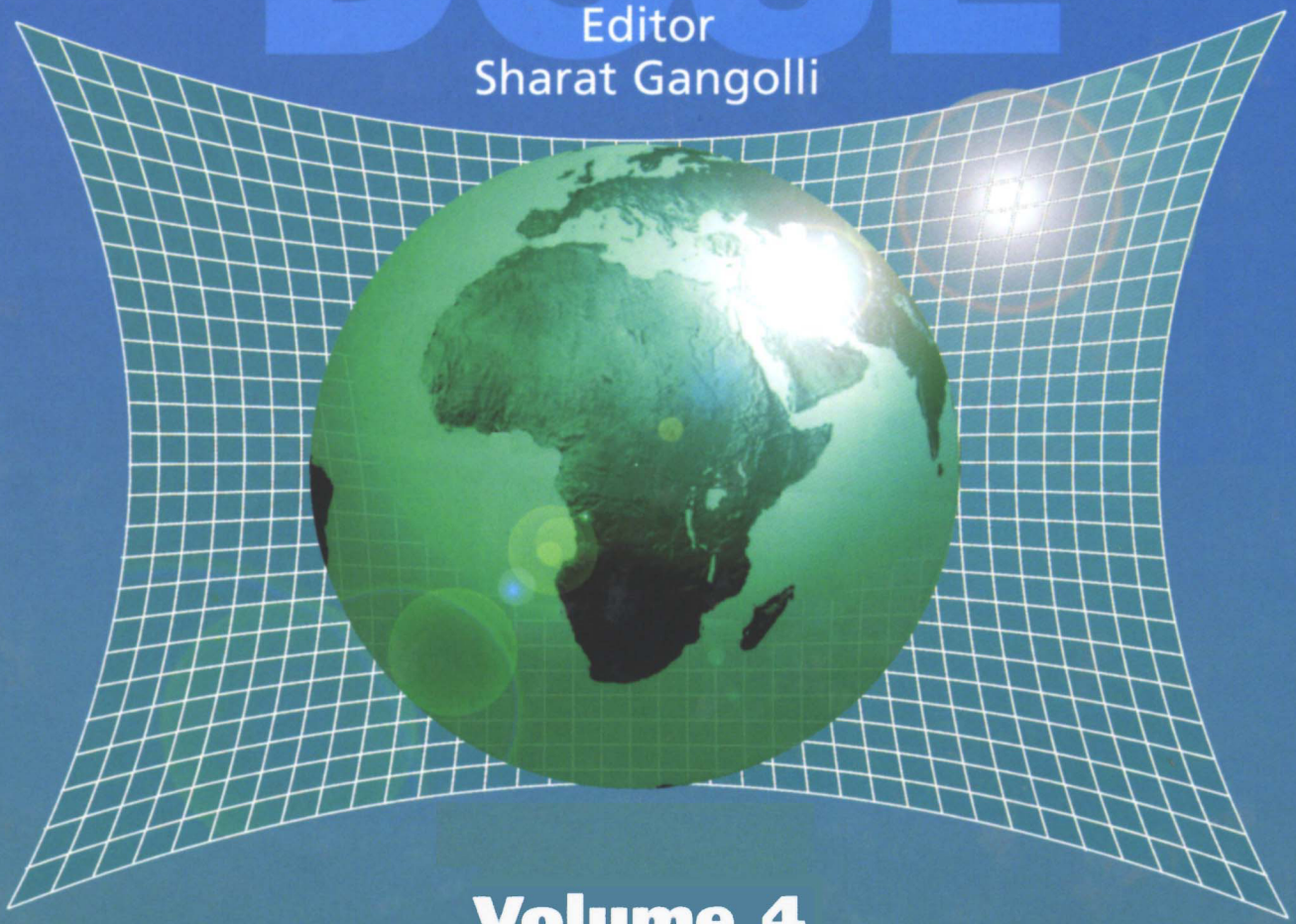
The Dictionary of Substances and their Effects

DOSE

Second Edition

Editor
Sharat Gangolli



Volume 4
E–J

The Dictionary of Substances and their Effects

Second Edition

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RS•C
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These headings only appear in an item when data have been identified for that heading. The user can, therefore, assume that the absence of a heading means that no relevant data were retrieved from the sources examined.

Dose No.

Each of the 4123 compounds in DOSE is identified by a unique, sequential alphanumeric DOSE No. For example, the first compound in DOSE, *A-α-C*, has DOSE No. *A1;* the last entry, *zoxazolamine*, has DOSE No. *Z25.*

Chemical name

In general, the chemical name is the common name of the substance, for example *nitrobenzene.* If it is not possible to allocate a precise chemical name (i.e. if the substance is of unknown or variable composition, or consists of biological materials), a short phrase appears instead, for example *chlorinated paraffins (C12, 60%).*

Molecular formula

This is the elemental composition of the compound. The elements appear alphabetically for inorganic compounds, i.e. Ag_2CO_3, Cl_2Cr, etc, but for organic compounds, carbon and hydrogen content are shown first followed by the other elements in alphabetical order, i.e. C_6H_5Br.

Molecular weight

This is directly calculated from the molecular formula. No molecular weights are given for polymers.

CAS Registry No.

The CAS Registry No. is a number sequence adopted by the Chemical Abstracts Service (American Chemical Society, Columbus, Ohio, USA) to uniquely identify specific chemical substances. The number contains no information relating to the chemical structure of a substance and is, in effect, a catalogue number relating to one of the millions of unique chemical substances recorded in the CAS Registry. New numbers are assigned sequentially to each new compound identified by Chemical Abstracts Service. This information is also provided in the full index of CAS Registry Numbers available at the end of Volume 7.

Synonyms

For common chemicals, several chemical names and numerous trade names may be applied to describe the chemical in question. Many of these names are identified to aid users on the range of names which have been used to describe each substance.

EINECS No.

This number is assigned by the European Commission to each record in the EINECS (European Inventory of Existing Commercial Chemical Substances) inventory. The numbers are in the format XXX-XXX-X, for example, *202-716-0* for *nitrobenzene.*

RTECS No.

The RTECS (Registry of Toxic Effects of Chemical Substances) number is a unique identifier assigned by NIOSH (National Institute of Occupational Safety and Health in the US) to every substance in the RTECS database. The number is in the format of two alphabetic characters followed by seven numeric characters, for example, *DA 6475000* for *nitrobenzene.*

Uses
Principal uses of the substances are given, with information on other significant uses in industrial processes.

Occurrence
Natural occurrences, whether in plants, animals or fungi are reported.

Physical properties

Melting/Boiling point
These data are derived from various sources.

Flash point
The flash point is the lowest temperature at which the vapours of a volatile combustible substance will sustain combustion in air when exposed to a flame. The flash point information is derived from various sources. Where possible the method of determination of the flash point is given.

Specific gravity (density)
The specific gravity of each substance has been derived from a variety of sources. Where possible the data have been standardised.

Partition coefficient
Partition coefficients, important for structure-activity relationship considerations, particularly in the aquatic environment, are indicated. Ideally the *n*-octanol/water partition coefficient is quoted. The major data source for this measurement is:

Sangster, J *J. Phys. Chem. Ref. Data* 1989, **18**(3), 1111-1229

Where no reference is quoted, it can be assumed that the information was derived from this source.

Volatility
The vapour pressure and vapour density are quoted where available. Where possible, the data have been standardised.

Solubility
Solubility data derived from several sources are quoted for both water and organic solvents where available.

Occupational exposure

Limit values
This field contains the occupational exposure limit values (or threshold limit values) from France, Germany, Japan, Sweden, UK and USA.

The airborne limits of permitted concentrations of hazardous chemicals represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. These limits are subject to periodic revision and vary between different countries. The term *threshold limit* relates primarily to the USA, but equivalent terms are available in most industrialised countries. The data relates to concentrations of substances expressed in *parts per million (ppm)* and *milligrams per cubic meter (mg* m^{-3}*)*.

French exposure limits are published by the French Ministry in Charge of Labour and presented in the report *Valeurs limites d'exposition professionnelle aux agents chimiques en France* (ND 1945-153-93). The values in DOSE have been taken from the 1998 edition. The FR-VLE values are short-term limits (15 minutes), and FR-VME values are long-term limits (8 hours).

German data currently include the national MAK values where available. The MAK value (Maximale Arbeitsplatz-Konzentration) is defined as the maximum permissible concentration of a chemical compound present in the air within a working area which, according to current knowledge, does not impair the health of the employee or cause undue annoyance. Under those conditions, exposure can be repeated and of long duration over a daily period of eight hours, constituting an average working week of 40 hours. MAK values are published by the Geschäftsstelle der Deutschen Forschungsgemeinschaft, Bonn, in "Maximum Concentrations at the Workplace and Biological Tolerance Values for Working Materials." The values in DOSE have been taken from the 1998 edition.

Japanese exposure limits are those recommended by the Japanese Society of Occupational Health. Unless otherwise indicated, these values are long-term exposure limits (the mean exposure concentration at or below which adverse health effects caused by the substance do not appear in most workers, working 8 hours a day, 40 hours a week under a moderate workload). The values in DOSE were published in 1997.

Swedish data can include short-term exposure limit, a level limit, or a ceiling limit. The values in DOSE were adopted in 1996.

In the UK occupational limits relating to airborne substances hazardous to health are published by the Health and Safety Executive annually in Guidance Note EH40. The values in the DOSE items have been taken from the 1999 edition.

There are Maximum Exposure Limits (MEL) in the UK which are subject to regulation and which should not normally be exceeded. They derive from Regulations, Approved Codes of Practice, European Community Directives, or from the Health and Safety Commission. In addition, there are Occupational Exposure Standards (OES) which are considered to represent good practice and realistic criteria for the control of exposure. In an analogous fashion to the USA Threshold Limits, there are long-term limits, expressed as time-weighted average concentrations over an 8-hour working day, designed to protect workers against the effects of long-term exposure. The short-term exposure limit is for a time-weighted average of 15 minutes. For those substances for which no short-term limit is listed, it is recommended that a figure of three times the long-term exposure limit averaged over a 15-minute period be used as a guideline for controlling exposure to short-term excursions.

The threshold limit values for the USA have been taken from the *Threshold Limit Values and Biological Exposure Indices, 1999* produced by the American Conference of Governmental Industrial Hygienists, Cincinnati, USA. The limits relate to *Threshold Limit – Time Weighted Average, Threshold Limit – Short Term Exposure Limit* and *Threshold Limit – Ceiling Limit.* The Threshold Limit Value – Time Weighted Average (TLV-TWA) allows a time-weighted average concentration for a normal 8-hour working day and a 40-hour working week, to which nearly all workers may be repeatedly exposed day after day, without adverse effect. The Threshold Limit Value – Short Term Exposure Limit (TLV-STEL) is defined as a 15-minute, time-weighted average which should not be exceeded at any time during a work day, even if the 8-hour time-weighted average is within the TLV. It is designed to protect workers from chemicals which may cause irritancy, chronic or irreversible tissue damage, or narcosis of sufficient degree to cause the likelihood of accidental injury. Many STELs have been deleted pending further toxicological assessment. With Threshold Limit – Ceiling Values (TLV-C) the concentration should not be exceeded during any part of the working day.

UN number

The United Nations Number is a four-figure code used to identify hazardous chemicals and is used for identification of chemicals transported internationally by road, rail, sea and air. In the UK this number is also called the "Substance Identification Number" or "SI Number".

HAZCHEM code

The Hazchem Code is used to instruct United Kingdom emergency services on equipment, evacuation and other methods of dealing with transportation incidents. It is administered by the Chemical Industries Association.

Conveyance classification

The information presented for the transportation of substances dangerous for conveyance by road is derived from the UK's Approved Carriage List, Health and Safety Commission, UK.

Supply classification

The information presented for the supply of substances is derived from the UK's Approved Supply List: information approved for the classification and labelling of substances and preparations dangerous for supply [Chemicals (Hazard Information and Packaging) Regulations 1999 (CHIP 99)*] Health and Safety Commission, UK.

Risk and safety phrases

Risk and safety phrases used in connection with DOSE items are approved phrases for describing the risks involved in the use of hazardous chemicals and have validity in the United Kingdom and throughout the countries of the European Community. The approved texts have designated R (Risk) and S (Safety) numbers from which it is possible to provide translations for all approved languages adopted by the European Community. The risk and safety phrases quoted in DOSE relate to the UK's Approved Supply List: information

*At the time of going to press the Health and Safety Commission, UK announced that an amendment (Amendment No. 2) to the CHIP 99 regulations is intended to come into force on 1 January 2000. The supply classifications and the risk and safety phrases reported in this edition of DOSE do not include any changes which are proposed in Amendment No. 2 to CHIP 99. These changes are incorporated in the updates to the electronic versions of DOSE released after 1 January 2000.

approved for the classification and labelling of substances and preparations dangerous for supply [Chemicals (Hazard Information and Packaging) Regulations, 1999 (CHIP 99)] Health and Safety Commission, UK. The risk and safety phrases should be used to describe the hazards of chemicals on data sheets for use and supply; for labelling of containers, storage drums, tanks etc., and for labelling of articles specified as dangerous for conveyance by road. (See also footnote on page xi.)

Ecotoxicity

Information is presented on the effects of chemicals on various ecosystems. Results of studies carried out on aquatic species, primarily fish and invertebrates, but also fresh water and marine microorganisms and plants are reported. Persistence and potential for accumulation in the environment and any available information on the harmful effects to non-target species, i.e. the unintentional exposure of terrestrial and/or aquatic species to a toxic substance is given. Ecotoxicology can be defined as that science involved in the study of the production of harmful effects by substances entering the natural environment, especially effects on populations, communities and ecosystems; or as the study of the effects of chemicals on ecosystems and their non-human components. An essential part of the ecotoxicology is the assessment of movement of potentially toxic imbalance through environmental compartments and through food webs.

Ecotoxicology, unlike human toxicology, is more concerned with the effects to populations than to individuals. Human toxicology is based on the extrapolation of data from many species to one species man, whereas ecotoxicology necessitates the extrapolation from a few species to many, or from limited field data to entire ecosystems.

Ecotoxicology must not be confused with environmental toxicology which is the direct effects of environmental chemicals to humans. The term environmental toxicology should only be applied to the study of direct effects of environmental chemicals on human beings. Although the main thrust of preventative toxicology is in the area of human health, it is becoming increasingly evident that human health is intimately connected with conditions in the natural environment. Chemicals released into the environment far from human habitation may become a health hazard for humans through food chain accumulation. Other chemicals may adversely affect crop growth or kill economically important fish stocks or bird life.

Fish toxicity

LC_{50} values, with duration of exposure, are quoted for two species of freshwater and one marine species if available. Any additional information on bioassay type (static or flow through) and water condition (pH, temperature, hardness or oxygen content) is reported.

Invertebrate toxicity

LC_{50} values with duration of exposure, are quoted for molluscs and crustaceans. EC_{50} values, i.e. concentrations which will immobilise 50% of an exposed population, are given for microbes, algae and bacteria. Values which will inhibit microbial or algal growth are reported. Duration of exposure is given when available.

Toxicity to other species

Toxicity to species other than mammals, birds, invertebrates and fish (e.g. reptiles, amphibians, plants, seaweeds), is reported here. LD_{50}, LC_{50} and EC_{50} values are given with duration of exposure, concentration and as much supplementary information as possible.

Bioaccumulation

Bioaccumulation, biomagnification and bioconcentration data are quoted primarily for fish, invertebrates, bacteria and algae. Bioaccumulation is the progressive increase in the amount of a chemical in an organism or part of an organism which occurs because the rate of intake exceeds the organism's ability to remove the substance from its body. Bioconcentration is a process leading to a higher concentration of a chemical in an organism than in its environment. Lastly, biomagnification is a sequence of processes in an ecosystem by which higher concentrations are attained in organisms at higher trophic levels, i.e. at higher levels in the food chain.

Environmental Fate

Degradation data are used to assess the persistence of a chemical substance in the environment, in water, soil and air. If the substance does not persist, information on the degradation products is also desirable. Intermediates may be either harmless or toxic substances which will themselves persist. Degradation occurs via two major routes, microbial degradation utilising microorganisms from a variety of habitats and decomposition by chemical methods. Microbial degradation is associated with the production of elemental carbon, nitrogen and sulfur from complex molecules. Standard biodegradation tests estimate the importance of microbial biodegradation as a persistence factor. Most tests use relatively dense microbial populations adapted to the compound being studied. Rapid degradation results in these tests implies that the compound will degrade under most environmental conditions, although specialised environments where degradation would not occur can exist. Compounds which are not readily degradable are likely to persist over a wide range of environmental situations.

Chemical degradation processes include photolysis, hydrolysis, oxidation and removal by reversible/irreversible binding to sediment. Factors which influence degradation rates, such as duration of exposure, temperature, pH, salinity, concentrations of test substance, microbial populations, and other nutrients, must also be taken into account.
Due care must also be given when metabolism results in the production of substances that are more toxic than their parents.

Nitrification inhibition

The nitrogen cycle is the major biogeochemical process in the production of nitrogen, an essential element contained in amino acids and proteins. Nitrogen is an essential element in microorganisms, higher plants and animals. Interference in the production of nitrogen from more complex molecules can be determined by standard tests using nitrogen-fixing bacteria. The degree of inhibition can be used to estimate the environmental impact of the test chemical.

Carbonaceous inhibition

Another major biogeochemical process is the recycling of carbon via the decomposition of complex organic matter by bacteria and fungi. In nature the process is important in the cycling of elements and nutrients in ecosystems. The degradation sequence occurs in stages, cellulose → cellobiose → glucose → organic acids and carbon dioxide. Chemical inhibition of microbial processes at all or any of these stages is reported here.

Anaerobic effects

Anaerobic microbial degradation of organic compounds occurs in the absence of oxygen and is an important degradation process in both the natural environment and in waste treatment plants. Data on the effects of chemicals on anaerobic systems are reported here. An important method uses anaerobic digestion tests which compare the production of methane and carbon dioxide by anaerobic microbes in a sludge sample with and without added test material. Methane production is at the end of the food chain process used by a wide range of anaerobic microorganisms.

Degradation studies

This section focuses on microbial degradation in both soil and water under anaerobic and aerobic conditions. The half-life of the chemical substance in the environment is reported with its degradation products where possible, giving an indication of the degree of its persistence. Water pollution factors: BOD (biochemical/biological oxygen demand), COD (chemical oxygen demand) and ThOD (theoretical oxygen demand) are stated, where available. BOD estimates the extent of natural purification which would occur if a substance were discharged into rivers, lakes or the sea. COD is a quicker chemical method for this determination which uses potassium dichromate or permanganate to establish the extent of oxidation likely to occur. ThOD measures the amount of oxygen needed to oxidise hydrocarbons to carbon dioxide and water. When organic molecules contain other elements nitrogen, sulfur or phosphorus, the ThOD depends on the final oxidation stage of these elements.

Abiotic removal

Information on chemical decomposition processes is contained in this section. The energy from the sun is able to break carbon-carbon, and carbon-hydrogen bonds, cause photodissociation of nitrogen dioxide to nitric oxide and atomic oxygen and photolytically produce significant amounts of hydroxyl radicals. Hydrolysis occurs when a substance present in water is able to react with the hydrogen or hydroxyl ions of the water. Therefore the extent of photolytic and oxidative reactions occurring in the atmosphere and hydrolysis in water can be used as a measure of environmental pollution likely to arise from exposure to a substance. Removal by activated carbon is also reported.

Adsorption and retention

The environmental impact of a chemical substance is determined by its ability to move through the environment. This movement depends on the affinity of the chemical toward particulate matter: soil and sediment. Chemicals which have a high affinity for adsorption are less readily transported in the gaseous phase or in solution, and therefore can accumulate in a particular medium. Chemical substances which are not readily adsorbed are transported through soil, air and aquatic systems.

Mammalian and avian toxicity

Studies on mammalian species are carried out to determine the potential toxicity of substances to humans. Avian species are studied primarily to assess the environmental impact on the ecosystem, however data from avian studies are also used for assessing human toxicity. This is specifically applied to pesticides, with neurotoxicology studies.

Procedures involve undertaking a series of established exposure studies on a particular substance using specific routes, oral, inhalation, dermal or injection for variable durations. Exposure durations include acute or single exposure to a given concentration of substance. Sub-acute or sub-chronic exposure, i.e. repeat doses over an intermediate time period, up to 4 weeks for sub-acute and 90 day/13 week (in rodents) or 1 year (in dogs) for sub-chronic studies. Chronic/long-term studies involve exposure to specific concentrations of chemical for a duration of 18 month-2 years. A variety of species are used in toxicity testing, most commonly rodents (rats, mice, hamsters) and rabbits, but tests can also be carried out on monkeys, domestic animals and birds.

Acute data

Single exposure studies quoting LD_{50}, LC_{LO}, LD_{LO}, TC_{LO} and TD_{LO} data.

Sub-acute and sub-chronic data

Results of repeat doses, intermediate duration studies are quoted. Priority is given to reporting the adverse effects on the gastro-intestinal, hepatic, circulatory, cardiopulmonary, immune, renal and central nervous systems.

Carcinogenicity and chronic effects

Information on the carcinogenicity of substances unequivocally proven to cause cancer in humans and laboratory animals, together with equivocal data from carcinogenicity assays in laboratory animals are reported. Additionally, treatment-related chronic adverse effects are reported. Criteria for inclusion required the study to report the species, duration of exposure, concentration and target organ(s); sex is also given where available.

Teratogenicity and reproductive effects

The results of studies carried out in intact animal and *in vitro* systems to determine the potential for teratogenic, foetotoxic and reproductive damage are reported here. Criteria for inclusion required the species, duration of exposure, concentration and details of the effect in relation to fertility to be stated. Adverse effects reported in this section include sexual organ dysfunction, developmental changes (to embryos and foetuses), malformations, increases in spontaneous abortions or stillbirths, impotence, menstrual disorders and neurotoxic effects on offspring.

Metabolism and toxicokinetics

Data are quoted on the metabolic fate of the substance in mammals, and includes adsorption, distribution, storage and excretion. Mechanisms of anabolic or catabolic metabolism, enzyme activation and half-lives within the body are reported when available. Additionally findings from *in vitro* studies are reported.

Irritancy

Chemical substances which cause irritation (itching, inflammation) to skin, eye and mucous membranes on immediate contact in either humans or experimental animals are reported here. Exposure can be intentional in human or animal experiments, or unintentional via exposure at work or accident to humans.

Sensitisation

Sensitisation occurs where an initial accidental or intentional exposure to a large or small concentration of substance causes no reaction or irritant effects. However, repeat or prolonged exposure to even minute amounts of a sensitising chemical causes increasingly acute allergic reactions.

Genotoxicity

Genotoxicity testing is carried out to determine the mutagenic and/or carcinogenic potential of a chemical substance. A standard series of tests are carried out under controlled laboratory conditions on an established set of test organisms. A hierarchical system using bacteria, yeasts, cultured human and mammalian cells, *in vivo* cytogenetic tests in mammals and plant genetics is used to assess the genotoxic potential of the substance under study. Bacteria, unlike mammals, lack the necessary oxidative enzyme systems for metabolising foreign compounds to the electrophilic metabolites capable of reacting with DNA. Therefore, bacteria are treated with the substance under study in the presence of a post-mitochondial supernatant (S9) prepared from the livers of mammals (usually rats). This fraction is supplemented with essential co-factors to form the S9 mix necessary for activation. DOSE reports published studies: giving the test organisms, whether metabolic activation (S9) was required, and the result, positive or negative.

Other effects

Other adverse effects (human)

Adverse effects to humans from single or repeat exposures to a substance are given. The section includes results of epidemiological studies, smaller less comprehensive studies of people exposed through their work environment and accidental exposure of a single, few or many individuals.

Any other adverse effects

Adverse effects to organisms or animals other than man are reported here.

Legislation
Any form of legislation, medical (food and drugs) or environmental from European, American and worldwide sources is reported.

Other comments
All other relevant information, including chemical instability and incompatibility, reviews, phytotoxicity and toxic effects associated with impurities, is contained in this section.

References
Contains references to data from above sections.

Indexes
The most convenient means of accessing a chemical in DOSE is via one of the indexes at the back of Volume 7. DOSE contains three indexes: chemical name and synonyms, CAS Registry Numbers and molecular formulae.

Index of chemical names and synonyms
Contains the name of the chemical used in DOSE together with a number of synonyms for that chemical. All names are arranged alphabetically.

Index of CAS Registry Numbers
Contains a list of the CAS Registry Numbers of the chemicals in DOSE in ascending order. This number is linked to the preferred DOSE name for that chemical and its DOSE number.

Index of molecular formulae
Contains a list of the molecular formulae of the chemicals in DOSE in alphabetical order for inorganic compounds, i.e. Ag_2CO_3, Cl_2Cr, etc., but for organic compounds, carbon and hydrogen content are shown first followed by the other elements in alphabetical order, i.e. C_6H_5Br. This number is linked to the preferred DOSE name for that chemical and its DOSE number.

Note

The Royal Society of Chemistry (RSC) has only assessed published information in compiling The Dictionary of Substances and their Effects. However, the RSC would welcome any relevant information on the chemicals that is not readily accessible, but in the public domain, for inclusion when the items in DOSE are updated.

If you have any relevant information, please contact:

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Cambridge CB4 0WF
UK
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Fax: +44 (0)1223 423429

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The Library and Information Centre (LIC) of the RSC offers a Document Delivery Service for items in chemistry and related subjects. Contact: Library and Information Centre, the Royal Society of Chemistry, Burlington House, Piccadilly, London W1V 0BN, UK.

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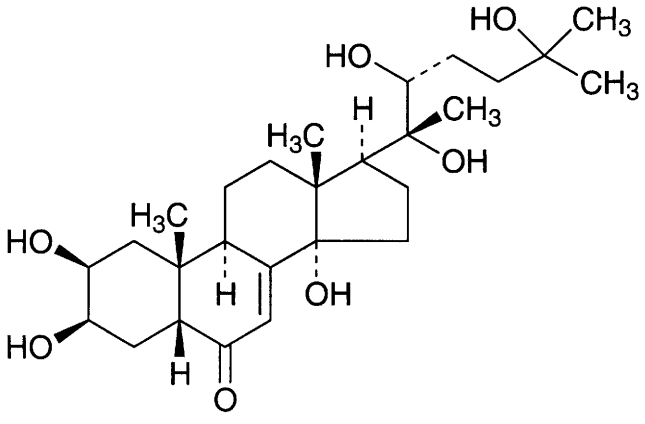
Fax: + 44 (0)20 7287 9798
Email: library@rsc.org

E1 β-ecdysterone



$C_{27}H_{44}O_7$ **Mol. Wt.** 480.64 **CAS Registry No.** 5289-74-7

Synonyms (2β,3β,5β,22*R*)-2,3,14,20,22,25-hexahydroxycholest-7-en-6-one; crustecdysone; ecdysone; 20-hydroxyecdysone; isoinokosterone; Polypodine A; viticosterone

RTECS No. FZ 8060000

Occurrence Moulting hormone in insects and crustaceans. Present in the wood of *Podocarpus elatus* and *Polypodium vulgare* and many other plants.

Physical properties

M. Pt. 245-247°C (97% purity)

Solubility Organic solvents: carbon tetrachloride

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse > 9000 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 6400 mg kg^{-1} (1).

Teratogenicity and reproductive effects

Subcutaneous ♂ rat, lowest toxic dose 350 μg kg^{-1} day^{-1} for 7 days (affected the prostate seminal vesicle, Cowper's gland and accessory glands) (1).

Other effects

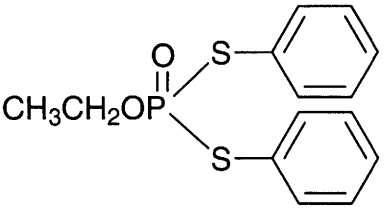
Any other adverse effects

Intraperitoneal mouse, single dose of 1 mg kg^{-1} increased the concentration of antibody-forming cells in the spleen of mice immunised with sheep red blood cells. The formation of proteins by human skin fibroblasts *in vitro* was also stimulated, but DNA formation in human lymphocytes *in vitro* stimulated by photohaemoglutinin was suppressed (2).

References

1. *Nippon Yakurigaku Zasshi* 1970, **66**, 551.
2. Sakhibov, A. D. et al *Dokl. Akad. Nauk SSSR* 1989, (8), 55-57 (Russ.) (*Chem. Abstr.* **112**, 192125v)

E2 edifenphos



$C_{14}H_{15}O_2PS_2$ **Mol. Wt.** 310.38 **CAS Registry No.** 17109-49-8

Synonyms *O*-ethyl *S,S*-diphenyl phosphorodithioate; EDDP; Hinosan; Hinorabacide

EINECS No. 241-178-1 **RTECS No.** TE 3850000

Uses Fungicide.

Physical properties

B. Pt. 154°C at 0.01 mmHg **Specific gravity** 1.23 at 20°C with respect to water at 4°C

Volatility v.p. 9.8×10^{-5} mmHg at 20°C

Solubility Water: 56 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, carbon tetrachloride, dioxane, heptene, methanol, xylene

Occupational exposure

Supply classification toxic

Risk phrases Toxic by inhalation, in contact with skin and if swallowed (R23/24/25)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S36/37, S45)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) tapmouth gudgeon fry 0.58 mg l^{-1} (1).

LC_{50} (96 hr) carp 2.5 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (48 hr) freshwater shrimp 1.2 mg l^{-1} (3).

Environmental fate

Abiotic removal

Hydrolysis in aqueous environment at 25°C, $t_{1/2}$ 19 days at pH 7, 2 days at pH 9 (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail, mallard duck 290, 2700 mg kg^{-1}, respectively (2).

LD_{50} oral rat, mouse, guinea pig, rabbit 100-350 mg kg^{-1} (1,4-6).

LD_{50} oral redwing blackbird >100 mg kg^{-1} (7).

LC_{50} (4 hr) inhalation rat 320-360 mg m^{-3} (2).

LD_{50} dermal rat 700-800 mg kg^{-1} (2).

LD_{50} intraperitoneal rat 26-67 mg kg^{-1} (8).

LD_{50} subcutaneous rat 132 mg kg^{-1} (9).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level for ♂ rats 5 mg kg^{-1} diet, for ♀ rats 15 mg kg^{-1} diet (2).

Metabolism and toxicokinetics
Rapidly absorbed following oral administration to rats and mice; 96% metabolised and eliminated from the body within 72 hr (2).

Genotoxicity

Bacillus subtilis H17 rec+, M45 rec- DNA damage negative (10).
In vitro mouse bone marrow cells, chromatid-type gaps, breaks, fragments and exchanges positive (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (12).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).
WHO Class Ib (14).
EPA Toxicity Class II (2).
ADI (human) 0.003 mg kg^{-1} body weight(2).

Other comments

Residues have been isolated from natural waters (3).

References

1. Miyashita, M. *Nippon Koshu Eisei Zasshi* 1988, **35**(6), 293-300 (Japan.) (*Chem. Abstr.* **109**, 224374g).
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Hatakeyama, S. et al *Chemosphere* 1991, **22**(1-2), 229-235.
4. *Nippon Noyaku Gakkaishi* 1982, **7**, 307.
5. *Pesticide Index* 1976, **5**, 91, College Science Publications, State College, PA, USA.
6. *Oyo Yakuri* 1968, **2**, 76.
7. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
8. Chen, T. S. et al *Toxicol. Appl. Pharmacol.* 1972, **23**, 519.
9. *Sci. Rep. Res. Inst., Tohoku Univ., Ser. C: Medicine* 1989, **36**(1-4), 10.
10. Shirasu, Y. et al *Mutat. Res.* 1976, **40**, 19-30.
11. Chunya, S. P. et al *Cytologia* 1984, **49**(4), 833-839.
12. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
13. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK
14. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

E3 EDTA

$$(HO_2CH_2C)_2NCH_2CH_2N(CH_2CO_2H)_2$$

$C_{10}H_{16}N_2O_8$ **Mol. Wt.** 292.25 **CAS Registry No.** 60-00-4

Synonyms *N,N'*-1,2-ethenediylbis[*N*-(carboxymethyl)glycine]; (ethylenedinitrilo)tetraacetic acid; edetic acid; versene acid; ethylenediaminetetraacetic acid

EINECS No. 200-449-4 **RTECS No.** AH 4025000

Uses Antioxidant in foods. Chelating agent.

Physical properties

M. Pt. 250 °C (decomp.)
Solubility Water: 500 mg l^{-1} at 25°C

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, channel catfish 129-159 mg l^{-1} (1,2).
LC_{50} (24 hr) rainbow trout 340 mg l^{-1} (3).

Invertebrate toxicity
LC_{50} (24 hr) *Artemia salina* 200 and 280 mg l^{-1} for saltwater and freshwater, respectively (3).
Toxicity threshold, cell multiplication inhibition *Pseudomonas putida* 105 mg l^{-1}, *Scenedesmus quadricauda* 11 mg l^{-1}, *Entosiphon sulcatum* 36 mg l^{-1} (4).

Environmental fate

Nitrification inhibition
Not inhibitory to ammonia oxidation by activated sludge at 350 mg l^{-1} (5).

Carbonaceous inhibition
Not inhibitory to biogas production in fluidised bed reactor at 83 mg l^{-1} (6).

Degradation studies
BOD_5 0.01 mg l^{-1} O_2 (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4000 mg kg^{-1} (8).
LD_{50} intraperitoneal mouse, rat 250, 400 mg kg^{-1}, respectively (9,10).

Teratogenicity and reproductive effects
Oral rat, lowest toxic dose, teratogenic effects 7630 mg kg^{-1} day^{-1} on days 7-14 of gestation (11).

Metabolism and toxicokinetics
In humans, poorly absorbed from gastro-intestinal tract, with only 2.5% of an oral dose of 3.0 g being excreted in the urine (12).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with metabolic activation negative (13).
In vitro mouse lymphoma L5178Y tk^+/tk^- forward mutation assay positive (14).

Other comments

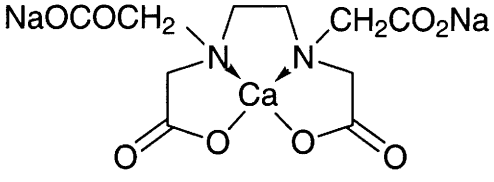
Residues have been isolated from wastewaters and natural waters (15).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).

References

1. Batchalder, T. L. et al *Bull. Environ. Contam. Toxicol.* 1980, **24**, 543-549.
2. McKee, J. E. et al *Water Quality Criteria* 2nd ed., 1963.
3. Jarcovic, M. et al *Arch. Fischereiwiss.* 1969, **20**, 178-181.
4. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
5. Tomlinson, T. G. et al *J. Appl. Bacteriol.* 1966, **29**(2), 266-291.
6. Witkowski, P. J. et al *Proc. 38th Ind. Waste Conf.* 1983, 839-845.
7. Masselli, J. W. et al *Rep. New Engl. Int. Water Pollut. Control Commun.* 1954.
8. *Material Safety Data Sheet* 1978, Dow Chemical Co.

9. *NTIS Report* AD691-490, Natl. Tech. Inf. Ser., Springfield, VA, USA.
10. *Arh. Hig. Rada Toksikol.* 1962, **13**, 295.
11. *Toxicol. Appl. Pharmacol.* 1977, **40**, 299.
12. Srbova, J. et al *Arch. Gewerbepathol. Gewerbehyg.* 1957, **15**, 572.
13. McCann, J. et al *Proc. Natl. Acad. Sci. U. S. A.* 1975, **72**(12), 5135-5139.
14. Wangenheim, J. et al *Mutagenesis* 1988, **3**(3), 193-205.
15. Frank, R. et al *Ecotoxicol. Environ. Saf.* 1990, **19**(1), 55-63.
16. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E4 EDTA calcium disodium salt



$C_{10}H_{12}CaN_2Na_2O_8$ **Mol. Wt.** 374.27 **CAS Registry No.** 62-33-9

Synonyms disodium [(ethylenedinitrilo)tetraacetato]calcium; calcium disodium EDTA; calcium disodium detate; Calcium Disodium Versenate; calcium EDTA; edetamine; edetate calcium; sodium calcium edetate; tetacin-calcium; Fetazine; Sequestrene Na2Ca

EINECS No. 200-529-9 **RTECS No.** EV 7700000

Uses Chelating agent. Antidote in heavy metal poisoning. Food preservative.

Physical properties

Solubility Water: 1 kg l^{-1} at 25°C

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 2340 mg l^{-1} static bioassay (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, dog 7000-12,000 mg kg^{-1} (2-4).

LD_{50} intraperitoneal rabbit 6000 mg kg^{-1} (4).

Metabolism and toxicokinetics

An intravenous dose of 3000 mg radiolabelled substance administered to two human volunteers was almost completely excreted in the urine within 12-16 hr (5).

Genotoxicity

Salmonella typhimurium TA97, TA102 with and without metabolic activation negative (6).

Other effects

Other adverse effects (human)

21/130 children treated for lead poisoning with 25 mg kg^{-1} by intramuscular injection every 12 hr and dimercaprol (3 mg kg^{-1} every 4 hr) for 5 days, developed nephrotoxicity which was attributed to EDTA disodium calcium (7).

Other adverse side-effects include thrombophlebitis, nausea, cramp, fever, malaise, myalgia, lachrymation, skin eruptions, transient hypotension and ECG abnormalities (8).

Any other adverse effects

Intraperitoneal mouse, 500 mg kg^{-1} had no effect on the hippocampal EEG and did not abolish Timm staining in the CA3 region after ≈ 1 hr (9).

Intravenous infusion to rats caused a marked depletion of collagen fibrils in the skin (dosage not specified) (10).

Other comments

Exchanges its calcium for lead or other heavy metal ions, forming water soluble complexes of the heavy metals (11).

References

1. Batchelder, T. L. et al *Bull. Environ. Contam. Toxicol.* 1980, **24**, 543-549.
2. *Material Safety Data Sheet* 1978, Dow Chemical Co.
3. *Toxicol. Appl. Pharmacol.* 1963, **5**, 142.
4. *Drugs in Japan: Ethical Drugs* 1990, 188.
5. Srbova, J. et al *Arch. Gewerbepathol. Gewerbehyg.* 1957, **15**, 572.
6. Fujita, H. et al *Kenkyu Nenpo – Tokyo-toritsu Eisei Kenkyusho* 1988, (39), 343-350 (Japan.) (*Chem. Abstr.* **110**, 230308a).
7. *Pediatrics* 1982, **70**, 259-262.
8. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
9. Negi, T. et al *Nippon Seirigaku Zasshi* 1987, **49**(11), 674-681 (Japan.) (*Chem. Abstr.* **108**, 68876u).
10. Braide, V. B. et al *Pharmacol. Res. Commun.* 1988, **20**(2), 133-146.
11. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

E5 EDTA copper complex

$C_{10}H_{14}CuN_2O_8$ **Mol. Wt.** 353.78 **CAS Registry No.** 54453-03-1

Synonyms dihydrogen [[*N*,*N*′-1,2-ethanediylbis-[*N*-(carboxymethyl)glycinato]](4-)-*N*,*N*′,O,O′, O $^{N,ON'}$]cuprate(2–); (ethylenedinitrilo)tetraacetic acid copper(II) complex; ethylenediaminetetraacetate copper chelate; Versene AG

EINECS No. 259-169-6 **RTECS No.** AH 4280000

Uses Algicide in swimming pools. In light-resistant, jet-printing inks.

Physical properties

M. Pt. 242°C (decomp.) **Specific gravity** 1.84

Occupational exposure

DE-MAK 1 mg m^{-3} (inhalable fraction of aerosol)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 555 mg l^{-1}. No adverse effect (96 hr) bluegill sunfish 320 mg l^{-1} (1).

Environmental fate

Adsorption and retention

EDTA complexes of copper and zinc were leached from podzolic soils easier than chlorides. EDTA treatments increased mobility of copper and zinc applied to soil as chlorides. Therefore, heavy metals may be leached by chelates from the root zone to decrease uptake by crops (2).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 2090 μg (Cu) kg^{-1} (3).

Sub-acute and sub-chronic data

Subcutaneous rabbit (5 months) administered wkly in diet (unspecified dose, as Cu salt). Copper residues detected in liver, spinal chord, kidneys, were 857, 45.9, 17.1 ppm dry weight, respectively (4).

Legislation

Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

World Health Organisation revised guidelines for water quality: copper guide level 1 mg l^{-1} (6).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Copper: guide level 100 μg l^{-1} at pumping/substations outlets; 3 mg l^{-1} after water has been standing 12 hr in the piping (7).

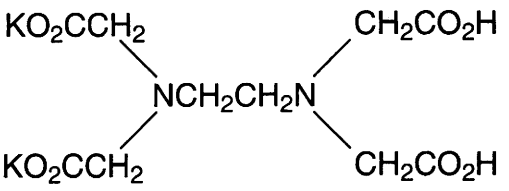
Other comments

5% solution inhibits corn seed germination (8).

References

1. Batchelder, T. L. et al *Bull. Environ. Contam. Toxicol.* 1980, **24**, 543-549.
2. Savich, V. I. et al *Zemledelie* 1990, **2**, 22-23 (Russ.) (*Chem. Abstr.* **112**, 197121a).
3. Nofre, C. et al *Pathol. Biol. (Paris)* 1963, **11**, 853-865.
4. Edington, N. et al *Nature (London)* 1966, **210**(5040), 1060-1062.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *Guidelines for Drinking Water Quality* 1984, **1**, 7, WHO, Geneva, Switzerland.
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. Szoke, P. et al *Novenytermeles* 1982, **31**(3), 207-215 (*Chem. Abstr.* **97**, 126323d)

E6 EDTA dipotassium salt



$C_{10}H_{14}K_2N_2O_8$ **Mol. Wt.** 368.43 **CAS Registry No.** 2001-94-7

Synonyms dipotassium EDTA; edetate dipotassium; (ethylenedinitrilo)tetracetic acid, dipotassium salt; potassium ethylenediaminetetraacetate

EINECS No. 217-895-0 **RTECS No.** AH 4310000

Uses As preservative in blood samples. Chelating agent. Antioxidant.

Physical properties

M. Pt. 272°C (decomp.)
Solubility Water: freely soluble

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2000 mg kg^{-1} (dihydrate) (1).

Irritancy
Dermal rabbit 500 mg caused mild irritation (exposure unspecified). 100 mg instilled into rabbit eye for 30 sec caused mild irritation (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium guide level 10 mg l^{-1}; maximum admissible concentration 12 mg l^{-1} (3).

References

1. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1606, Sigma-Aldrich, Milwaukee, WI, USA.
2. *Food Chem. Toxicol.* 1982, **20**, 573.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

E7 EDTA disodium salt

$$(HO_2CH_2C)_2NCH_2CH_2N(CH_2CO_2Na)_2$$

$C_{10}H_{14}N_2Na_2O_8$ **Mol. Wt.** 336.21 **CAS Registry No.** 139-33-3

Synonyms disodium (ethylenedinitrilo)tetraacetic acid; disodium *N,N'*-1,2-ethanediylbis[*N*-(carboxymethyl)glycine]; edetate disodium; disodium edetate; disodium EDTA; disodium ethylenebis(iminodiacetic acid)

EINECS No. 205-358-3 **RTECS No.** AH 4375000

Uses Sequestering and pharmaceutic aid. Anticoagulant. Used in photography, cleaning agents, electroplating baths. Hair waving and dyeing preparations. Preservative.

Physical properties

M. Pt. 252°C (dihydrate crystals decomp.)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit mouse 2000-2300 mg kg^{-1} (1,2).
LD_{50} intraperitoneal mouse 260 mg kg^{-1} (1).
LD_{50} intravenous rabbit, mouse 47, 56 kg^{-1}, respectively (1,3).

Teratogenicity and reproductive effects

Oral rat (7-15 day gestation) 12.8 g kg^{-1} day^{-1} caused teratogenic effects (4).
Oral rat (1-22 day gestation) 31.4 g kg^{-1} day^{-1} caused reproductive effects (4).

Genotoxicity

Salmonella typhimurium TA97, TA102 with and without metabolic activation negative (5).
In vitro Chinese hamster lung fibroblasts 0.5 mg ml^{-1} showed weak clastogenic response prior to toxicity (6).
Staphylococcus aureus 196E *in vitro* 0.3-0.6 g l^{-1} inhibited cell growth. Addition of Fe^{3+}, Zn^{2+} or Ca^{2+} eliminated inhibition (7).
Staphylococcus epidermidis in vitro 20 mg l^{-1} inhibited cell growth (8).

Other comments

Disodium EDTA may be used in retention enemas without significant clinical side-effects (9).

References

1. *Jpn. J. Pharmacol.* 1956, **52**, 113.
2. *Fed. Proc.* 1968, **27**, 465.
3. U.S. Army Armament Res. Dev. Command, NIOSH Exchange Chemicals, NX No. 03781.
4. *Science* 1972, **173**, 62.
5. Fujita, H. et al *Kenkyu Nenpo. – Tokyo-toritsu Eisei Kenkyusho* 1988, **39**, 343-350 (Japan.) (*Chem. Abstr.* 1989, **110**, 230308a).
6. Ashby, J. et al *Mutat. Res.* 1986, **163**(1), 63-73.
7. Kraniak, J. M. et al *J. Food Sci.* 1988, **53**(3), 910-913.
8. Root, J. L. et al *Antimicrob. Agents Chemother.* 1988, **32**(11), 1627-1631.
9. Rabau, M. Y. et al *Gen. Pharmacol.* 1991, **22**(2), 329-330

E8 EDTA tetrasodium salt

$$(NaO_2CH_2C)_2NCH_2CH_2N(CH_2CO_2Na)_2$$

$C_{10}H_{12}Na_4N_2O_8$ **Mol. Wt.** 380.17 **CAS Registry No.** 64-02-8

Synonyms edetate sodium; *N,N'*-1,2-ethanediylbis[*N*-(carboxymethyl)glycine]tetrasodium salt; (ethylenedinitrilo)tetraacetic acid tetrasodium salt; ethylenediaminetetraacetic acid, tetrasodium salt; tetrasodium ethylenediaminetetraacetate; sodium edetate; Aroquest 100; Hamp-ene 100; Sequestrene; Trilon B

EINECS No. 200-573-9 **RTECS No.** AH 5075000

Uses Chelating agent. Preparation of cosmetics. Cross-linking catalyst.

Physical properties

M. Pt. > 300°C
Solubility Water: 90% at 25°C

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 490-1030 mg l^{-1} static bioassay (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2000-4000 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 330 mg kg^{-1} (3).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation and 100 mg instilled into rabbit eye for 24 hr caused moderate irritation (4).

References

1. Batchelder, T. L. et al *Bull. Environ. Contam. Toxicol.* 1980, **24**, 543-549.
2. *Material Safety Data Sheet* 1978, Dow Chemical Co.
3. *Rev. Epidemiol.* 1962, **10**, 391.
4. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 306, Prague, Czechoslovakia

E9 EDTA trisodium salt

$$Na_2OCH_2C(HO_2CH_2C)NCH_2CH_2N(CH_2CO_2Na)_2$$

$C_{10}H_{13}Na_3N_2O_8$ **Mol. Wt.** 358.19 **CAS Registry No.** 150-38-9

Synonyms trisodium ethylenediaminetetraacetate trihydrate; *N,N'*-1,2-ethandiylbis[*N*-(carboxymethyl)glycine] trisodium salt; (ethylenedinitrilo)tetraacetic acid, trisodium salt; edetate trisodium; Sequestrene trisodium; trisodium resenate

EINECS No. 205-758-8 **RTECS No.** AH 5250000

Uses Food additive. Organic synthesis. Chelating agent.

Physical properties

M. Pt. >300°C (monohydrate) **Partition coefficient** log P_{ow} –3.65 (1)
Solubility Water: 10 g l^{-1} at 22°C

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 2150 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 300 mg kg^{-1} (3).

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice via food. Negative results were reported in ♂ and ♀ rats and mice (4).

Teratogenicity and reproductive effects
In vitro vaccinia virus growth in monkey kidney cells, teratogenic assay positive (5).
Lowest toxic dose, teratogenic effects in rodents (unspecified) 250 mg kg^{-1} (5).

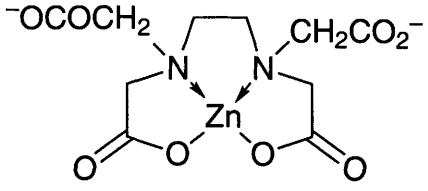
Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (6).
In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations negative (6).

References

1. McCoy, G. D. et al *Carcinogenesis (London)* 1990, **11**(7), 1111-1117.
2. *Litton Bionetis* 1972 Progress Report NIH-NCI-E-C-72-3252.
3. *Rev. Epidemiol.* 1962, **10**, 391.
4. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-011, NIEHS, Research Triangle Park, NC, USA.
5. Kello, S. J. *Mol. Toxicol.* 1987, 1(2-3), 261-276.
6. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50

E10 EDTA zinc salt



$C_{10}H_{12}N_2O_8Zn$ **Mol. Wt.** 353.60 **CAS Registry No.** 12519-36-7

Synonyms
Uses Component in some fertilisers.

Physical properties

Solubility Water: freely soluble

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 685 mg l^{-1} static bioassay (1).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. Batchelder, T. L. et al *Bull. Environ. Contam. Toxicol.* 1980, **24**, 543-549.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E11 EDTPA

$$(H_2O_3PH_2C)_2NCH_2CH_2N(CH_2PO_3H_2)_2$$

$C_6H_{20}N_2O_{12}P_4$ **Mol. Wt.** 436.13 **CAS Registry No.** 1429-50-1

Synonyms ethylenediaminetetramethylphosphonic acid; {1,2-ethanediylbis[nitrilobis(methylene)]} tetrakis (phosphonic acid); *N,N,N',N'*-ethylenediaminetetramethylende phosphonic acid; Dequest 2040; editempa; EDPA; EDTF; EDTMP

EINECS No. 215-851-5

Uses Chelating agent. Corrosion inhibitor. Scale inhibitor.

Physical properties

M. Pt. 214°C (decomp.)
Solubility Water: freely soluble

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Oral rat (13 wk) 0, 5, 50 or 500 mg kg^{-1} day^{-1} The high dose caused mild anaemia which was resolved in a 9-wk recovery period (1).

Metabolism and toxicokinetics
Poorly absorbed from the gastro-intestinal tract of rats following administration in the feed. Most of the absorbed dose was rapidly excreted in the urine or sequestered in the bone. Administration by gavage led to 4- to 6-fold increase in bone levels (1).

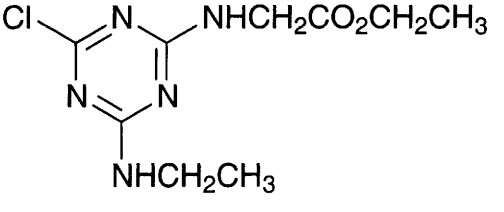
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (2).

References

1. Calvin, G. et al *Food Chem. Toxicol.* 1988, **26**(7), 601-610.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E12 eglinazine-ethyl



$C_9H_{14}ClN_5O_2$ **Mol. Wt.** 259.70 **CAS Registry No.** 6616-80-4

Synonyms *N*-[4-chloro-6-(ethylamino)-1,3,5-triazin-2-yl]glycine, ethyl ester
Uses Superseded herbicide.

Physical properties

M. Pt. 228-230°C **Volatility** v.p. 2×10^{-7} mmHg at 20°C
Solubility Water: 300 mg l^{-1} at 25°C. Organic solvents: acetone, hexane, xylene

Environmental fate

Degradation studies
$t_{1/2}$ in soil 12-18 days (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse >10 g kg^{-1} (1).
LD_{50} oral guinea pig >3375 mg kg^{-1} (1).
LD_{50} dermal rat, rabbit > 10 g kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse >7100 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 9th ed., 1991, British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E13 eicosanoic acid

$$CH_3(CH_2)_{18}CO_2H$$

$C_{20}H_{40}O_2$ **Mol. Wt.** 312.54 **CAS Registry No.** 506-30-9
Synonyms arachic acid; arachidic acid
EINECS No. 208-031-3 **RTECS No.** JX 3780000
Occurrence Occurs in peanut, vegetable and fish oils.

Physical properties

M. Pt. 74-76°C **B. Pt.** 328°C **Specific gravity** 0.8240 at 100°C with respect to water at 4°C
Solubility Organic solvents: miscible with benzene, chloroform, diethyl ether, ethanol, light petroleum

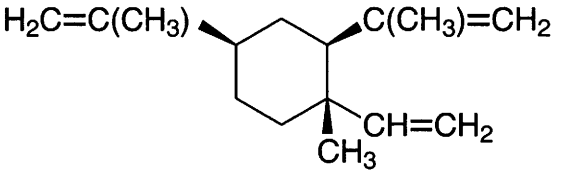
Mammalian & avian toxicity

Carcinogenicity and chronic effects
Urinary bladder implant mouse (11 month) 25 mg pellet induced local squamous metaplasia in 5/52, local benign tumours in 10/52, and local carcinomas in 8/52 treated mice (1).

References

1. Bryan, G. T. et al *Cancer Res.* 1966, **26**, 105-109

E14 β-elemene



$C_{15}H_{24}$ **Mol. Wt.** 204.36 **CAS Registry No.** 33880-83-0

Synonyms cyclohexane, 2,4-diisopropenyl-1-methyl-1-vinyl-, (1α,2β,4β)-; cyclohexane, 1-ethenyl-1-methyl-2,4-bis(1-methylethenyl)-, [1*S*-(1α,2β,4β)]-

EINECS No. 251-713-0

Uses The compound has antitermite properties (1).

Occurrence Natural component of many plant oils, including many used in foods, herbs and oriental medicines (2).

Also in some woods, including Yakusugi bogwood (1).

Physical properties

B. Pt. 122-123°C **Specific gravity** 0.882-0.900 at 20°C

Ecotoxicity

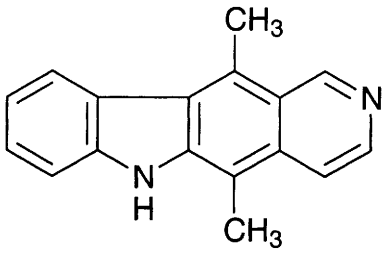
Invertebrate toxicity

Compound has termiticidal properties (1).

References

1. Yatogi, M. et al *Mokuzai Gakkaishi* 1991, **37**(4) 345-351.
2. Xizhong, M. et al *Beijing Huagong Xueyuan Xuebao, Ziran Kexueban* 1990, **17**(4), 111-113 (Ch.) (*Chem. Abstr.* **115**, 35813n)

E15 ellipticine



$C_{17}H_{14}N_2$ **Mol. Wt.** 246.31 **CAS Registry No.** 519-23-3

Synonyms 5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazole

EINECS No. 208-264-0 **RTECS No.** UU 8825000

Uses Antineoplastic agent.

Occurrence Present in *Ochrosia elliptica, O. sandwicensis, O. viellardii, O. silvatica.*

Physical properties

M. Pt. 311-315°C (decomp.)

Solubility Organic solvents: ethyl acetate

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 178-204 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 150 mg kg^{-1} (2).

Genotoxicity

Neurospora crassa H12 forward mutation assay, positive (3).

T4 rFC11 bacteriophage reversion assay positive (4).

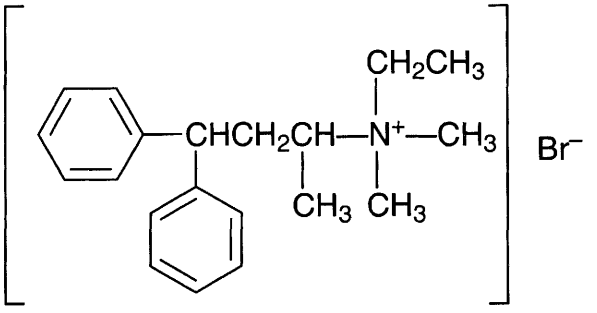
In vitro mouse lymphoma L5178Y tk^+/tk^- cells, chromosome aberrations positive (5).

In vitro Chinese hamster ovary cells, sister chromatid exchanges and mutation induction at multiple genetic loci positive (6).

References

1. Rakieten, et al *U.S. Gov. Res. Dev. Rep.* 1967, **38**.
2. *Biomedicine* 1974, **21**, 101.
3. Gupta, R. *Mutat. Res.* 1990, **240**(2), 47-58.
4. De Marini, D. M. et al *Teratog., Carcinog., Mutagen.* 1988, **8**(5), 293-301.
5. Moore, M. M. et al *Environ. Mutagen.* 1987, **9**(2), 161-170.
6. Singh, B. et al *Cancer Res.* 1983, **43**(2), 575-584

E16 emepronium bromide



$C_{20}H_{28}NBr$ **Mol. Wt.** 362.35 **CAS Registry No.** 3614-30-0

Synonyms benzenepropanaminium bromide; Cetiprin; *N*-ethyl-*N*,*N*,α-trimethyl-γ-phenylbenzenepropanaminium bromide; ethyldimethyl(1-methyl-3,3-diphenylpropyl) ammonium bromide; Hexanium; Riprin; Uroripirin

EINECS No. 222-786-6 **RTECS No.** BQ 4240000

Uses Anticholinergic, antispasmodic drug.

Physical properties

M. Pt. 204°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1000 mg kg^{-1} (1).

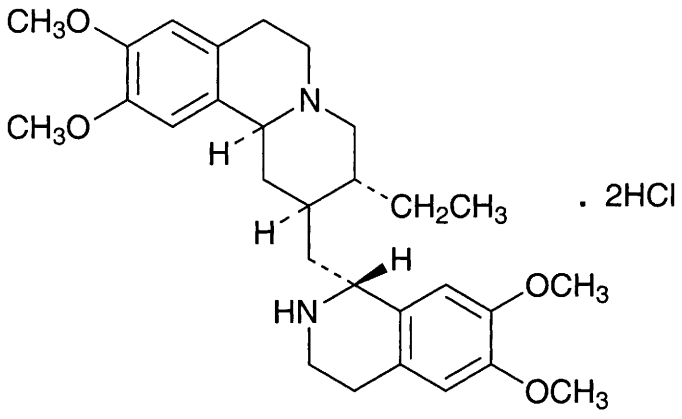
Metabolism and toxicokinetics

Gastro-intestinal absorption in mice increased from 1-7% as assessed by urinary excretion. In the oral dose range of 0.1-40 mg kg^{-1} 50% of the dose was excreted unchanged, but at a dose of 80 mg kg^{-1} 80% was excreted unchanged. No dose-dependent urinary excretion was observed following intravenous administration (2).

References

1. *Reg. Tox. Effect. Chem. Subst.* 1989, German (East) Patent Doc. 139212.
2. Hallen, B. et al *Pharmacol. Toxicol. (Copenhagen)* 1987, **60**(3), 199-215

E17 emetine hydrochloride



$C_{29}H_{42}Cl_2N_2O_4$ **Mol. Wt.** 553.57 **CAS Registry No.** 316-42-7

Synonyms emetine dihydrochloride; hemometine; ([2*S*-[2α(*S**),3β,11β]]-3-ethyl-1,3,4,6,7,11*b*-hexahydro-2-[(1,2,3,4-tetrahydro-1- isoquinolinyl)methyl]-2*H*-benzo[*a*]quinolizine) dihydrochloride; 6′,7′,10,11-tetramethoxyemetan dihydrochloride

EINECS No. 206-259-8 **RTECS No.** JY 5250000

Uses Antiamoebic drug.

Occurrence Alkaloid obtained from ground roots of *Uragoga ipecacuanha.*

Physical properties

M. Pt. 235°C (decomp.)

Solubility Water: 143 g l^{-1}. Organic solvents: chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 56 mg kg^{-1} (1).

LD_{50} oral rat, mouse 12, 15 μg kg^{-1}, respectively (2).

LD_{50} subcutaneous mouse 37 mg kg^{-1} (3).

LD_{50} intraperitoneal rat, mouse 17, 62 mg kg^{-1}, respectively (4).

Metabolism and toxicokinetics

After injection in humans, emetine is concentrated in the liver, kidneys, lungs and spleen. Excretion is slow and detectable, concentrations may persist in the urine for up to 60 days (5).

Sensitisation

Eczematous, urticarial and purpurial skin lesions have been reported in patients (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6).

Other effects

Other adverse effects (human)

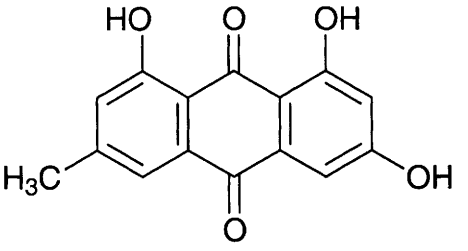
Administration is commonly associated with aching, tenderness, stiffness and weakness of the muscles in the area

of injection. Diarrhoea, nausea and vomiting are common. Cardiovascular effects, including changes in the ECG, are considered the most serious adverse effects (5).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *Antibiot. Chemother. (Basel 1959-70)* 1958, **8**, 297.
3. *J. Pharm. Pharmacol.* 1964, **16**, 65.
4. *J. Pharmacol. Exp. Ther.* 1948, **94**, 431.
5. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
6. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 7), 1-119

E18 emodin



$C_{15}H_{10}O_5$ **Mol. Wt.** 270.24 **CAS Registry No.** 518-82-1

Synonyms 1,3,8-trihydroxy-6-methyl-9,10-anthracenedione; 6-methyl-1,3,8-trihydroxyanthraquinone; Natural Yellow 14; C.I. 75440

EINECS No. 208-258-8 **RTECS No.** CB 7920600

Uses Purgative agent.

Occurrence Isolated from several herbs (1).

Physical properties

M. Pt. 255°C (decomp.)

Solubility Water: Practically insoluble. Organic solvents: benzene, carbon disulfide, carbon tetrachloride, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling >100 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 35 mg kg^{-1} (3).

Metabolism and toxicokinetics

Metabolised by rat hepatic microsomes *in vitro* to give 2-hydroxyemodin, 4-hydroxyemodin, 5-hydroxyemodin, 7-hydroxyemodin, ω-hydroxyemodin and emodic acid (4).

Genotoxicity

Salmonella typhimurium TA1535, TA1537 with metabolic activation positive (5,6).

Escherichia coli WP2, CM871, mutagenicity assay with metabolic activation positive (7).

In vitro Chinese hamster ovary cells, sister chromatid exchanges positive (7).

In vitro V79 cells mutation assay positive (8).
In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (9).
In vivo mouse bone marrow cells, micronuclei formation negative (10).

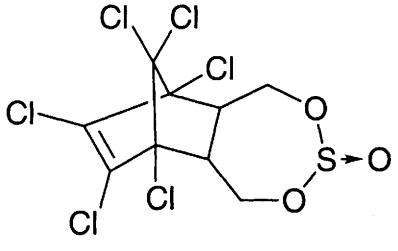
Other comments

Immunosuppressive and vasorelaxant actions have been observed in human mononuclear cells *in vitro* and rat thoracic aortic rings (1).

References

1. Huang, H. C. et al *Environ. J. Pharmacol.* 1991, **198**(2,3), 211-213.
2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
3. *J. Agric. Food Chem.* 1979, **27**, 1342.
4. Morooka, N. et al *Agric. Biol. Chem.* 1990, **54**(5), 1247-1252.
5. Boesch, R. et al *Mutat. Res.* 1987, **188**(3), 161-168.
6. Tanaka, H. et al *Mutat. Res.* 1987, **176**(2), 165-170.
7. von Wright, A. et al *Mutat. Res.* 1992, **269**(1), 27-33.
8. Westendorf, J. et al *Mutat. Res.* 1990, **240**(1), 1-12.
9. Williams, G. et al *Mutat. Res.* 1982, **97**, 359-370.
10. Mengs, U. et al *Mutat. Res.* 1997, **393**(3), 289-293

E19 endosulfan



$C_9H_6Cl_6O_3S$ **Mol. Wt.** 406.93 **CAS Registry No.** 115-29-7

Synonyms (1,4,5,6,7,7-hexachloro-8,9,10-trinorborn-5-en-2,3-ylenebismethylene) sulfite; C,C'-(1,4,5,6,7,7-hexachloro-8,9,10-trinorborn-5-en-2,3-ylene)(dimethyl sulfite); 6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3-oxide; 1,4,5,6,7,7-hexachloro-5-norbornene-2,3-dimethanol cyclic sulfite; Endotox; Afidan; Agaclor; Cloca; End; Fan; Hildan

EINECS No. 204-079-4 **RTECS No.** RB 9275000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 70-100°C (commercial material), 109.2°C (α-form), 213.3°C (β-form) **B. Pt.** 106°C at 0.7 mmHg (with partial decomp.) **Specific gravity** 1.745 at 20°C **Partition coefficient** log P_{ow} 4.74 (α-form), 4.79 (β-form) (both at pH 5) **Volatility** v.p. 9×10^{-3} mmHg at 80°C
Solubility Water: 0.32 mg l^{-1} (α-form), 0.33 mg l^{-1} (β-form) both at 22°C. Organic solvents: dichloromethane, ethanol, ethyl acetate, hexane, toluene

Occupational exposure

FR-VME 0.1 mg m^{-3}
UK-LTEL 0.1 mg m^{-3} **UK-STEL** 0.3 mg m^{-3}
US-TWA 0.1 mg m^{-3}
Supply classification toxic, dangerous for the environment
Risk phrases Toxic in contact with skin and if swallowed – Irritating to the eyes – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R36, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) golden orfe 0.002 mg l^{-1} (1).
LC_{50} (96 hr) rainbow trout 0.3 μg l^{-1} (2).
LC_{50} fathead minnow 0.86 μg l^{-1} flow through bioassay: maximum acceptable toxicant concentration 0.20 μg l^{-1} (3).
Common Indian freshwater catfish were exposed to 96-hr LC_{50}, 0.007-0.013 ppm, for 4 days. Stressed fish showed liver damage (degeneration of cytoplasm, pycnosis of nuclei, loss of glycogen and stasis of bile duct lumen) and kidney damage (shrinkage of glomeruli, cytoplasmic damage and epithetial desquamation in tubules and extensive degeneration of haemopoietic stroma); intestinal damage was negligible (4).

Invertebrate toxicity
LC_{50} (24 hr) freshwater rotifer 5.15 ppm (5).
LC_{50} (96 hr) *Pteronarcys californica* 2.3 μg l^{-1} (6).
LC_{50} (96 hr) *Gammarus fasciatus* 5.8 μg l^{-1} (7).
EC_{50} (24, 48 hr) *Daphnia magna* 240 and 60 μg l^{-1}, respectively (8).
Growth of *Anabaena* and *Aulosira fertilissima* was adversely effected at concentrations of 1 μg l^{-1}. Inhibition was significant, >50% at 20 μg l^{-1} (9).
LC_{50} (96 hr) juvenile *Procambarus clarkii* 24 ppb, adult crayfish 423 ppb. Published LC_{50} values indicate freshwater crayfish are more tolerant than marine decapods (10).

Bioaccumulation
Palaemonetes pugio (96 hr) exposure to 0.16-1.75 μg l^{-1}, bioconcentration factor range 81-245 (11).
Marine pin perch (96 hr) exposure to 0.15-0.26 μg l^{-1}, bioconcentration factor range 1046-1299 (12).
Rotifers were exposed to 1.5-2.0 ppm for 24, 48, 72 and 96 hr. Highest accumulation occurred 24 hr after initial exposure to 1.5 ppm of the toxicant. A steady-state concentration was reached between 24 and 48 hr, followed by a gradual decrease until 96 hr (5).
Accumulation in tissues of *Scylla serrata* was highest in hepatopancreas, intermediate in muscle and lowest in gills. Residue levels deceased by 30% in all tissues after depuration (13).
Residues were estimated in 20 freshwater edible fish. Residue accumulation showed a definite relation with the feeding habits of the fish. Omnivorous fish were highly contaminated > carnivorous > herbivorous. *Heteropneustes fossilis* was most contaminated, with residue concentrations of 0.312 ppm (14).

Environmental fate

Nitrification inhibition
Nitrification was assayed in a sandy loam (pH 5.7), silt loam (pH 5.0) and a clay loam (pH 4.9) soil, using both soil perfusion and batch incubation techniques. Significant differences in nitrification were evident in the three soils: sandy loam ≥90% of added ammonium was converted into nitrate within 30 days, while silt loam required 40 days to achieve similar nitrate levels. Activity in clay loam was slow, only 5% of added ammonium was converted

into nitrate in 70 days. At high concentrations of 500 and 1000 ppm the commercial preparation was consistently more toxic than the technical material (15).

Degradation studies

^{14}C-endosulfan incubated with active soil fungi formed endosulfan sulfate as the major metabolite whereas the endodiol was the major product formed by active soil bacteria (16).

A majority of endosulfan metabolites produce conjugates with plant carbohydrates. Ultimate molecular degradation occurs comparatively slowly. Can persist for ≥18 months in soil (17,18).

Technical endosulfan (α and β isomers) individually incorporated into soil at the rate of 1 kg active ingredient ha^{-1} showed that α-endosulfan decomposed fairly rapidly, i.e. 90% in 30 days with the simultaneous formation of endosulfan sulfate (50%), whereas β-endosulfan disappeared slowly, i.e. 60-65% in 30 days. The formulated endosulfan 35% emulsifiable concentration showed 87% disappearance of the α-isomer and 70% of the β-isomer within 30 days (19).

Degraded by *Pseudomonas* sp. Maximum degradation occurred on day-10 with endodiol the only metabolite in the culture extract The species were capable of utilising endosulfan as the sole carbon source (20).

Degradation was studied after incubation in sterilised and non-sterilised soils. In sterilised soils the extracted residues were 80%, bound residues were 6-14% and total residues 90-102%, presenting small variation in 160 days incubation. In non-sterilised soil (160-day incubation) extracted residues were 38-45%, bound residues 23-34 and total residues 68-73%. Carbon dioxide evolution was low and no great mineralisation occurred within a 48-day incubation period (21).

Abiotic removal

Stable to sunlight. Stable during storage in the absence of moisture. Slowly hydrolysed in aqueous acid and alkalis with the formation of the diol and sulfur dioxide (22).

Moderately stable in water, $t_{1/2}$ 4 days. 30% persisted in river water for 2 wk following initial treatment (100%) and 5% remained after 4 wk (17,18).

In river water in sealed glass jar under sunlight and artificial fluorescent light, initial concentration 10 μg l^{-1}, percentage original compound found after 1 hr 100%, 1 wk 30%, 2 wk 30%, 4 wk 0% (23).

Adsorption and retention

Binding in three types of Sudanese agricultural soils under laboratory conditions was studied. Binding did not exceed 4% of the applied radioactivity after an incubation period of 10 wk (24).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck 205-245 mg kg^{-1} (22).

LD_{50} oral rat 70-110 mg kg^{-1} (22).

LC_{50} (4 hr) inhalation ♂ rat 34.5, ♀ 12.6 μg l^{-1} in air (22).

LD_{50} dermal rabbit 359 mg kg^{-1} (25).

Sub-acute and sub-chronic data

In 2-yr feeding trials rat, dog receiving 30 mg kg^{-1} diet showed no ill-effects (22).

Intragastrial rat (10 month), 99-350 mg kg^{-1} (total dose) administered as 2 mg kg^{-1} day^{-1} caused death (26).

Dermal ♂ rat (30 day) 18.7, 37.5 and 62.5 mg kg^{-1} day^{-1} and ♀ rat 10, 20 and 32 mg kg^{-1} day^{-1} caused hyperexcitability, tremor, dyspnoea and salivation. No deaths occurred and signs of toxicity subsided within 1 wk. Residues were detected in fatty tissues of rats receiving highest doses (27).

Carcinogenicity and chronic effects

Oral rat (duration unspecified) 5.5 and 11 mg kg^{-1} caused loss in body weight, increased liver, kidney and adrenal weights and death (28).

Oral (78 wk) ♂, ♀ Osborne-Mendel rat, ♂, ♀ B6C3FI mouse, 952 and 408 ppm ♂ rat, and 445 and 223 ppm ♀ rat, 6.9 and 3.5 ppm ♂ mouse, and 3.9 and 2.0 ppm ♀ mouse. Doses for ♂ rat and mouse were too toxic to obtain carcinogenic data. In ♀ rat and mouse it was found not to be carcinogenic (29).

Groups of 50 rats were fed with 3, 7, 5, 15 and 75 ppm of endosulfan in diet and groups of 50 mice with 2, 6 and 18 ppm of endosulfan, for 24 months. Significant reduction in the body weights of both ♂ and ♀ rats were only

observed in rats fed 75 ppm in diet. The kidneys were identified as the target organ based on the increased incidence of enlargement in ♀s and the slight increased incidence of progressive glomerulonephrosis and renal aneurysms in ♂s fed on 75 ppm in diet. A dietary intake of 15 ppm, equivalent to a daily intake of 0.6 mg kg^{-1} body weight, was seen as the no-observed-effect level (NOEL) in rats. Corresponding NOELs of 0.84 mg kg^{-1} and 0.97 mg kg^{-1} body weight in ♂ and ♀ mice were selected from observations of increased mortalities in ♀s and a slight reduction in body weight gain in ♂s fed with 18 ppm in diet. Evaluation of tumour data revealed no differences between treated rodents and controls and endosulfan was not considered to have carcinogenic potential (30).

Teratogenicity and reproductive effects

No inhibition of reproductive function of rats in a three generation study for a 5 mg kg^{-1} dose (17).
Gavage rat (6-15 days gestation) 0.5 and 1.5 mg kg^{-1} did not cause teratogenic effects (17).

Metabolism and toxicokinetics

In rats, following oral administration, endosulfan was metabolised to α-hydroxyendosulfan and endosulfandiol, which were excreted in the urine. No accumulation occurred in milk, fat or muscle (22).

Irritancy

652 subjects were patch tested with 1% endosulfan (mixed isomers). Results were evaluated at 48 and 72 hr; irritation reactions were observed (31).

Genotoxicity

Saccharomyces cerevisiae T_2 without metabolic activation induced mitotic recombination (32).
Salmonella typhimurium TA97a, TA98, TA100 with metabolic activation negative (33).
Salmonella typhimurium TA97a modified assay using preincubation procedure with and without metabolic activation positive (34).
Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (35).
In vitro mouse lymphoma L5178Y tk^+/tk^- positive (36).
In vitro peripheral human lymphocytes, 5 and 100 μg ml^{-1} negative (37).
In vivo oral mice, meiotic germ cells increased polyploidy, aneuploidy and chromosomal aberrations (38).
In vivo mice induction of dominant lethal mutations and dose-dependent increase in sperm abnormality. No change in sperm motility observed (39).
In vivo intraperitoneal mice, bone marrow chromosomal aberrations and clastogenic effects observed (40).

Other effects

Other adverse effects (human)

61 ♂ pesticide workers were analysed for mutation in peripheral lymphocytes. The frequency of sister chromatid exchanges was significantly higher among pesticide applicators at all durations of exposure (41).

Any other adverse effects

Attributed endocrine disruption effects in wildlife. Avian reproduction impaired, reduced egg production (42).
Oral house sparrow (exposure duration and concentration unspecified) maximum cholinesterase inhibition occurred in the oesophagus 32%, proventriculus 20%, intestine (small) 16%, (large) 19%, and liver 10% (43).
Acute endosulfan poisoning in rodents and cats affects the central nervous system and effects include increased reflex excitability, tremor, muscle cramp, clonic and clonictonic convulsions, excessive salivation, vomiting, irregular breathing, leukocytosis, eosinophilia and an increase in blood sugar level. During pathanatomical investigations dystrophic changes were observed in the parenchymatous organs and persisted for 1 month after a single LD_{50} dose (26).
Haemodynamic disturbances of brain and parenchymatous nerve cells were noted during the early stages of the poisoning. Dystropic and occasional inflammation, necrobiotic damage to the brain, kidneys, adrenal glands and heart cells were observed (44).
Chronic exposure in rats caused increased activity of drug-metabolising enzymes and inhibited androgen-biotransforming enzyme activities. These biochemical changes were reversed when exposure ceased (45).
No oestrogenic effect observed in rats (46).

I_{50} value (inhibition of 50% of enzyme activity) for serum enzyme aspartate amino transferase (species unspecified) 3.13×10^{-4} M (47).

Legislation

WHO Toxicity Class II (48).
EPA Toxicity Class I (formulation) (1).
Tolerable daily intake (human) 0.002 mg kg^{-1} (17).

Other comments

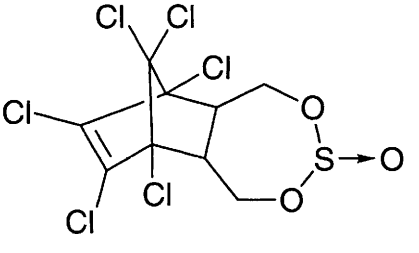
Studies conducted to investigate a possible synergistic increase in oestrogenic potency between the weakly oestrogenic organochlorines dieldrin and endosulfan showed no synergism in the displacement of 3H-E2 from rat uterine oestrogen receptors nor in inducing the proliferation of MCF-7 breast cancer cells (an oestrogen-dependent response). In addition, endosulfan or dieldrin (0.1 mg $animal^{-1}$ day^{-1}) alone or in combination, injected intraperitoneally for 3 days, did not stimulate any uterotrophic activity and had no effect on pituitary prolactin or other endocrine-related endpoints in immature ♀ rats (49).
Endosulfan exists as a mixture of two isomers, pure α-endosulfan 64-67% of the isomeric mixture (CAS RN 959-98-8) and pure β-endosulfan 29-32% of the isomeric mixture (CAS RN 33213-65-8). The ratio of α-isomer: β-isomer in commercial endosulfan is 4:1.
Toxicology hazards and human health effects reviewed (50-52).
Endosulfan residues were not detected by chemical analysis in foodstuffs. Endosulfan does not accumulate in plant tissues. The usual metabolites of endosulfan are detectable at a level of 0.1 mg kg^{-1} on plants (leaf and fruit) (53).
Implications of dermal exposure during pesticide application to tropical crops (in the Philippines, Thailand, Tanzania and Malawi) are discussed (54).
Incompatible with strongly alkaline materials.

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Schoettger, R. A. *Toxicology of Thiodan in Several Fish and Aquatic Invertebrates* 1970, Bureau of Sport Fisheries and Wildlife Investigation in Fish Control 35, Govt. Print. Off Washington, DC, USA.
3. Macek, K. J. et al *Toxicity of Four Pesticides to Water Fleas and Fathead Minnows* 1976, EPA 600/3-76-099, US EPA, Duluth, MN, USA.
4. Narain, A. S. et al *Acta Hydrochim. Hydrobiol.* 1991, **19**(2), 235- 243.
5. Fernandez-Casalderrey, A. et al *Comp. Biochem. Physiol., C: Comp. Pharmacol. Toxicol.* 1991, **100C**(1-2), 61-63.
6. Sanders, H. O. et al *Limnol. Oceanogr.* 1968, **13**(1), 112.
7. Sanders, H. O. *Toxicity of Pesticides to the Crustacean Gammarus lacustris* 1969, Bureau of Sport Fisheries and Wildlife Technical Paper 25, Gov. Print. Off., Washington, DC, USA.
8. Sanders, H. O. et al *Trans. Am. Fish. Soc.* 1965, **95**, 165.
9. Tandon, R. A. et al *Environ. Pollut.* 1988, **52** (1), 1-9.
10. Naqvi, S. M. et al *Environ. Pollut.* 1987, **48**(4), 275-288.
11. Schimmel, S. C. et al *Aquatic Toxicology and Hazard Evaluation* 1977, 241, American Society for the Testing of Materials.
12. Ernst, W. *Chemosphere* 1977, **6**, 731.
13. Biswas, R. et al *Natl. Acad. Sci. Lett. (India)* 1989, **12**(7), 257-259.
14. Verma, D. K. et al *Acta Hydrochim. Hydrobiol.* 1991, **19**(4), 431- 433.
15. Stratton, G. W. *Toxic. Assess.* 1990, **5**(4), 319-336.
16. Martens, R. *Appl. Environ. Microbiol.* 1976, **31**, 853.
17. Pavlov, A. V. (Ed.) *Pesticides. Hygiene of the Use and Toxicology* 1986, 50-51, Urozhai, Kiev, USSR.
18. Melnikov, N. N. et al *Pesticides: Chemistry, Technology and Use* 1987, 358-361, Moscow, USSR.
19. Akhter, S. et al *Karachi Univ. J. Sci.* 1985, **13**(2), 191-197.
20. Kshemkalyani, S. B. et al *Indian J. Environ. Health* 1987, **29**(2), 145-152.
21. Monteiro, R. T. R. et al *Rev. Bras. Cienc. Solo* 1989, **13**(2), 163-168.
22. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
23. Eichelberger, J. W. et al *Environ. Sci. Technol.* 1971, **5**, 541.

24. El Zorgani, G. A. et al *Quantif. Nat. Bioavailability Bound ^{14}C-Pestic. Residues Soil Plant Food Proc. Final Res. Coord. Meet.* 1985, 51-56, IAEA, Vienna, Austria.
25. *Pesticide Dictionary* 1976, Meister Publishing Co., Willoughby, OH, USA.
26. Antronovich, E. A. *Pesticides. Hygiene Toxicology and Clinical Signs of Poisoning* 1965, 169-176, Kiev, USSR.
27. Dikshith, T. S. S. et al *Vet. Hum. Toxicol.* 1988, **30**(3), 219-224.
28. *Scientific Reviews of Soviet Literature of Toxicity and Hazards of Chemicals* 1991, UNEP/IRPTC, Geneva, Switzerland.
29. *Bioassay of Endosulfan* 1978, TRS No. 62, Dept HEW Publication No. (NIH) 78-1312.
30. Hack, R. et al *Food Chem. Toxicol.* 1995, **33**(11), 941-950.
31. Lisi, P. et al *Contact Dermatitis* 1986, **15**(5), 266-269.
32. L'vova, T. S. *Reports 14th Ann. Conf. Eur. Soc. Environ. Mutagen.* 1984, 305-306, Moscow, USSR.
33. Pednekar, M. D. et al *Bull. Environ. Contam. Toxicol.* 1987, **38**(6), 925-933.
34. Pandey, N. et al *Mutat. Res.* 1990, **242**(2), 121-125.
35. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
36. McGregor, D. B. et al *Environ. Mol. Mutagen* 1988, **12**(1), 85-154.
37. L'vova, T. S. *Tzitol Genet.* 1984, **6**, 455-457.
38. Usha, R. et al *IRCS Med. Sci.* 1986, **14**(11), 1125-1126.
39. Pandey, N. et al *Mutat. Res.* 1990, **242**(1), 1-7.
40. Sharma, A. K. et al *Cytologia* 1991, **56**(1), 73-78.
41. Rupa, D. S. et al *Environ. Mol. Mutagen* 1991, **18**(2), 136-138.
42. *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* 1997, EPA/630/R-96/012, Risk Assessment Forum, US Environmental Agency, Washington, DC 20460, USA.
43. Bakhre, P. P. et al *J. Curr. Biosci.* 1990, **7**(1), 4-8.
44. Medvea, L. I. (Ed.) *Pesticides. Hygience of the Use and Toxicology* 1977, 65-66, Moscow, USSR.
45. Singh, S. K. et al *Indian J. Biochem. Biophys.* 1989, **26**(4), 262-267.
46. Raizada, R. B. et al *Natl. Acad. Sci. Lett. (India)* 1991, **14**(2), 103-107.
47. Sekeroglu, M. R. et al *J. Environ. Sci. Health, Part A: Environ. Sci. Eng. Toxic Hazard. Subst. Control* 1997, **A32**(7), 1975-1980.
48. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
49. Wade, M.G. et al *Reprod. Toxicol.* 1997, **11**(6), 791-798.
50. Maier-Bode, H. *Res. Rev.* 1968, **22**, 1-44.
51. *Environmental Health Criteria* 1984, **40**, WHO, Geneva, Switzerland.
52. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(3), 61-65.
53. Spynu, E. I. *Industrial Toxicology and Clinical Signs of Occupational and Chemical Etiology* 1962, 98-101, Moscow, USSR.
54. Ambridge, E. M. et al *Med. Lav.* 1990, **81**(6), 457- 462

E20 β-endosulfan



$C_9H_6Cl_6O_3S$ **Mol. Wt.** 406.93 **CAS Registry No.** 33213-65-9

Synonyms 6,9-methano-2,4,3-benzodioxathiepin, 6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-, 3-oxide, (3α,5aα,6β,9β,9aα)-; *exo*-1,4,5,6,7,7-hexachloro-5-norbornene-2,3-dimethanol; β-benzoepin; Endotox; Afidan; Chimac endo; End; Fan; Hildan; α-Thionex; Thiodan II

RTECS No. RB 9875200

Uses Insecticide. Acaricide.

E19 end

Physical properties

M. Pt. 213.3°C **Partition coefficient** log P_{ow} 4.79 at pH 5 **Volatility** v.p. 9.0×10^{-6} mmHg at 80°C
Solubility Water: 0.33 mg l^{-1} at 20°C. Organic solvents: dichloromethane, ethanol, ethyl acetate, hexane, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) snakehead fish 66 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (96 hr) *Daphnia magna* 53 μg l^{-1} (2).
LC_{50} (48 hr) *Daphnia magna* 60 μg l^{-1} (3,4).
LC_{50} (24 hr) *Daphnia magna* 240 μg l^{-1} (3,4).
LC_{50} (96 hr) *Palaemon macrodactylus* 17 μg l^{-1} (2).
LC_{50} (96 hr) *Pteronarcys californica* 2.3 μg l^{-1} (5).
LC_{50} (96 hr) *Ischnura* sp. 71.8 μg l^{-1} (2).
♂, ♀ Louisiana crayfish (20 wk) during mating at 600 ppb caused no effect on number of eggs produced. Hatchings (9, 23, 27 wk) exposed to 2, 10, 15 ppb caused insignificant differences in weight gain to controls (6).

Bioaccumulation

Estuary animals, common edible cockle, soft clam, lugworm, brown shrimp, common sole, gave wet tissue residues 0.3-1.3 mg g^{-1} (7).
Bioaccumulation (96 hr) *Lagodon rhomboides, Leiostomus xanthurus, Mugil cephalus* gave bioconcentration factors of 1000-1344 at concentrations 0.05-0.49 μg l^{-1} (8).
Exposure of three species of freshwater fish at 0.7-16 μg l^{-1} metabolised β-endosulfan to sulfate, diol, ether and lactone. Fish contained endosulfan residues and the authors concluded β-endosulfan to be stable in the environment (9).
Indian major carp (96 hr), metabolites reported in liver were endosulfan lactone, alcohol, sulfate and ether. All compounds except the ether metabolite were reported in kidney, but none were recorded in muscle, which was the principal storage site of β-endosulfan. At sublethal concentrations, metabolism of total proteins, glycogen and total lipids of kidney, liver and muscle are affected (10).

Environmental fate

Degradation studies

Soils incubated under N_2/CO_2 conditions, endosulfan sulfate was the major product (11).
^{14}C endosulfan incubated with active soil fungi formed endosulfan sulfate as the major metabolite while endothiol was the major product formed by active soil bacteria (12).
Under flooded conditions, the diol was produced in greater amounts than the sulfate, the hydroxy-ether was also formed (13).

Adsorption and retention

Degradation of ^{14}C-endosulfan after incubation with three soil types (160 days); in sterilised soil extracted residues were 80%, bound residues 6-14%, and for non-sterilised soil 38-43% and 23-34%, respectively. Evolution of CO_2 was 0.3-0.4% in both sterilised and non-sterilised soils (14).
Concentrations of 0.013-14.9 ppm were found in silt loam soil, loamy sand and organic muck soil, the latter at the highest levels, in soils of Canadian vegetable farms (15).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck 205-245 mg kg^{-1} (16).
LD_{50} oral ring-necked pheasant 620-1000 mg kg^{-1} (16).
LD_{50} oral rat 240 mg kg^{-1} (16).
LD_{50} oral dog 76 mg kg^{-1} (16).
LD_{50} dermal rabbit 359 mg kg^{-1} (16).

Sub-acute and sub-chronic data
Oral dog (1 yr) 3 mg kg^{-1} in diet. No adverse effect reported (16).
Oral rat (1 month) 3 mg kg^{-1} day^{-1} via gavage increased monooxygenase activity of the liver (17).
Oral ♂ rat (10 wk) 1, 5 mg kg^{-1} day^{-1} 5 × wk^{-1} did not enhance enzyme-altered foci incidence (18).

Carcinogenicity and chronic effects
Oral rat (2 yr) 30 mg kg^{-1} in diet. No adverse effects reported (16).

Metabolism and toxicokinetics
Metabolised to the corresponding sulfate which is toxicologically similar to the sulfite (endosulfan). No accumulation occurs in milk, fat or muscle. Excreted as conjugates of the diol (19).
Following oral administration in rats, metabolised to α-hydroxyendosulfan and endosulfandiol which are excreted in the urine (20).

Irritancy
Of 357 subjects patch-tested at 0.5, 1% concentrations, one person showed irritant reaction (21).

Sensitisation
Of 357 subjects, no allergic reaction was experienced at 0.5, 1% concentration (21).

Genotoxicity

In vitro Escherichia coli PQ37 SOS-Chromotest with and without metabolic activation negative (22).
In vitro Chinese hamster lung fibroblast (V-79) with and without metabolic activation in metabolic cooperation assay, positive and *in vitro* rat liver WB epithelial cell positive (18).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (23).
Included in Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (24).
WHO Toxicity Class II (25).
EPA Toxicity Class I (formulation, tech.) (16).
Partition coefficient exceeds EU limit of 3.0.
Tolerable daily intake human 0.006 mg kg^{-1} (16).

Other comments

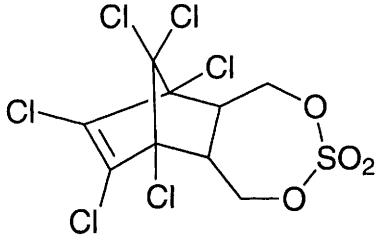
Harmless to wildlife and to honeybees (16,20).
Human health effects and toxicity reviewed (26,27).

References

1. Devi, A. O. *Bull. Environ. Contam. Toxicol.* 1981, **27**, 239.
2. Schoettger, R. A. *Toxicology of Thiodan in Several Fish and Aquatic Invertebrates* 1970, Bureau of Sport Fisheries and Wildlife Investigation in Fish Control 35, Govt. Printing Office, Washington, DC, USA.
3. Sanders, H. O. et al *Trans. Am. Fish Soc.* 1966, **65**, 165-169.
4. Frear, D. E. H. et al *J. Econom. Entomol.* 1967, **60**, 1228-1238.
5. Sanders, H. O. et al *Limnol. Oceanogr.* 1968, **13**(1), 112-117.
6. Nagvi, S. M. et al *J. Environ. Sci. Health, Part B* 1991, **B26**(4), 437-447.
7. Goerke, H. et al *Mar. Pollut. Bull.* 1979, **10**, 127-133.
8. Schimmel, S. C. et al *Aquatic Toxicology and Hazard Evaluation* 1977, 241, Am. Soc. Testing Materials.
9. Novak, B. et al *J. Environ. Sci. Health, Part B* 1989, **B24**(1), 97-109.
10. Rao, D. M. R. *Pestic. Biochem. Physiol.* 1989, **33**(3), 220-229.
11. Vershueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold, New York, NY, USA.
12. Martens, R. *Appl. Environ. Microbiol.* 1976, **31**, 853.
13. Martens, R. *Bull. Environ. Contam. Toxicol.* 1977, **17**, 438.

14. Monteiro, R. T. R. et al *Rev. Bras. Cienc. Solo* 1989, **13**(2), 163-168 (Port.) (*Chem. Abstr.* **113**, 147207h).
15. Szeto, S. Y. et al *J. Agric. Food Chem.* 1991, **39**(9), 1679-1684.
16. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
17. Aslanyan, G. T. et al *Biol. Zh. Arm.* 1987, **40**(10), 864-866 (Russ.) (*Chem. Abstr.* **108**, 162959v).
18. Hodstroem, S. et al *Pharmacol. Toxicol. (Copenhagen)* 1988, **62**(4), 230-235.
19. Maier-Bode, H. *Res. Rev.* 1968, **22**, 1.
20. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
21. Lisi, P. et al *Contact Dermatitis* 1987, **17**(4), 212-218.
22. Mersch-Sundermann, V. *Zentralbl. Hyg. Umweltmed.* 1989, **189**(2), 135-146 (Ger.) (*Chem. Abstr.* **112**, 113966u).
23. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
24. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
25. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
26. *Environ. Health Crit.* 1984, **40**, World Health Organisation, Geneva, Switzerland.
27. *NTIS Report* PB88-180229.GAR, 1987, EPA/600/8-88/034, Natl. Tech. Inf. Ser., Springfield, VA, USA

E21 endosulfan sulfate



$C_9H_6Cl_6O_4S$ **Mol. Wt.** 422.93 **CAS Registry No.** 1031-07-8

Synonyms 6,9-methano-2,4,3-benzodioxathiepin 3,3-dioxide; 1,4,5,6,7,7-hexachloro-5-norbornene-2,3-dimethanal cyclic sulfate; benzoepin sulfate; endosulfan cyclic sulfate; Thiodan sulfate

RTECS No. RB 9150000

Physical properties

M. Pt. 181°C **Partition coefficient** log P_{ow} 3.66 (1)
Solubility Water: 0.22 mg l^{-1} at 22°C

Ecotoxicity

Bioaccumulation
Bioconcentration factor ranged from 223-29,430 in algae and 935-1741 in fish (2).

Environmental fate

Degradation studies
$t_{1/2}$ for degradation by soil microorganisms 11 wk. Metabolites include endosulfan ether, endosulfan α-hydroxyether and endosulfan lactone (3).

Abiotic removal
Evaporation from river water, estimated $t_{1/2}$ 43 hr (4).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 1.23 hr (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 18 mg kg^{-1} (6).

Sub-acute and sub-chronic data

Gavage rat (1 month) 3 mg kg^{-1} day^{-1} induced increases in liver weight and liver monooxygenase activity (7).

Metabolism and toxicokinetics

Metabolites identified following intraperitoneal administration to rats were hydroxyether and lactone (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (11).

Other comments

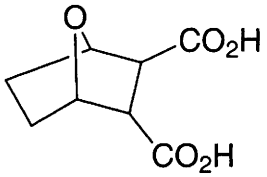
Metabolite of endosulfan in soils (12).
Reviews on toxicity listed (13).
Juvenile fathead minnows were used to compare San Diego's potable water supplies. Trace amounts of organic, inorganic chemicals and pesticides were found in fish tissue after exposure to water supplies. Differences in survival, growth and swimming performance were evident after 90-180 day exposures (14).

References

1. Paldahan, M. A. *Water-Related Environmental Fate of 129 Priority Pollutants* 1979, **2**, WEPA-440/4-78-029a.
2. *Endosulfan: Its Effects on Environmental Quality* 1975, 39, National Research Council, Canada, NRCC No. 14098.
3. Miles, J. R. W. et al *Bull. Environ. Contam. Toxicol.* 1979, **23**, 613-619.
4. Greve, P. A. et al *J. Water Pollut. Control Fed.* 1971, **42**, 2338-2348.
5. *GEMS: Graphical Exposure Modeling System: Fate of Atmospheric Pollutants* 1981, US EPA, Office of Toxic Substances, Washington, DC, USA.
6. *NTIS Report* PB85-143766, Natl. Tech. Inf. Ser., Springfield, VA, USA.
7. Aslanyan, G. T. et al *Biol Zh. Arm.* 1987, **40**(10), 864-866 (Russ.) (*Chem. Abstr.* **108**, 162959v).
8. Menzie, C. M. *Metabolites of Pesticides, Update II* 1978, 133, U.S. Dept. Int. Fish Wildlife Service, Special Scientific Report No. 212, Washington, DC, USA.
9. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
10. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
12. Monteiro, R. T. R. et al *Rev. Bras. Cienc. Solo* 1989, **13**(2), 163-168 (Port.) (*Chem. Abstr.* **113**, 147207h).
13. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
14. de Peyster, A. et al *J. Toxicol. Environ. Health* 1993, **39**(1), 121-142

E21 end

E22 endothal



$C_8H_{10}O_5$ **Mol. Wt.** 186.16 **CAS Registry No.** 145-73-3

Synonyms endothall; 7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid; 1,2-dicarboxy-3,6-endoxo-cyclohexane; 3,6-epoxycyclohexane-1,2-dicarboxylic acid; 3,6-endoxohexahydrophthalic acid; Accelerate; Aquathol; Asepta Prebetox

EINECS No. 205-660-5 **RTECS No.** RN 7875000

Uses Herbicide. Defoliant. Plant growth regulator.

Physical properties

M. Pt. 144°C (monohydrate) **Specific gravity** 1.431 at 20°C **Partition coefficient** log P_{ow} 1.91 (1)
Solubility Water: 100 g l^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, 1,4-dioxane, isopropanol, methanol

Occupational exposure

Supply classification toxic
Risk phrases Harmful in contact with skin – Toxic if swallowed – Irritating to eyes, respiratory system and skin (R21, R25, R36/37/38)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37/39, S45)

Ecotoxicity

Invertebrate toxicity
EC_{50} (10 day) *Chlorococcum, Dunaliella tertiolecta, Isochrysis galbana, Phaeodactylum tricornutum* 15-50 mg l^{-1} (2).

Environmental fate

Degradation studies
Biodegradation in a shake-flask study using an oligomesotrophic reservoir water was $t_{1/2}$ 8.35 days (3). Incubation of ^{14}C-ring-labelled endothal with *Arthrobacter* sp. revealed that ^{14}C was incorporated into cellular amino acids, proteins, nucleic acids and lipids and was released as carbon dioxide. The major metabolite was glutamic acid. Minor metabolites included aspartic acid, citric acid, alanine and phosphate esters (4).

Abiotic removal
Endothal is stable to oxidation, hydrolysis and photolysis (5).

Adsorption and retention
K_p for lake sediment 0.4-0.9 (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 35-51 mg kg^{-1} (7,8).
LD_{50} dermal rat >1000 mg kg^{-1} (9).
LD_{50} intraperitoneal mouse 14 mg kg^{-1} (10).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 1000 mg kg^{-1} diet (11).

Metabolism and toxicokinetics
Following oral administration to rats of 5 mg kg^{-1} ^{14}C-labelled endothal, ≈90% of the dose was excreted in the faeces, ≈7% in the urine and ≈3% was expired as carbon dioxide; ≈20% of the dose excreted in the faeces was unchanged endothal. The remaining dose was presumed to be excreted as an endothal conjugate. 95% of the administered dose was excreted within 48 hr. No radioactivity was detected in the pups of lactating dams (12).

Irritancy
80 mg instilled into rabbit eye for 24 hr caused severe irritation. Several animals died within 24 hr as a result of systemic effects resulting from this route of application (13).

Genotoxicity

Salmonella typhimurium TA92, TA98, TA100, TA1535, TA1537, TA2637 with and without metabolic activation negative (14).
Drosophila melanogaster sex-linked recessive lethal assay positive (15).
In vitro human lymphocytes sister chromatid exchanges negative (16).
In vitro BALB/C 3T3 cells with and without metabolic activation malignant transformation positive (17).

Other effects

Any other adverse effects
Intraperitoneal mouse single dose of 75 mg kg^{-1} caused extreme liver enlargement and congestion. Hepatic glycolysis was increased and hepatic ATP decreased (18).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (19).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (20).
EPA Toxicity Class II (11).

Other comments

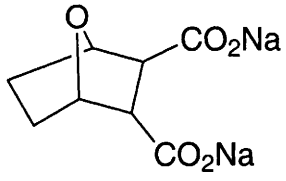
Physical properties, environmental fate, metabolism, mammalian toxicity, mutagenicity and health advisories reviewed (1,21-23).
Endothal exists as a mixture of three stereoisomers of which the (1*R*,2*S*,3*R*,4*S*)-isomer is the most herbicidally active (11).

References

1. *Drinking Water Health Advisory: Pesticides* 1989, 381-394, Lewis Publishers, Chelsea, MI, USA.
2. Walsh, G. E. *Hyacinth Control J.* 1972, **10**, 45-48.
3. Reinert, K. H. et al *Environ. Toxicol. Chem.* 1986, **5**, 449-461.
4. Sikka, H. C. et al *J. Agric. Food Chem.* 1973, **21**, 402.
5. Reinert, K. H. *Bull. Environ. Contam. Toxicol.* 1984, **32**, 557.
6. Simsiman, G. V. et al *Water, Air, Soil Pollut.* 1975, **4**, 399-413.
7. Simsiman, G. V. et al *Res. Rev.* 1976, **62**, 131-174.
8. Tweedy, B. G. et al *Herbicides – Chemistry, Degradation and Mode of Action* 1976, 815-833, Marcel-Dekker Inc., New York, NY, USA.
9. *Fundam. Appl. Toxicol.* 1986, **7**, 299.
10. *J. Agric. Food Chem.* 1987, **35**, 823.
11. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
12. Soo, A. et al *J. Agric. Food Chem.* 1967, **15**, 1018-1021.
13. *Summary Data, Primary Eye Irritation in the Rabbit and Inhalation Toxicity in Several Species (Endothal)* 1975, USEPA, EPA Accession No. 246012, Pharmacology Research Inc.

14. Remondelli, P. et al *Medecine Biologie Environment* 1986, **14**, 377-386.
15. Sandler, L. et al *The Induction of Sex-Linked Recessive Lethal Mutations in Drosophila melanogaster* 1981, Report to Municipality of Metropolitan Seattle, WA, USA.
16. Vighusson, N. V. *Evaluation of the Mutagenic Potential of Aquathol K by Induction of Sister Chromatid Exchanges in Human Lymphocytes in vitro* 1981, EPA Accession No. 245680, Report to Municipality of Metropolitan Seattle, WA, USA.
17. *Evaluation of Aquathol K in the in vitro Transformation of BALB/3T3 Cells With and Without Metabolic Activation Assay* 1981, Project No. 20992, Litton Biometrics Inc., WA, USA.
18. Graziano, M. J. et al *Toxicol. Lett.* 1987, **37**(2), 143-148.
19. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
20. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
21. *Dangerous Prop. Ind. Mater. Rep.* 1988, **8**(6), 51-56.
22. *IPCS Environmental Health Criteria No. 132* WHO, Geneva, Switzerland.
23. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, **3**, 344-348, Lewis Publishers, Chelsea, MI, USA

E23 endothal sodium



$C_8H_8Na_2O_5$ **Mol. Wt.** 230.13 **CAS Registry No.** 129-67-9

Synonyms 7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid, disodium salt; endothall sodium; disodium 3,6-endoxohexahydrophthalate; disodium 3,6-epoxycyclohexane-1,2-dicarboxylate; Hydrothol; Niagorathal

EINECS No. 204-959-8 **RTECS No.** RN 8225000

Uses Herbicide.

Physical properties

M. Pt. 144°C
Solubility Water: miscible

Occupational exposure

Supply classification toxic
Risk phrases Harmful in contact with skin – Toxic if swallowed – Irritating to eyes, respiratory system and skin (R21, R25, R36/37/38)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37/39, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, largemouth bass, king salmon 125-136 mg l^{-1} (1).

Environmental fate

Abiotic removal

No degradation occurred when irradiated at 254 nm (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 51-197 mg kg^{-1} (3-5).

LD_{50} dermal rabbit, rat 100, 750 mg kg^{-1}, respectively (6,7).

Sub-acute and sub-chronic data

Oral rat (4 wk) 40 or 400 mg kg^{-1} day^{-1}. The low dose caused slight liver degeneration and focal haemorrhage areas in the kidney. Most rats receiving the high dose died within 1 wk (8).

Carcinogenicity and chronic effects

Oral dog (2 yr) 0, 2, 6 or 16 mg kg^{-1} day^{-1} caused no signs of toxicity. Increased stomach and small intestine weights were observed in the 6 and 16 mg kg^{-1} groups (9).

Teratogenicity and reproductive effects

Oral rat (3 generations) 0, 5, 15 or 120 mg kg^{-1} day^{-1}. Pups in the 5 mg kg^{-1} group were normal, pups in the 15 mg kg^{-1} group had decreased body weights at 21 days of age, and pups in the 120 mg kg^{-1} group did not survive for more than 1 wk (10).

Oral rat 0, 10, 20 on 30 mg kg^{-1} day^{-1} on days 6-19 of gestation. Fatalities were reported in the 20 and 30 mg kg^{-1} groups. There were no observable signs of teratogenicity in any treated group (11).

Other effects

Other adverse effects (human)

A suicide victim injected 7-8 g in solution. Autopsy revealed focal haemorrhage and oedema in the lungs, and gross haemorrhage of the gastro-intestinal tract (12).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (13).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).

WHO Toxicity Class II (15).

Other comments

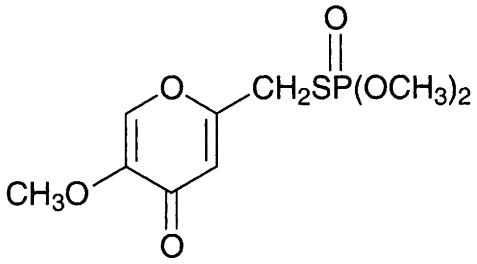
Physical properties, environmental fate, metabolism, mammalian toxicity, mutagenicity and health advisories reviewed (16).

References

1. Walker, C. R. *Water Sewage Works* 1964, **111**(3), 113-116.
2. Mitchell, L. C. *J. Assoc. Off. Anal. Chem.* 1961, **44**, 643-712.
3. Simiman, G. V. et al *Res. Rev.* 1976, **62**, 131-174.
4. Tweedy, B. G. et al *Herbicides. Chemistry, Degradation and Mode of Action* 1976, 815-833, Marcel Dekker Inc., New York, NY, USA.
5. *Guide to Chemicals Used in Crop Protection* 1973, **6**, 248, Information Canada, Ottawa, Canada.
6. *Pharm. J.* 1960, **185**, 361.
7. *Q. BULL. – Assoc. Food Drug Off. U.S.* 1952, **16**, 3.
8. Brieger, H. *Preliminary Studies on the Toxicity of Endothall* 1966, EPA Pesticide Petition No. 7F0570, EPA Accession No. 246012.
9. Keller, J. *Two Year Chronic Feeding Study of Disodium Endothall to Beagle Dogs* EPA Pesticide Petition No. 7F0570, EPA Accession No. 246012.
10. *Three-Generation Rat Productive Study, Disodium Endothall* 1965, EPA Pesticide Petition No. 7F0570, EPA Accession No. 246012, Scientific Associates.

11. *A Dose Range-Finding Teratology Study of Endothall Technical and Disodium Endothal in Rats* EPA Accession No. 071249, Science Applications Inc.
12. Allender, W. J. *J. Anal. Toxicol.* 1983, **7**, 79-82.
13. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
14. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
15. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
16. *Drinking Water Health Advisory: Pesticides* 1989, 381-394, Lewis Publishers, Chelsea, MI, USA

E24 endothion



$C_9H_{13}O_6PS$ **Mol. Wt.** 280.24 **CAS Registry No.** 2778-04-3

Synonyms *O,O*-dimethyl *S*-(5-methoxy-4-oxo-4*H*-pyran-2-yl) phosphorothioate; 5-methoxy-2-(dimethoxyphosphinylthiomethyl) 4-pyrone; Endocide

EINECS No. 220-472-3 **RTECS No.** TF 8225000

Uses Superseded insecticide and acaricide.

Physical properties

M. Pt. 96°C

Solubility Water: 1500 g l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform, olive oil

Occupational exposure

Supply classification toxic

Risk phrases Toxic in contact with skin and if swallowed (R24/25)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Ecotoxicity

Fish toxicity

Goldfish survived exposure to 10 ppm for 14 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 17, 23 mg kg^{-1}, respectively (2,3).

LD_{50} dermal rat 130 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Oral rat (7 wk) 50 mg kg^{-1} diet caused no adverse effects (1).

Other effects

Any other adverse effects
Inhibits acetylcholinesterase activity (5).

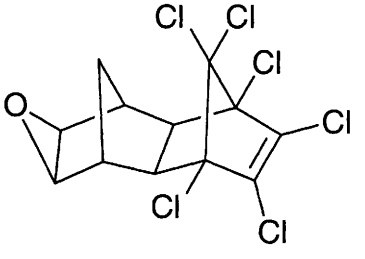
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

References

1. *The Pesticide Manual* 5th ed., 1974, British Crop Protection Council, Worcestershire, UK.
2. *World Rev. Pest Control* 1964, **4**, 36.
3. *USDA Information Memorandum* 1966, **20**, 10, Agricultural Research Service, Beltsville, MD, USA.
4. *Pharm. J.* 1960, **185**, 361.
5. Morgan, D. P. *Recognition and Management of Pesticide Poisonings* 1982, 2, USEPA 540/0-80-005, Washington, DC, USA.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E25 endrin



$C_{12}H_8Cl_6O$ **Mol. Wt.** 380.91 **CAS Registry No.** 72-20-8

Synonyms hexachloroepoxyoctahydro-*endo,endo*-dimethanonaphthalene; 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-*endo,endo*-1,4:5,8-dimethanonaphthalene; mendrin; nendrin; hexadrin; Endrix; Endrical

EINECS No. 200-775-7 **RTECS No.** IO 1575000

Uses Superseded insecticide.

Physical properties

M. Pt. 226-230°C (decomp. >245°C) **Specific gravity** 1.64 at 20°C **Partition coefficient** log P_{ow} 6.31 (1)
Volatility v.p. 2.7×10^{-7} mmHg at 25°C
Solubility Water: 0.25 μg l^{-1} at 25°C. Organic solvents: acetone, benzene, carbon tetrachloride, hexane, xylene

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.1 mg m^{-3}
UK-LTEL 0.1 mg m^{-3} **UK-STEL** 0.3 mg m^{-3}
US-TWA 0.1 mg m^{-3}
Supply classification very toxic, dangerous for the environment
Risk phrases Toxic in contact with skin – Very toxic if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24, R28, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S22, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout, coho salmon, fathead minnow 0.5-0.7 μg l^{-1} (2,3).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 1.9 μg l^{-1} (4).
LC_{50} (96 hr) *Gammarus lacustris, Orconectes nais, Asellus brevicaudus* 1.5-3.0 μg l^{-1} (5,6).
LD_{50} to bees by three routes oral, contact and by dusting, 0.46 μg bee^{-1}, 0.65 μg bee^{-1} and 2.02 μg bee^{-1}, respectively (7,8).

Bioaccumulation
Bioconcentration factor in fathead minnow, channel catfish, flagfish, sheepshead minnow, snail, mussels, oyster, grass shrimp 1600-15,000 (9).
Bioconcentration factor in the algae *Microcystis aeruginosa, Anabaena cylindrica, Scenedesmus quadricauda* and *Oedogonium* spp. 140-222 (9).

Environmental fate

Degradation studies
$t_{1/2}$ in anaerobic sewage sludge 5-14 days (10).
$t_{1/2}$ in soil 4-8 yr (11).

Abiotic removal
Photooxidation by UV light in aqueous medium at 90-95°C, as determined by carbon dioxide evolution, 25% after 15 hr, 50% after 41 hr, 75% after 172 hr (12).

Adsorption and retention
Calculated K_{oc} of 34,000 indicates that endrin is likely to be immobile in soil (13).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, redwing blackbird, starling, quail 1.3-4.2 mg kg^{-1} (14-16).
LD_{50} dermal rat, rabbit 12, 60 mg kg^{-1}, respectively (17).
LD_{50} intravenous mouse 2.3 mg kg^{-1} (18).

Sub-acute and sub-chronic data
LC_{50} (5 day) bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck 14-22 mg kg^{-1} diet (19).

Carcinogenicity and chronic effects
No adequate data for evaluation of carcinogenicity to humans, insufficient evidence of carcinogenicity to animals, IARC classification group 3 (20).

National Toxicology Program tested rats and mice via feed. Negative results were reported in ♂ and ♀ rats and mice (21).

Teratogenicity and reproductive effects

Chicken embryo 0.1 mg egg^{-1} day^{-1} on days 5-10 induced malformation which was linked to the embryonic γ-aminobutyric acid (pro) receptor complex (22).

Metabolism and toxicokinetics

Oral rats were fed radiolabelled endrin at 30 mg kg^{-1} in diet for 8 days. 60-70% was excreted in faeces within 24 hr, after 72 hr faecal excretion was 80%. Only 0.05% was detected in urine while 3-4 mg kg^{-1} was stored in adipose tissue (23).

Oral rabbit two single doses of 4.7 mg in olive oil 14 days apart. Between days 1 and 13, 37% was excreted via the urine and 49% in the faeces. On day-50, 50% had been excreted in the urine as metabolites and 47% in the faeces as unchanged compound (24).

Major route of metabolism identified (unspecified species) as the formation of *anti*-12-hydroxyendrin and its sulfate and glucuronide conjugates (25).

Irritancy

Dermal rabbit (14 wk) 75 or 150 mg kg^{-1} for 2 hr day^{-1} 5 day wk^{-1} on intact or abraded skin. No skin irritation observed (26).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (27).
Escherichia coli PQ37 SOS-Chromotest with and without metabolic activation negative (28).
In vitro mouse lymphoma L5178Y cells, tk^+/tk^- forward mutation negative (29,30).
In vitro Chinese hamster ovary cells, chromosomal aberrations negative, sister chromatid exchanges positive (31).

Other effects

Other adverse effects (human)

In mild cases of poisoning, dizziness, weakness of the legs, abdominal discomfort, nausea and vomiting have been reported. Temporary deafness, disorientation and aggressiveness have also been reported. Onset of poisoning is variable and can occur 30 min to 10 hr after oral or dermal exposure. Severe poisoning is manifested by epileptic fits and violent limb convulsions. Fatalities occur within 2-12 hr; in survivors recovery is rapid within 24 hr (32).

Any other adverse effects

After agrochemical application of endrin, four species of aquatic birds were found dead with a mean concentration of 0.11 mg kg^{-1} endrin in the brain; common egrets were also found dead, brain concentration 0.25 mg kg^{-1}, and liver/kidneys concentration 0.08 mg kg^{-1} (33).

Effects to central nervous system in experimental animals exposed to 0.2 mg kg^{-1} include considerable changes to EEG activity and convulsions (34).

Legislation

Endrin is included in Schedule 5 (Release into Water: Prescribed Substances) and Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (35).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (36).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (37).

Quality objective under EC Directives 86/280/EEC and 88/347/EEC 0.005 μg l^{-1} for all waters. A 'standstill' provision applies to concentrations in sediments, molluscs, shellfish and/or fish. Limit value under EC Directives 86/280/EEC and 88/347/EEC 2 μg l^{-1} in effluent and 3 g $tonne^{-1}$ of total production capacity for industrial plants producing endrin (38).

Other comments

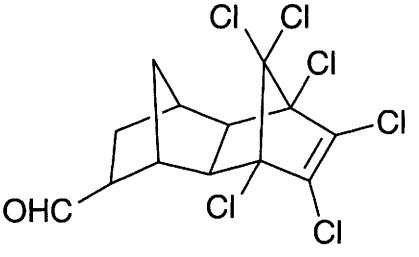
Residues have been isolated from water, soil, crops, birds and fish (39).
Environmental fate reviewed (39).
Mammalian toxicology and carcinogenicity reviewed (34,40).
Toxicology (34,41), effects on human milk (42) and on drinking water reviewed (43).

References

1. McCoy, G. D. et al *Carcinogenesis (London)* 1990, **11**(7), 1111-1117.
2. Jarvinen, A. W. et al *Ecotoxicol. Environ. Saf.* 1988, **15**(1), 78-95.
3. Katz, M. *Trans. Am. Fish Soc.* 1961, **90**(3), 264-268.
4. Vighi, M. et al *Chemosphere* 1987, **16**(5), 1043-1051.
5. Sanders, H. O. *Toxicity of Pesticides to the Crustacean, Gammarus lacustris* 1969, Bureau of Sport Fisheries and Wildlife, Tech. Paper 25, Washington, DC, USA.
6. Sanders, H. O. *The Toxicities of Some Insecticides to Four Species of Molocostracan Crustacea* 1972, Fish Pesticide Research Laboratory, Columbia, MO, USA.
7. Oomen, P. A. *Meded. Fac. Landbouwwet. Rijksuniv. Ghent* 1986, **51**(3b), 1205- 1213.
8. Atkins, E. L. et al *Toxicity of Pesticides and Agrochemicals to Honeybees* 1973, Dept. of Entomology, U C Riverside, CA, USA.
9. *Ambient Water Quality Criteria: Endrin* 1980, EPA 440/5-80-047, USEPA.
10. Hill, D. W. et al *J. Water Pollut. Control Fed.* 1967, **39**, 1259-1277.
11. Menzie, C. M. *Ann. Rev. Entomol.* 1972, **17**, 199-222.
12. Knoevenagel, K. et al *Arch. Environ. Contam. Toxicol.* 1976, **4**, 324- 333.
13. Swann, R. L. et al *Res. Rev.* 1983, **85**, 17- 28.
14. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
15. *World Rev. Pest Control* 1970, **9**, 119.
16. *Toxicol. Appl. Pharmacol.* 1973, **25**, 42.
17. *Special Publication of the Entomological Society of America* 1978, **78-1**, 13, College Park, MD, USA.
18. *Toxicol. Appl. Pharmacol.* 1972, **23**, 408.
19. Hill, E. F. et al *Lethal Dietary Toxicities of Environmental Pollutants to Birds* 1975, U.S. Fish and Wildlife Service, Wildlife Report No. 191, Washington, DC, USA.
20. *IARC Monograph* 1987, **Suppl. 7**, 63.
21. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-012, NIEHS, Research Triangle Park, NC, USA.
22. Siefert, J. *Bull. Environ. Contam. Toxicol.* 1989, **42**(5), 707-715.
23. *Evaluation of Pesticide Residues in Food* 1971, FAO/WHO, Geneva, Switzerland.
24. Bedford, C. T. et al *Xenobiotica* 1975, **5**(8), 485-500.
25. Bedford, C. T. et al *Pestic. Sci.* 1986, **17**, 659-667.
26. Treon, J. F. et al *J. Agric. Food Chem.* 1955, **3**(1), 842- 848.
27. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
28. Mersch-Sundermann, V. et al *Zentralbl. Hyg. Umweltmed.* 1989, **189**(2), 135-146 (Ger.) (*Chem. Abstr.* **112**, 113966u).
29. Garrett, N. E. et al *Mutat. Res.* 1986, **168**(3), 301-325.
30. Ennever, F. K. et al *Environ. Mutagen.* 1986, **8**(6), 849-865.
31. Rosenkranz, H. S. et al *Mutagenesis* 1990, **5**(6), 559-571.
32. Jacobziner, H. et al *N. Y. State J. Med.* 1959, **59**, 2017-2022.
33. Vermeer, K. et al *Environ. Pollut.* 1974, **7**, 217-236.
34. *IPCS Environmental Health Criteria No. 130* 1992, World Health Organisation, Geneva, Switzerland.
35. *S. I. 1991, No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
36. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
37. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
38. *DoE Circular 7/89: Water and the environment. The implementation of EC directives on pollution caused by certain dangerous substances discharged into the aquatic environment* 1989, HMSO, London, UK.
39. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, **3**, 349- 361, Lewis Publishers, Chelsea, MI, USA.
40. *IARC Monograph* 1974, **5**, 157.

41. Shigeoka, T. *Mathematical Models for Environmental Fate and Exposure of Chemicals in An International Reference Manual on Chemical Safety* 1994, 90-109, Richardson, M.L. (Ed.), VCH Publ., Weinheim, Germany.
42. Richardson, M.L. (Ed.) *An International Reference Manual on Chemical Safety* 1994, 157-170, VCH Publ., Weinheim, Germany.
43. Richardson, M.L. (Ed.) *An International Reference Manual on Chemical Safety* 1994, 353-370, VCH Publ., Weinheim, Germany

E26 endrin aldehyde



$C_{12}H_8Cl_6O$ **Mol. Wt.** 380.91 **CAS Registry No.** 7421-93-4

Synonyms 2,2a,3,3,4,7-hexachlorodecahydro-(1α,2β,2aβ,4β,4aβ,5β,6aβ,6bβ,7*R*)-1,2,4-metheno-cyclopenta[*cd*]pentalene-5-carboxaldehyde

Physical properties

M. Pt. 235°C (decomp.) **Partition coefficient** log P_{ow} 4.7 (1) **Volatility** v.p. 2×10^{-7} mmHg at 25°C
Solubility Water: 0.25 mg l^{-1} at 23°C

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor 2200 indicates that the potential for environmental accumulation is likely (1).

Environmental fate

Adsorption and retention
Calculated K_{oc} 8500-45,000 indicates significant soil adsorption (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related compounds: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (4).

Other comments

Impurity and metabolite of endrin (5).

References

1. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.

3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
5. Callahan, M. A. et al *Water-Related Environmental Fate of 129 Primary Pollutants* 1979, **1**, US EPA- 440/4-79-029 A

E27 enflurane

CHF_2OCF_2CHClF

$C_3H_2ClF_5O$ **Mol. Wt.** 184.49 **CAS Registry No.** 13838-16-9

Synonyms 2-chloro-1-(difluoromethoxy)-1,1,2-trifluoroethane; 2-chloro-1,1,2-trifluoroethyl difluoromethyl ether; Ohio 347; Methylflurether; ethrane

EINECS No. 237-553-4 **RTECS No.** KN 6800000

Uses Anaesthetic.

Physical properties

B. Pt. 56.5°C **Specific gravity** 1.5167 at 25°C with respect to water at 25°C
Solubility Organic solvents: fats and oils

Occupational exposure

DE-MAK 20 ppm (150 mg m^{-3})
SE-LEVL 10 ppm (80 mg m^{-3}) **SE-STEL** 20 ppm (150 mg m^{-3})
UK-LTEL 50 ppm (383 mg m^{-3})
US-TWA 75 ppm (566 mg m^{-3})

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 5000-5450 mg kg^{-1} (1).
LC_{50} (3 hr) inhalation mouse, rat 8100, 14,000 ppm, respectively (2).
LD_{50} intraperitoneal mouse, rat 3900, 6000 mg kg^{-1}, respectively (1).
LD_{50} subcutaneous rat, mouse 19,500, 38,800 mg kg^{-1}, respectively (3).

Carcinogenicity and chronic effects
Inadequate evidence of carcinogenicity to humans and animals, IARC classification group 3 (4).
LC_{Lo} (78 wk) inhalation mouse 3000 ppm 4 hr day^{-1} caused increased incidence of liver tumours to 36% compared with 24% in controls, however this was judged not to be significant for carcinogenic effects to be positive in this study (5).

Metabolism and toxicokinetics
Enflurane is absorbed on inhalation. The blood/gas coefficient is low. Mostly excreted unchanged through the lungs (6).

Sensitisation
Asthma and bronchospasm have been reported in patients (6).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation negative (7).
Drosophila melanogaster sex-linked recessive lethal assay negative (8).

In vitro Chinese hamster lung cells, sister chromatid exchanges negative (9).
In vivo mouse, dominant lethal assay negative (10).

Other effects

Other adverse effects (human)

Elevated levels of serum fluoride have been reported in patients, but renal damage is rare (6).
Enflurane has been associated with liver damage (6).
Psychophysiological performance was impaired in volunteers exposed for 4 hr to 112 mg m^{-3} enflurane plus 615 mg m^{-3} nitrous oxide (11).

Any other adverse effects

Inhalation rat, repeated treatment (duration unspecified) 3% mixture with oxygen caused a decrease in the liver cytoplasmic NAD/NADH ratio, but did not alter the mitochondrial ratio. The blood cell cytosolic NAD/NADH ratio decreased slightly whereas the total NAD content was increased. Serum transaminase activities were not increased, indicating the absence of significant toxic effects on the liver (12).

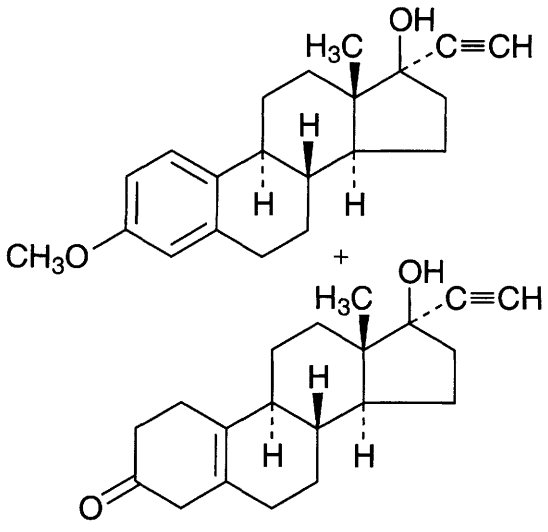
Other comments

Mammalian toxicity and carcinogenicity for volatile anaesthetics reviewed (13).
Reviews on toxicity listed (14).

References

1. *Drugs. Int. J. Current Ther. Appl. Pharmacol. Rev.* 1982, **6**, 143.
2. *Iyakuhin Kenkyu* 1981, **12**, 668.
3. *Yakkyoku* 1981, **32**, 491.
4. *IARC Monograph* 1987, **Suppl. 7**, 93-95.
5. *Anesthesiology* 1982, **56**, 9.
6. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
7. Baden, J. M. et al *Anesthesiology* 1977, **46**, 346-350.
8. Baden, J. M. et al *Br. J. Anaesth.* 1987, **59**(6), 772-775.
9. Trudnowski, R. J. et al *J. Med. (Westbury, N.Y.)* 1987, **18**(1), 55-60.
10. Wharton, R. S. et al *Anethesiology* 1981, **54**, 505-510.
11. Bruce, D. L. et al *Anesthesiology* 1975, **42**, 194-196.
12. Lusini, P. et al *Minerva Anestesiol.* 1987, **53**(3), 57-62, (Ital.) (*Chem. Abstr.* **107**, 190944j).
13. *IARC Monograph* 1976, **11**, 285-293.
14. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E28 Enovid



CAS Registry No. 8015-30-3

Synonyms (17α)-19-norpregna-1,3,5(10)-trien-20-yn-17-ol, mixture with (17α)-3-methoxy-19-norpregna-1,3,5(10)-trien-20-yn-17-ol; Enavid; Infecundin; menstranol-norethynodrel mixture

Uses Oral contraceptive.

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Oral monkey (2 yr) 2.6 mg day^{-1} per animal increased plasma renin activity, which is linked to the mechanism of hypertension produced by use as an oral contraceptive (1).

Teratogenicity and reproductive effects

LD_{Lo} subcutaneous rat, single dose of 1.25 mg kg^{-1} 1 day before mating caused reproductive effects (2).

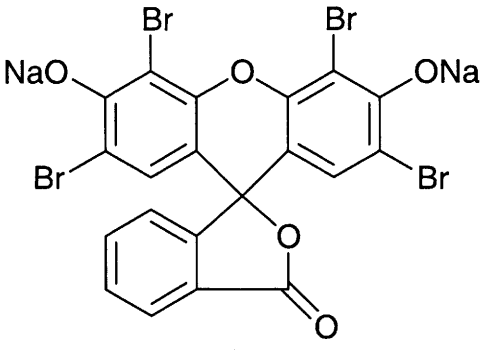
Other comments

Mammalian toxicity and carcinogenicity reviewed (3-5).

References

1. Milanian, I. et al *Indian J. Med. Res.* 1986, **84**, 640-644.
2. *Endocrinology (Baltimore)* 1965, 77, 873.
3. *IARC Monograph* 1987, **Suppl. 7**, 288, 295.
4. *IARC Monograph* 1979, **21**, 46, 57.
5. *IARC Monograph* 1974, **6** , 191

E29 eosin



$C_{20}H_6Br_4Na_2O_5$ **Mol. Wt.** 691.86 **CAS Registry No.** 17372-87-1

Synonyms C.I. 45380; 2′,4′,5′,7′-tetrabromo-3′,6′-dihydroxyspiro[isobenzofuran-1(3*H*),9′-[9*H*]xanthen]-3-one, disodium salt; disodium 2′,4′,5′,7′-tetrabromofluorescein; tetrabromofluorescein; Eosin Yellowish; D & C Acid Red No. 87; D & C Red No. 22; Japan Red No. 103; Solvent Red 43; Sodium eosin; Food Red 103; Water Red 2

EINECS No. 241-409-6 **RTECS No.** LM 5850000

Uses Catalyst. Analytical reagent in fluorimetry. Photosensitiser. Dyestuff used in inks, biological staining, cosmetics (lipstick) and textiles. Dye intermediate in the production of red inks and toners.

Physical properties

M. Pt. 295-296°C

Solubility Water: freely soluble. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2350 mg kg^{-1} (1).

LD_{Lo} subcutaneous rat 1500 mg kg^{-1} (2).

LD_{50} intravenous mouse 550 mg kg^{-1} (3).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (4).

Subcutaneous rat (23 month) 500 mg kg^{-1} wk^{-1} for 13 wk, followed by 250 mg kg^{-1} wk^{-1} for 21 months. 1/20 rats developed cysticercus sarcoma of the liver, 3/20 developed mammary fibroadenomas and 2/20 developed local sarcomas at the site of injection (2,5).

Subcutaneous rat (830 day) ≈45 mg kg^{-1} 2 × wk^{-1} for 590 days (♂) or 618 days (♀). The median survival times were 770 days for ♂ and 465 days for ♀. One treated ♀ rat developed a mammary fibroadenoma, and one control ♀ rat had a mammary fibrosarcoma. Few animals survived the period of study. There were no controls for the study (6).

Oral rat (830 day) 0 or 500 mg kg^{-1} (free acid) day^{-1} for 654 days. Maximum total dose 304.5 g $animal^{-1}$. The median survival times were 469 daysfor ♂ and 778 days for ♀ rats. 1/10 ♀ developed a mammary fibrosarcoma. 1/10 ♀ control developed a fibrosarcoma of the stomach (5).

Metabolism and toxicokinetics

Excreted in the bile following intravenous administration to rats (7).

Following intravenous administration of the free acid to rats, eosin disodium salt was excreted unchanged, with 50-70% in the bile and 2-6% in the urine. After oral administration of 500 mg kg^{-1}, 94% was excreted unchanged in the faeces and urine (8).

Binds non-covalently to proteins to form protein-dye complexes (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (10).
In the *rec* assay, which gives an indication of repairable DNA damage, it was not more toxic to *Bacillus subtilis* M45 (*rec*$^-$) than to H17 (*rec*$^+$), suggesting that it does not damage DNA (11).
A CASE study applied to a Gene-Tox derived *Salmonella typhimurium* mutagenicity database predicted marginal activity (12).

Legislation

Approved by USFDA for use in drugs and cosmetics except for use in eye area (13).
Halogens and their covalent compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).

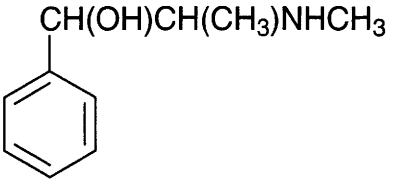
Other comments

Physical properties, use, analysis, carcinogenicity, mammalian toxicity and mutagenicity reviewed (15).
In bioreactor tracer studies for wastewater treatment the compound was stable over time, showed good solubility and did not change colour between pH 6.5-6.8 (16).
To evaluate the acute toxicity to fish its photodecomposed products were isolated and identified; the toxicity was measured with photo-irradiation, and, as with other xanthene dyestuffs, was attributed to liberated halogens (17).
The drug and cosmetic grade used in the US contains maximum amounts of: 2 mg kg^{-1} lead, 0.2 mg kg^{-1} arsenic, 3 mg kg^{-1} other heavy metals, 10% volatile matter at 135°C, 1% insoluble matter (alkaline solution), 0.5% diethyl ether extracts (from alkaline solutions), 5% sodium chlorides and sulfates, 1% mixed oxides and 0.02% free bromine. Must contain a minimum of 85% pure dye.

References

1. *Eastern Pharmacist* 1981, **24**, 125.
2. Umeda, M. *Gann* 1955, **46**, 367-368.
3. *Toxicol. Appl. Pharmacol.* 1978, **44**, 225.
4. *IARC Monographs* 1987, **Suppl. 7**, 63.
5. Umeda, M. *Gann* 1956, **47**, 51-78.
6. Hiller, F. K. *Arzneim.-Forsch.* 1962, **12**, 587-588.
7. Varga, F. et al *Arch. Toxicol. Suppl.* 1989, **13**, 309-311.
8. Webb, J. M. et al *J. Pharmacol. Exp. Ther.* 1962, **137**, 141-147.
9. Gangolli, S. D. et al *Food Cosmet. Toxicol.* 1972, **10**, 449-462.
10. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141.
11. Kada, T. in *New Methods in Environmental Chemistry and Toxicology* 1973, 127-133, Academic Scientific Books, Tokyo, Japan.
12. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
13. *Fed. Regist.* 1982, **47**, 53843.
14. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
15. *IARC Monograph* 1977, **15**, 183-193.
16. Jimenez, B. et al *Biotechnol. Technol.* 1988, **2**(2), 77-82.
17. Tonogai, Y. et al *J. Toxicol. Sci.* 1979, **4**, 115

E30 ephedrine



$C_{10}H_{15}NO$ **Mol. Wt.** 165.24 **CAS Registry No.** 299-42-3

Synonyms (1*R*,2*S*)-(–)-ephedrine; (1*R*,2*S*)-[α-(1-methylamino)ethyl]benzyl alcohol; Biophedrin

EINECS No. 206-080-5 **RTECS No.** KB 0700000

Uses Catalyst. Chemical intermediate. Nasal decongestant.

Occurrence Alkaloid obtained from *Ephedra* sp.

Physical properties

M. Pt. 34°C **B. Pt.** 255°C (decomp.) **Flash point** 85°C **Specific gravity** 1.124

Solubility Water: 50 g l^{-1}. Organic solvents: chloroform, diethyl ether, ethanol, liquid paraffin

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed (R22)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – Avoid contact with the eyes (S2, S22, S25)

Mammalian & avian toxicity

Acute data

LD_{50} redwing blackbird 560 mg kg^{-1} (1).

LD_{50} oral rat, mouse, 60, 1250 mg kg^{-1}, respectively (2,3).

LD_{50} subcutaneous rat 300 mg kg^{-1} (4).

LD_{50} intraperitoneal mouse 350 mg kg^{-1} (5).

Carcinogenicity and chronic effects

Oral rat, mouse (2 yr) 125 and 250 mg kg^{-1} diet, respectively, did not show evidence of carcinogenicity (6).

Teratogenicity and reproductive effects

Intraperitoneal rat 0.1, 1.0, 10 or 50 mg kg^{-1} on days 9, 10 or 11 of gestation induced cardiovascular malformations in 8-27% of animals in all treated groups (7).

Metabolism and toxicokinetics

Completely absorbed from the gastro-intestinal tract. Resistant to metabolism by monoamine oxidase and is largely excreted unchanged in the urine together with small amounts of hepatic metabolites. Plasma $t_{1/2}$ 3-6 hr depending on urinary pH; elimination is enhanced and $t_{1/2}$ is shorter in acid urine (8).

Genotoxicity

In vitro mouse lymphoma L5178Y mutagenicity assay without metabolic activation positive (9).

In vitro Nigella sativa L. meristematic cells induced depression of mitotic index and an increase in chromosomal aberrations at metaphase, anaphase and telophase (10).

Other effects

Other adverse effects (human)

Major adverse effects among patients are those of adrenergic and central nervous system stimulation (8).

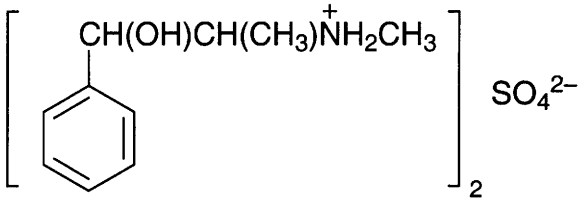
Any other adverse effects

Inhibits acetylcholinesterase activity (11).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *Arzneim.-Forsch.* 1973, **23**, 1125.
3. Usdin, E. et al *Psychotropic Drugs and Related Compounds* 2nd ed., 1972, 341, Washington, DC, USA.
4. *Arch. Int. Pharmacodyn. Ther.* 1942, **68**, 339.
5. *Pharm. Chem. J. (Engl. Transl.)* 1969, **3**, 203.
6. *National Toxicology Program Research and Testing Division* 1986, Report No TR-307, Research Triangle Park, NC, USA.
7. Kanai, T. *Tokyo Joshi Ika Daigaku Zasshi* 1987, **57**(7), 347-357 (Japan.) (*Chem. Abstr.* **107**, 72592v).
8. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
9. McGregor, D. B. et al *Mol. Mutagen.* 1988, **11**(4), 523-544.
10. Mogili, T. et al *Indian. Bot. Rep.* 1986, **5**(2), 214-217.
11. Ngiam, T. L. et al *Chem. Pharm. Bull.* 1989, **37**(9), 2423-2426

E31 ephedrine sulfate



$C_{20}H_{32}N_2O_6S$ **Mol. Wt.** 428.55 **CAS Registry No.** 134-72-5

Synonyms 1-[α-(1-methylamino)ethyl]benzyl alcohol sulfate; 1-phenyl-2-methylaminopropanol sulfate; isofedrol

EINECS No. 205-154-4 **RTECS No.** KB 2625000

Uses Nasal decongestant.

Physical properties

M. Pt. 245°C (decomp.) **Partition coefficient** log P_{ow} 1.39 (1)

Solubility Water: 83 g l^{-1}. Organic solvents: ethanol

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed (R22)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – Avoid contact with the eyes (S2, S22, S25)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit 400, 825 mg kg^{-1}, respectively (2).
LD_{50} subcutaneous rat, rabbit 320, 380 mg kg^{-1}, respectively (2).
LD_{50} intravenous rabbit, rat 73, 102 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal mouse 400 mg kg^{-1}, respectively (3).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via feed. No evidence of carcinogenicity was demonstrated in ♂ and ♀ rats and mice (no chemically related increase in malignant or benign neoplasms) (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (5).
In vitro Chinese hamster ovary cells, chromosomal aberrations negative, sister chromatid exchanges positive (6).

Other effects

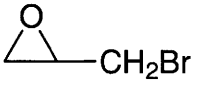
Other adverse effects (human)

Administration during pregnancy has been reported to cause foetal tachycardia (7).

References

1. McCoy, G. D. *Carcinogenesis (London)* 1990, **11**(7), 1111- 1117.
2. *J. Pharmacol. Exp. Ther.* 1948, **94**, 150.
3. *Toxicol. Appl. Pharmacol.* 1974, **28**, 227.
4. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-307, NIEHS, Research Triangle Park, NC, USA.
5. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
6. Rosenkranz, H. S et al *Mutagenesis* 1990, **5**(6), 559-571.
7. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK

E32 epibromohydrin



C_3H_5BrO **Mol. Wt.** 136.98 **CAS Registry No.** 3132-64-7

Synonyms 2-(bromomethyl)oxirane; (bromomethyl)ethylene oxide; 1-bromo-2,3-epoxypropane; bromohydrin

EINECS No. 221-525-3 **RTECS No.** TX 4115000

Uses Alkylating agent. Chemical intermediate. Flame retardant. Sporicide.

Physical properties

M. Pt. –40°C **B. Pt.** 134-136°C **Flash point** 56°C **Specific gravity** 1.601 at 20°C **Partition coefficient** log P_{ow} 0.85 (1) **Volatility** v.p. 2 mmHg at 25°C
Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2558 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (14 day) guppy 0.71 mg l^{-1} (1).

Not toxic to brown trout, bluegill sunfish, yellow perch and goldfish exposed to 5 ppm for 24 hr. Test conditions: pH 7, dissolved oxygen content 7.5 ppm, total hardness (soap method) 300 ppm, methyl orange alkalinity 310 ppm, free carbon dioxide 5 ppm, temperature 12.8°C (2).

Bioaccumulation

Calculated bioconcentration factor of 0.85 indicates that environmental accumulation is unlikely (3).

Environmental fate

Abiotic removal

Hydrolysis in water estimated $t_{1/2}$ 16 days at pH 7 and 25°C. 1-Bromo-2,3-propanediol is a possible product, although in the presence of anions such as chloride, 1-bromo-3-chloro-2-propanol is formed (4).

Volatilisation from a model river water at 1 m depth $t_{1/2}$ 2.5 days (5).

Reaction with photochemically produced hydroxyl radicals in the atmosphere, calculated $t_{1/2}$ ≈28 days (6).

Adsorption and retention

Calculated K_{oc} 22 indicates that epibromohydrin will not adsorb to soil and sediments (5).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 300 mg kg^{-1} (7).

Genotoxicity

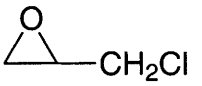
Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive (8).

In vitro Chinese hamster V79 cells, sister chromatid exchanges positive (3).

References

1. Deneer, J. W. et al *Aquat. Toxicol.* 1988, **13**(3), 195-204.
2. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-897-002; PB 87-200-275, Washington DC, USA.
3. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
4. Santodonato, J. et al *Investigations of Selected Potential Environmental Contaminants: Epichlorohydrin and Epibromohydrin* 1980, US EPA 560/11-80/006.
5. Lyman, W. J. *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1990, American Chemical Society, Washington, DC, USA.
6. Atkinson, R. *Environ. Toxicol. Chem.* 1988, **7**, 435-442.
7. *Arzneim.-Forsch.* 1987, **17**, 145.
8. Canter, D. A. et al *Mutat. Res.* 1986, **172**(2), 105-138

E33 epichlorohydrin



C_3H_5ClO **Mol. Wt.** 92.52 **CAS Registry No.** 106-89-8

Synonyms (chloromethyl)oxirane; (chloromethyl)ethylene oxide; 1-chloro-2,3-epoxypropane; 3-chloro-1,2-epoxypropane; chloropropylene oxide; 3-chloro-1,2-propylene oxide; 1,2-epoxy-3-chloropropane; (DL)-α-epichlorohydrin

EINECS No. 203-439-8 **RTECS No.** TX 4900000

Uses Cross-linking agent for cyclodextrins. Synthesis of glycerin, epoxy resins and epichlorohydrin elastomers. Solvent. Fumigant.

Physical properties

M. Pt. -57°C (99% pure) **B. Pt.** 115-117°C **Flash point** 33°C **Specific gravity** 1.1812 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.30 (1) **Volatility** v.p. 16 mmHg at 25°C ; v.den. 3.29
Solubility Water: 6.4% at 20°C. Organic solvents: miscible with acetone, carbon tetrachloride, chloroform, diethyl ether, trichloroethylene

Occupational exposure

FR-VLE 2 ppm (10 mg m^{-3})
SE-LEVL 0.5 ppm (1.9 mg m^{-3}) **SE-STEL** 1 ppm (4 mg m^{-3})
UK-LTEL MEL 0.5 ppm (1.9 mg m^{-3}) **UK-STEL** MEL 1.5 ppm (5.8 mg m^{-3})
US-TWA 0.5 ppm (1.9 mg m^{-3})

UN No. 2023 **HAZCHEM Code** 2W **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Flammable – Toxic by inhalation, in contact with skin and if swallowed – Causes burns – May cause sensitisation by skin contact (R45, R10, R23/24/25, R34, R43)
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
LC_{50} (14 day) guppy 0.66 mg l^{-1} (1).
LC_{50} (24 hr) goldfish 23 mg l^{-1} (2).
LC_{50} (96 hr) bluegill sunfish, inland silverside 18-35 mg l^{-1} (3).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 670 ppm, Microtox test (4).
EC_{50} (48 hr) *Daphnia magna* 24 mg l^{-1} (5).

Bioaccumulation
Calculated bioconcentration factor 4.6, indicates that environmental accumulation is unlikely (6).

Environmental fate

Degradation studies
3-14% reduction in ThOD with sewage seed in 5 days (7,8).

Abiotic removal

Hydrolysis to 1-chloropropan-2,3-diol in aquatic environment, $t_{1/2}$ ≈8 days. Evaporation from model river water of 1 m depth, $t_{1/2}$ 29 hr (9).

In sea water, additional reaction with chloride ions reduces overall $t_{1/2}$ to ≈5.3 days (6,10).

Reaction with photochemically produced hydroxyl radicals, $t_{1/2}$ 4 days. When irradiated in the presence of 5 ppm nitric oxide to simulate photochemical fog conditions, $t_{1/2}$ 16 hr (11,12).

Adsorption and retention

Calculated K_{oc} 123, indicates that epichlorohydrin will not absorb strongly to soil and sediments (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, guinea pig 240-280 mg kg^{-1} (13,14).

LC_{50} (9 min) inhalation mouse 72 g m^{-3} (13).

LD_{50} dermal rabbit 760 mg kg^{-1} (13).

LD_{50} intraperitoneal rabbit, rat, mouse, guinea pig 120-170 mg kg^{-1} (13).

Carcinogenicity and chronic effects

Inadequate evidence of carcinogenicity to humans, sufficient evidence of carcinogenicity to animals, IARC classification group 2A (15).

Dermal mouse (19 month) 2 mg 3 × wk^{-1}. No skin tumours were observed. The median survival time was 506 days (16).

Dermal mouse, inhalation promotion experiment (13 month) 2 mg epichlorohydrin, followed 2 wk later by 2.5 μg phorbol myristate 3 × wk^{-1} for the duration of the experiment, caused statistically significant increase in skin papillomas and skin carcinomas (16).

Subcutaneous mouse (19 month) 1 mg wk^{-1} caused a statistically significant increase in local sarcomas and local adenocarcinomas. The median survival time was 486 days (16).

Intraperitoneal mouse (15 month) 1 mg wk^{-1} 11/30 mice developed papillary tumours of the lung compared with 10/30 lung tumours in controls (16).

Teratogenicity and reproductive effects

Oral ♂ rat (21 day) 12.5, 25 or 50 mg kg^{-1} day^{-1} and oral ♀ rat (14 day) 25, 50 or 100 mg kg^{-1} day^{-1}. Fertility was totally impaired in the high-dose ♂ rats; ♀ rats showed no reproductive change relative to controls (17).

Irritancy

Dermal rabbit (24 hr) 10 mg caused irritation (18).

Sensitisation

Sensitisation and dermatitis have been reported (19).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive (20).

Drosophila melanogaster sex-linked recessive lethal assay negative (21).

In vitro human fibroblasts, unscheduled DNA synthesis with and without metabolic activation positive (22).

In vitro Chinese hamster ovary cells, chromosomal aberration positive (23).

In vitro Chinese hamster V79 cells, sister chromatid exchanges, without metabolic activation positive (24).

In vitro human diploid fibroblasts (VH-10), DNA strand breaks positive (25).

In vivo rat gastric mucosa, unscheduled DNA synthesis positive (26).

Other effects

Other adverse effects (human)

Inhalation exposure of humans to 0.3 mg m^{-3}, which is the threshold odour concentration, produced changes in the electroencephalogram pattern, whereas 0.2 mg m^{-3} was inactive (27).

In a cohort study of 606 exposed workers in European factories no excess of cancers were observed. The study was regarded as inconclusive because of the small cohort and short follow-up (15,28).
Two cohort studies of exposed workers in USA showed a slight non-statistically significant excess of lung cancer (29).
In one severe case of inhalation poisoning, initial irritation of the eyes and throat was followed by chronic asthmatic bronchitis. Successive biopsies established a high degree of fatty infiltration of the liver (30).

Any other adverse effects
Oral rat, single dose of 125 mg kg^{-1} caused renal insufficiency within 24-48 hr in 80% of treated animals (27).

Legislation

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (31).

Other comments

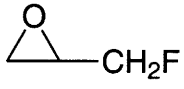
Physical properties, analysis, carcinogenicity, mammalian toxicity and mutagenicity reviewed (19,32-34).
Environmental fate reviewed (35).
Reviews on toxicity are listed (36).
Autoignition temperature 411°C.

References

1. Krijgsheld, K. R. et al *Chemosphere* 1986, **15**, 881-893.
2. *Shell Industrie Chemicalien Gids* 1975, 'S-Gravenhage, Netherlands.
3. Dawson, G. W. et al *J. Hazard. Mater.* 1975/77,**1**, 303-318.
4. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
5. Gersich, F. M. et al *Arch. Environ. Contam. Toxicol.* 1986, **15**(6), 741-749.
6. Santodonato, J. et al *Investigation of Selected Potential Environmental Contaminants: Epichlorohydrin and Epibromohydrin* 1980, US EPA 560/11-80-006.
7. Bridie, A. L. et al *Water Res.* 1979, **13**, 627-630.
8. Anderson, G. E. *Human Exposure to Atmospheric Concentrations of Selected Chemicals* 1983, **1**, USEPA, Office of Air Quality Planning and Standards, Research Triangle Park, NC, USA.
9. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw Hill, New York, NY, USA.
10. Mabey, W. M. et al *J. Phys. Chem. Ref. Data* 1978, **7**, 383-415.
11. Dilling, W. L. et al *Environ. Sci. Technol.* 1976, **10**, 351-356.
12. Cupitt, L. T. *Fate of Toxic and Hazardous Materials in the Air Environment* 1983, USEPA, 600/3-80/084.
13. Lawrence, W. H. et al *J. Pharm. Sci.* 1972, **61**, 1712-1717.
14. *Gig. Sanit.* 1968, **33**(1), 46.
15. *IARC Monograph* 1987, **Suppl. 7**, 202-203.
16. van Duuren, B. L. et al *J. Natl. Cancer Inst.* 1974, **53**, 695-700.
17. Toth, G. P. et al *Fundam. Appl. Toxicol.* 1989, **13**(1), 16-25.
18. *J. Ind. Hyg. Toxicol.* 1948, **30**, 63.
19. *Chemical Safety Data Sheets* 1989, **1**, 126-129, The Royal Society of Chemistry, London, UK.
20. Canter, D. A. et al. *Mutat. Res.* 1986, **172**(2), 105-138.
21. Velasquez, A. et al *Rev. Bras. Genet.* 1989, **12**(3), 515-524.
22. Robinson, D. E. et al *Prog. Mutat. Res.* 1981, **1**, 517-527.
23. Asita, A. *Mutagenesis* 1989, **4**(6), 432-436.
24. von der Hude, W. et al *Environ. Mutagen.* 1987, **9**(4), 401-410.
25. Kolman, A. et al *Environ. Mol. Mutagen.* 1997, **30**(1), 40-46.
26. Burlinson, B. *Carcinogenesis (London)* 1989, **10**(8), 1425-1428.
27. Pallade, S. et al *Arch. Mal. Prof. Med. Trav. Secur. Soc.* 1968, **29**, 679-688.
28. Tassingnon, J. P. et al *Int. Arch. Occup. Environ. Health* 1983, **51**, 325-336.
29. Enterline, P. E. *Ann. N.Y. Acad. Sci.* 1982, **381**, 344-349.
30. Schultz, C. *Dtsch. Med. Wochenschr.* 1964, **89**, 1342-1344.

31. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
32. *Appl. Occup. Environ. Hyg.* 1990, 5(9), 629-633.
33. *IPCS Environmental Health Criteria No. 33* 1984, World Health Organisation, Geneva, Switzerland.
34. *IARC Monograph* 1976, **11**, 131-139.
35. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1989, **1**, 319-324.
36. *ECETOC Technical Report No. 71* 1996, European Chemical Industry Ecology and Toxicology Centre, B-1160 Brussels, Belgium

E34 epifluorohydrin



C_3H_5FO **Mol. Wt.** 76.07 **CAS Registry No.** 503-09-3

Synonyms 1,2-epoxy-3-fluoropropane; (fluoromethyl)oxirane

EINECS No. 207-960-1 **RTECS No.** TZ 3325000

Uses Organic synthesis.

Physical properties

B. Pt. 85-86°C **Flash point** 4°C **Specific gravity** 1.067 at 20°C with respect to water at 4°C
Solubility Water: > 1 g l^{-1} at 16°C. Organic solvents: acetone, dimethyl sulfoxide

Occupational exposure

UN No. 1992

Mammalian & avian toxicity

Acute data
LC_{Lo} inhalation rat 111 mg m^{-3} (exposure not specified) (1).
LD_{50} intravenous mouse 180 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive; TA98 with and without metabolic activation negative (3).
Escherichia coli WP2 *uvrA* without metabolic activation positive (4).
In vitro Chinese hamster V79 cells induced sister chromatid exchanges (5).

Other effects

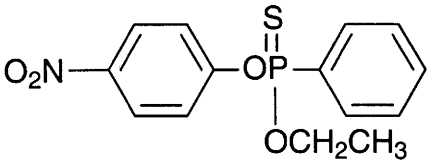
Any other adverse effects
Extremely destructive to tissue of the upper respiratory tract, eyes and skin (6).

References

1. *Progess Report* 1943, 12, Natl. Defence Res. Com., Office of Scientific Research and Development.
2. *Report* NX 00407, US Army Armament Research and Development Command, Chemical Systems Laboratory, Aberdeen Proving Ground, MD 21010, USA.

3. Zeiger, E. et al *Environ. Mol. Mutagen* 1992, **19**(Suppl. 21), 2-141.
4. Hemminki, K. et al *Arch. Toxicol.* 1980, **46**(3/4), 277-285.
5. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
6. Lenga, R. E. (Ed.) *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1518, Milwaukee, WI, USA

E35 EPN



$C_{14}H_{14}O_4NPS$ **Mol. Wt.** 323.31 **CAS Registry No.** 2104-64-5

Synonyms *O*-ethyl *O*-(4-nitrophenyl) phosphonothioate; *O*-ethyl *O*-(*p*-nitrophenyl) phosphonothioate; ethyl *p*-nitrophenyl thionobenzenephosphonate

EINECS No. 218-276-8 **RTECS No.** TB 1925000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 34.5°C **B. Pt.** 215°C at 5 mmHg **Specific gravity** 1.268 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} >5.02 **Volatility** v.p. 9.5×10^{-7} mmHg at 25°C
Solubility Water: Practically insoluble. Organic solvents: acetone, benzene, dioxane, isopropanol, methanol, toluene, xylene

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.5 mg m^{-3}
US-TWA 0.1 mg m^{-3}
Supply classification very toxic, dangerous for the environment
Risk phrases Very toxic in contact with skin and if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R27/28, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S22, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (duration unspecified) rainbow trout, bluegill sunfish 0.21, 0.37 mg l^{-1} respectively (1).
LC_{50} (48 hr) killifish 0.58 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (96 hr) *Gammarus lacustris, Gammarus fasciatus* and *Palaemonetes kadiakensis* 0.56-15 µg l^{-1} (3,4).

Bioaccumulation
Bioconcentration factor for pinfish, sheepshead minnow and topmouth gudgeon 700-7700 (5).
Bioaccumulation factor for killifish (whole body) 1124 (2).

Environmental fate

Degradation studies

$t_{1/2}$ in soil 30-90 days, depending on soil type and moisture condition. Under submerged conditions, $t_{1/2}$ 3-15 days. Degradation products included EPN-oxon, des-ethyl EPN-oxon, *p*-nitrophenol, *O*-(ethylthio)methyl phenylphosphonothioate, *O*-Et-*O*-Me-phenylphosphonate and, after acid treatment, *O*-Et-*H*-phenylphosphonate and *H*-phenylphosphonate (6).

When phenyl-^{14}C-labelled compound was foliarly applied to cotton plants, $t_{1/2}$ 1 wk. Initial metabolism was principally through hydrolysis and oxidation to phenylphosphonic acid. Further metabolism resulted in bound residues, $t_{1/2}$ in soil 2-4 wk (7).

Abiotic removal

Reacted with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 5 hr (8).

Adsorption and retention

Calculated K_{oc} of 2340-2960 indicates moderate to high adsorption to soil and sediments (9).

Mammalian & avian toxicity

Acute data

LD_{50} redwing blackbird, starling, coturnix, quail 3, 8, 10, 50 mg kg^{-1} (10,11).

LD_{50} oral rat, mouse, 7, 12 mg kg^{-1}, respectively (12).

LD_{50} dermal rat, rabbit, cat 25, 30, 45 mg kg^{-1}, respectively (12-14).

Sub-acute and sub-chronic data

LC_{50} (5 day) oral bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck 170-1075 mg kg^{-1} diet (15).

Carcinogenicity and chronic effects

Oral rat (2 yr) no-adverse-effect level 75-150 mg kg^{-1} diet. Retarded growth was observed at 3 × these doses (1).

Oral dog (1 yr) no adverse effect level 2 mg kg^{-1} day^{-1} (16).

Metabolism and toxicokinetics

In mammals, metabolism involves desulfuration and removal of *p*-nitrophenol, and also reduction of the nitro group to an amino group (17,18).

Other effects

Any other adverse effects

Inhibits cholinesterase activity (13).

Sub-chronic exposure of rodents resulted in a marked suppression of the humoral immune function and caused moderate histological changes to the lymphoid organs without any significant clinical effects (19).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (20).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (21).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (22).

WHO Toxicity Class Ia (23).

EPA Toxicity Class I (13).

Other comments

Residues have been isolated from crops, water and sediments (5).

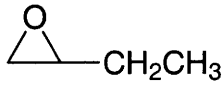
Environmental fate reviewed (5).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.

2. Tsuda, T. et al *Chemosphere* 1997, **35**(5), 939-949.
3. Sanders, H. O. *Toxicity of Pesticides to the Crustacean, Gammarus lacustris* 1969, Bureau of Sport, Fisheries and Wildlife Tech. Paper 25, Washington, DC, USA.
4. Sanders, H. O. *The Toxicities of Some Insecticides to Four Species of Malocostracan Crustacea* 1972, Fish Pesticide Research Laboratory, Columbia, MO, USA.
5. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, **3**, 362- 368, Lewis Publishers, Chelsea, MI, USA.
6. Wakabayashi, T. et al *Nippon Noyaku Gakkaishi* 1983, **8**, 155-165.
7. Chrzanowski, R. L. et al *J. Agric. Food Chem.* 1982, **30**, 155-161.
8. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
9. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw Hill, New York, USA.
10. Schafer, E. W. *Toxicol. Appl. Pharmacol.* 1972, **21**, 315-330.
11. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
12. *Agric. Biol. Chem.* 1962, **26**, 257.
13. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
14. *Toxicol. Lett.* 1980, **1000**(Sp.1), 141.
15. Hill, E. F. et al *Lethal Dietary Toxicities of Environmental Pollutants to Birds* 1975, US Fish and Wildlife Service, Report Wildlife No. 191, Washington, DC, USA.
16. Hodge, H. C. et al *J. Pharmacol. Exp. Ther.* 1954, **112**, 29.
17. Hitchcock, M. et al *Biochem. Pharmacol.* 1967, **16**, 1801-1811.
18. Chrzarowski, R. L. et al *J. Agric. Food Chem.* 1981, **29**, 580.
19. Moon, C. K. et al *Arch. Pharmacol. Res.* 1988, **9**(3), 175-187.
20. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
21. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
22. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
23. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

E36 1,2-epoxybutane



C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 106-88-7

Synonyms ethyloxirane; 1-butene oxide; 1,2-butane oxide; 1-butylene oxide; ethylethylene oxide; α-butylene oxide

EINECS No. 203-438-2 **RTECS No.** EK 3675000

Uses Used in fuel or oil products. Intermediate for various polymers, stabilisers for chlorinated solvents.

Physical properties

M. Pt. –150°C **B. Pt.** 63°C **Flash point** –12°C (closed cup) **Specific gravity** 0.837 at 20°C
Volatility v.p. 141 mmHg at 20°C ; v.den. 2.49
Solubility Water: 82.4 g l^{-1} at 25°C. Organic solvents: acetone, ethanol

Occupational exposure

UN No. 3022 (stabilised) **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid
Supply classification highly flammable, harmful

Risk phrases Highly flammable – Harmful by inhalation, in contact with skin and if swallowed – Irritating to eyes, respiratory system and skin – Possible risk of irreversible effects (*R11, R20/21/22, R36/37/38, R40*)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not empty into drains – Wear suitable protective clothing and gloves (S2, S9, S16, S29, S36/37)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 500 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 4000 ppm (2).

Sub-acute and sub-chronic data
Inhalation rats, guinea pigs, rabbits 7-hr exposures at 400 mg m^{-3} can be tolerated for long periods (3).
Inhalation rats, mice (14 day) 400-6400 ppm. Rats exposed to 3200 and 6400 ppm died and mice exposed to 1600, 3200 and 6400 ppm died. Compound-related lesions included pulmonary haemorrhage and rhinitis in rats at 1600 ppm and nephrosis in mice at 800 and 1600 ppm (4).
Inhalation rats, mice (13 wk) 50-800 ppm, no compound related mortality was observed in rats; all mice exposed to 800 ppm died. Inflammation of nasal turbinates was seen in rats exposed to 800 ppm, but not at lower concentrations. Renal tubular necrosis was seen in mice at 800 ppm, but not at lower concentrations (4).

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice via inhalation. Rats were exposed to 0, 200 or 400 ppm 6 hr day^{-1} 5 day wk^{-1} for 103 wk, and mice to concentrations of 0, 50 or 100 ppm for 102 wk. ♂ rats showed an increased incidence of papillary adenomas of the nasal cavity, and alveolar/bronchiolar carcinomas and alveolar/bronchiolar adenomas and carcinomas combined. Equivocal evidence in ♀ rats shown by the presence of papillary adenomas of the nasal cavity. No evidence of carcinogenicity in ♂ or ♀ mice exposed to 50 or 100 ppm. Exposure was associated with adenomatous hyperplasia and inflammatory lesions in nasal cavity in rats and inflammatory lesions (4-6).

Teratogenicity and reproductive effects
Inhalation rabbit (10-24 day gestation) 1000 ppm for 7 hr day^{-1} caused (unspecified) reproductive effects (7).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye (24 hr) caused moderate irritation (8).

Genotoxicity

Salmonella typhimurium TP135, TP137, TP138 without metabolic activation positive (9).
Salmonella typhimurium TA1535/psk1002 without metabolic activation positive (10).
Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive. TA98, TA1537 with and without metabolic activation negative (11).
Escherichia coli PQ 37, SOS-Chromotest, without metabolic activation negative (12).
In vitro mouse lymphoma L5178Y tk^+/tk^- positive (13).
In vitro Chinese hamster V79 cells without metabolic activation sister chromatid exchanges positive (14).
Drosophila melanogaster induced significant increases in sex-linked recessive lethal mutations (4).

Other effects

Other adverse effects (human)
Irritant and a sensitiser (15).

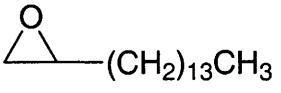
Other comments

Odour threshold, absolute limit of detection 0.07 mg m^{-3} (16).
Reviews on human health effects, experimental toxicology, workplace experience and epidemiology listed (17).

References

1. Duvel, W. A. et al *J. Water Pollut. Control Fed.* 1975, **47**(1).
2. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
3. Clayton, G. D. et al (Eds.) *Patty's Industrial Hygiene and Toxicology* 1967, **Vol. 2**, Interscience Publishers, New York, NY, USA.
4. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-329, NIEHS, Research Triangle Park, NC, USA.
5. Dunnick, J. K. *Natl. Toxicol. Program. Tech. Rep. Ser.* 1988, **329**, 1-176.
6. Dunnick, J. K. et al *Toxicology* 1988, **50**(1), 69-82.
7. *NTIS Report* BP81-168510, Natl. Tech. Inf. Ser., Springfield, VA, USA.
8. Marhold, J. *Prehled Prumyslove Toxikologie: Organicke Latky*, 1986, Prague, Czechoslovakia.
9. Popkin, D. J. et al *Mutat. Res.* 1989, **224**(4), 453-464.
10. Nakamura, S. et al *Mutat. Res.* 1987, **192**, 239-246.
11. Canter, D. A. et al *Mutat. Res.* 1986, **172**(2), 105-138.
12. von der Hude, W. et al *Mutat. Res.* 1990, **231**(2), 205-218.
13. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1987, **9**(2), 143-160.
14. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
15. Keith, L. H. et al (Ed.) *Compendium of Safety Data Sheets for Research and Industrial Chemicals* 1985, Part II, 796-797.
16. Hellmann, T. M. et al *Chem. Eng. Prog.* 1973, **69**, 9.
17. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E37 1,2-epoxyhexadecane



$C_{16}H_{32}O$ **Mol. Wt.** 240.43 **CAS Registry No.** 7320-37-8

Synonyms tetradecyloxirane; hexadecene epoxide

EINECS No. 230-786-2 **RTECS No.** ML 9450000

Uses Intermediate in organic synthesis.

Physical properties

M. Pt. 21-22°C **B. Pt.** 270-275°C **Flash point** 93°C (closed cup) **Specific gravity** 0.846 at 20°C
Solubility Water: <0.1 g l^{-1}. Organic solvents: dimethyl sulfoxide

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Dermal mouse (44 wk) 53 g kg^{-1} (total dose) applied intermittently caused some evidence of tumorigenic activity described as an equivocal tumorigenic agent (1).

Genotoxicity

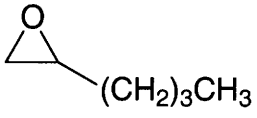
Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (2).
In vitro Chinese hamster V79 cells without metabolic activation sister chromatid exchange negative (3).
In vitro mouse lymphoma L5178Y tk^+/tk^- positive (4).

References

1. *J. Natl. Cancer Inst.* 1967, **39**, 1217.

2. Canter, D. A. et al *Mutat. Res.* 1986, **172**(2), 105-138.
3. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
4. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **12**(1), 85-154

E38 1,2-epoxyhexane



$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 1436-34-6

Synonyms butyl oxirane; 2-butyloxirane; 1-hexene epoxide; 1-hexene oxide; 1,2-hexene oxide

EINECS No. 215-864-6 **RTECS No.** MO 3630000

Uses Organic synthesis.

Physical properties

B. Pt. 118-120°C **Flash point** 15°C **Specific gravity** 0.831 at 20°C **Partition coefficient** log P_{ow} 1.82 (1)

Ecotoxicity

Fish toxicity

LC_{50} (14 day) guppy 19 mg l^{-1} static bioassay (1).

Mammalian & avian toxicity

Irritancy

Irritating to the skin. Vapour or mist is irritating to the mucous membranes and upper respiratory tract (species unspecified) (2).

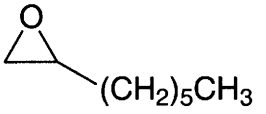
Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (3).
Escherichia coli PQ37, SOS-Chromotest with and without metabolic activation negative (3).
In vitro Chinese hamster V79 lung cells, sister chromatid exchanges positive (4).

References

1. Deneer, J. W. et al *Aquat. Toxicol.* 1988, **13**(3), 195-204.
2. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1523, Sigma-Aldrich, Milwaukee, WI, USA.
3. von der Hude, W. et al *Mutat. Res.* 1990, **231**(2), 205-218.
4. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70

E39 1,2-epoxyoctane



$C_8H_{16}O$ **Mol. Wt.** 128.21 **CAS Registry No.** 2984-50-1

Synonyms 1,2-epoxy-*n*-octane; octylene epoxide

EINECS No. 221-047-5 **RTECS No.** RG 9625000

Uses Organic synthesis.

Physical properties

B. Pt. 62.5-63°C at 17 mmHg **Flash point** 37°C **Specific gravity** 0.839 at 20°C
Partition coefficient log P_{ow} 2.88 (1)

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy 8 mg l^{-1} static bioassay (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Inhalation mouse (duration unspecified), total dose of 2 mg induced malignant lymphomas in 6/30 mice. No skin tumours or pulmonary adenomas were reported (2).

Irritancy
Irritating to the skin. Vapour or mist is irritating to the mucous membranes and upper respiratory tract (species unspecified) (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (4).
Escherichia coli PQ37 SOS-Chromotest with and without metabolic activation negative (4).
In vitro Chinese hamster V79 lung cells, without metabolic activation sister chromatid exchanges negative (5).
In vitro primary rat hepatocytes, without metabolic activation unscheduled DNA synthesis negative (6).

References

1. Deneer, J. W. et al *Aquat. Toxicol.* 1988, **13**(3), 195-204.
2. Kotin, P. et al *Radiat. Res.* 1963, (Suppl. 3), 193-211.
3. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1524, Sigma-Aldrich, Milwaukee, WI, USA.
4. von der Hude, W. et al *Mutat. Res.* 1990, **231**(2), 205-218.
5. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
6. von der Hude, W. et al *Mutat. Res.* 1990, **245**(3), 145-150

E40 EPTC

$$CH_3CH_2SC(O)N(CH_2CH_2CH_3)_2$$

$C_9H_{19}NOS$ **Mol. Wt.** 189.32 **CAS Registry No.** 759-94-4

Synonyms *S*-ethyl dipropylthiocarbamate; *S*-ethyl dipropylcarbamothioate; ethyl *N,N*-dipropylthiocarbamate; Agrisan; Alirox; Beskor; Corncide; Eptam; Genep; Torbin; Verdasan; Witox; Zean

EINECS No. 212-073-8 **RTECS No.** FA 4550000

Uses Herbicide. Germination inhibitor.

Physical properties

M. Pt. <–30°C **B. Pt.** 127°C at 20 mmHg **Specific gravity** 0.9546 at 30°C **Partition coefficient** log P_{ow} 3.2
Volatility v.p. 3×10^{-3} mmHg at 35°C
Solubility Water: 365 mg l^{-1} at 20°C. Organic solvents: miscible with benzene, ethanol, toluene, xylene

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 19, 27 mg l^{-1}, respectively (1,2).
LC_{50} (48 hr) killifish >10 mg l^{-1} (3).

Invertebrate toxicity
EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 49.8 mg l^{-1} Microtox test (4).
LC_{50} (96 hr) *Gammarus fasciatus* 23 mg l^{-1} (5).
LC_{50} (48 hr) *Penaeus aztecus* 0.63 mg l^{-1} (3).
LC_{50} (24 hr) *Callinectes sapidus* >20 mg l^{-1} (2).
EC_{50} (96 hr) *Crassostrea virginica* 5 mg l^{-1} (2).
LD_{50} bees 0.011 mg bee^{-1} (1).

Environmental fate

Degradation studies
Undergoes rapid microbial degradation in soil to a mercaptan residue, an amino residue and CO_2 (6).
Decomposes in 4-6 wk in warm, moist soil (1).
Soil $t_{1/2}$ ≈7 days at 21-32°C (7).
75-100% disappearance from soils within 28 days (8).
Decomposition by soil microbes of soil treated with 6 kg ha^{-1} occurred in 5-7 days in loamy and brown forest soil types. In brown forest soils with 16-yr previous EPTC exposure, decomposition time was 10 days (9).
Degradation occurs more rapidly in soils of low pH and high C/N ratio (10).
Degradation of ^{14}C-labelled EPTC and unlabelled EPTC by an isolated *Rhodococcus* sp. yielded *N,N*-dipropyl EPTC (a product of α-propyl hydroxylation) and EPTC-sulfoxide (sulfur oxidation) (11).

Abiotic removal
Soil moisture affects $t_{1/2}$ values. Treated soils at 10 μg g^{-1} were analysed at 0, 7, 28, 56, 112 day intervals, $t_{1/2}$ values of ≈25 days in sandy loam and ≈44 days in loamy sand were recorded at 25°C (12).

Adsorption and retention

Poorly absorbed but readily volatilised from six types of soil studied (13).

Fairly persistent in soil and may reach water. Likely to persist in water, but there is no information on leaching from soil or on persistence in water (14).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling >100 mg kg^{-1} (15).

LD_{50} oral ♂ rabbit 2550 mg kg^{-1}, ♀ rabbit 2525 mg kg^{-1} (7).

LC_{50} (1 hr) inhalation rat 31 mg l^{-1} (2).

LD_{50} dermal rabbit >5000-10,000 mg kg^{-1} (3,7).

Sub-acute and sub-chronic data

LC_{50} (7 day) oral bobwhite quail 20,000 mg kg^{-1} (2).

Oral rat (90 day) NOEL 16 mg kg^{-1} day^{-1} (1).

Oral dog (90 day) NOEL 20 mg kg^{-1} day^{-1} (1).

Oral rat (21 day) 326 mg kg^{-1} day^{-1} showed no symptoms other than excitability and weight loss (7).

Carcinogenicity and chronic effects

Oral mouse (2 yr) NOEL 20 mg kg^{-1} day^{-1} (7).

Metabolism and toxicokinetics

27-45% of an (unspecified) administered dose to rats was metabolised via the following intermediates: thiocarbamate, thiocarbamate sulfoxide, *S*-(*N*,*N*-dialkylcarbamoyl)glutathione, *S*-(*N*,*N*-dialkylcarbamoyl)cysteine, *S*-(*N*,*N*-dialkylcarbamoyl)mercapturic acid, and *S*-(*N*,*N*-dialkylcarbamoyl)mercaptoacetic acid (6).

Irritancy

Mild skin and eye irritant, rabbits (1,7).

Sensitisation

Non-sensitiser to guinea pig skin (1).

Genotoxicity

Escherichia coli and *Saccharomyces cerevisiae* gene conversion and mitotic recombination negative (16).

Other effects

Other adverse effects (human)

In a field study of exposure in mixing, loading and application of EPTC, the total absorbed dose was 5.6 mg day^{-1} (0.074 mg kg^{-1}) for a 75 kg worker applying EPTC to 120 acres soil day^{-1}. The dermal absorption rate by rats was detected to be 14.7% per 24 hr and on the basis of this absorption rate, a worker exposure of 0.074 mg kg^{-1} (body weight) day^{-1}, and a no-observable-effect level of 5.0 mg kg^{-1} day^{-1} from animal toxicity studies, margins of safety of 68-340 were detected for workers applying the herbicide (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (18).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (19).

Advisory value for EPTC is 50 μg l^{-1}. Included under Statutory Instrument No. 1147, 1989 (20).

WHO Toxicity Class II (21).

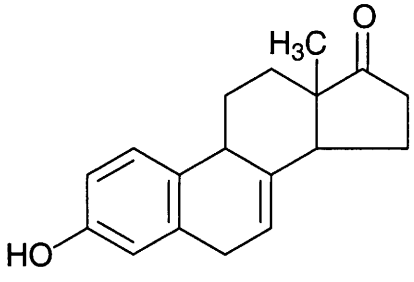
Other comments

Metabolic pathways reviewed (22).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *Technical Information* 1973, No. A-10177, Stauffer Chemical Company.
3. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold, New York, NY, USA.
4. Kaiser, K. L. E. *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
5. Sanders, H. O. *J. Water Pollut. Control. Fed.* 1970, **42**(8, Part 1), 1544-1550.
6. Hubbell, J. P. et al *J. Agric. Food Chem.* 1977, **25**, 404.
7. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
8. Edwards, C. A. *Residue Rev.* 1966, **13**, 83.
9. Nagy, I. et al *Proc. Brit. Crop. Prot. Conf. – Weeds* 1987, (2), 525-530.
10. Ghani, A. et al *N.Z. J. Agric. Res.* 1986, **29**(3), 469-474.
11. Dick, W. A. et al *ACS Symp. Ser.* 1990, **426**, 98-112.
12. Singh, G. et al *Environ. Pollut.* 1990, **66**(3), 253-262.
13. Ekler, Z. *Pestic. Sci.* 1988, **22**(2), 145-157.
14. *Guidance on Safeguarding the Quality of Public Water Supplies* Dept. of the Environment, Welsh Office, HMSO, London, UK.
15. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
16. Emnova, E. E. et al *Genetika (Moscow)* 1986, **22**(10), 2416-2422 (*Chem. Abstr.* **106**, 80111g).
17. Knaak, J. B. et al *ACS Symp. Ser.* 1989 **382**, 288-303.
18. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
19. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
20. *S. I. 1989 No. 1147 The Water Supply (Water Quality) Regulations* 1989, HMSO, London, UK.
21. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
22. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

E41 equilin



$C_{18}H_{20}O_2$ **Mol. Wt.** 268.36 **CAS Registry No.** 474-86-2

Synonyms 3-hydroxyestra-1,3,5(10),7-tetraen-17-one; 1,3,5,7-estratetraen-3-ol-17-one

EINECS No. 207-488-6 **RTECS No.** KG 6650000

Uses Commercial conjugated oestrogen preparations which are used in the treatment of patients with vulvar dystrophies and female hypogonadism and following ovariectomy, and also in the chemotherapy of mammary carcinoma, contain 20-35% sodium equilin sulfate (1).

Occurrence Steroidal hormone isolated from urine of pregnant mares.

Physical properties

M. Pt. 238-240°C (orthorhombic sphenoidal plates from ethyl acetate)
Solubility Water: sparingly soluble. Organic solvents: acetone, dioxane, ethanol, ethyl acetate

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Limited evidence for carcinogenicity of conjugated oestrogens to animals (2).
TD_{50} subcutaneous mouse 112 mg kg^{-1} administered intermittently over 56 wk resulted in neoplastic effects (3).
TD_{50} implant castrated ♂ hamster 640 mg kg^{-1} intermittently over 38 wk, equivocal tumorigenic response (4).

Other effects

Other adverse effects (human)
Human studies strongly suggest that the administration of conjugated oestrogens (an amorphous mixture, principally of sodium oestrone sulfate and sodium equilin sulfate) is causally related to an increased incidence of endometrial carcinoma (5).

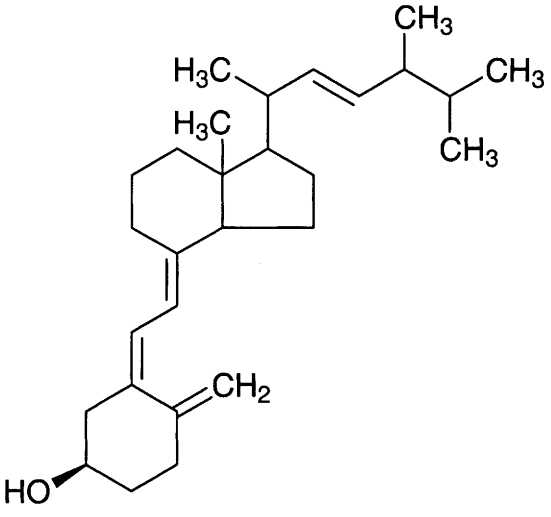
Other comments

Carcinogenic risk to humans of conjugated oestrogens reviewed (6).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
2. *IARC Monograph* 1987, **Suppl. 7**, 68.
3. *Z. Krebsforsch.* 1949, **56**, 482.
4. Li, J. J. et al *Cancer Res.* 1983, **43**, 5200.
5. *IARC Monograph* 1979, **21**, 156.
6. *IARC Monograph* 1979, **21**, 147-159

E42 ergocalciferol



$C_{28}H_{44}O$ **Mol. Wt.** 396.66 **CAS Registry No.** 50-14-6

Synonyms (3β,5*Z*,7*E*,22*E*)-9,10-secoergosta-5,7,10(19),22-tetraen-3-ol; Deltalin; Hyperkil; Sorexa; vitamin D_2

EINECS No. 200-014-9 **RTECS No.** KE 1050000

Uses Antirachitic vitamin. Nutrient or dietary supplement. Used for control of rodents by multiple feeding, often in admixture with warfarin to increase its efficacy.

Occurrence Occurs in some natural sources, including mammalian fats and fish oils.

Physical properties

M. Pt. 115-118°C

Solubility Water: 50 mg l^{-1}. Organic solvents: acetone, benzene, hexane

Ecotoxicity

Invertebrate toxicity

Not dangerous to bees (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 56 mg kg^{-1} (1).

LD_{50} oral mouse 23.7 mg kg^{-1} (1).

LD_{50} oral, intravenous, intramuscular intraperitoneal dog 4-10 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rat (7 days) 0, 0.39, 0.63, 1.00% or 0, 0.0195, 0.0315, 0.050% in diet. All rats in 0.39-1.00% groups expired on days 2 and 3. Some rats in the 0.0195-0.05% group died on days 3-6. In expired and surviving rats, kidney and heart were mineralised. Renal tubule injuries and pulmonary bleeding were also noted (3).

TD_{Lo} (72 wk) oral woman, 12.6 mg kg^{-1} caused weight loss/anorexia, nausea and vomiting (4).

Teratogenicity and reproductive effects

TD_{Lo} (9-19 day pregnant) oral rat, 55 mg kg^{-1} caused developmental abnormalities to musculoskeletal system (5).

TD_{Lo} (9 day pregnant) oral rat, 34 mg kg^{-1} caused both maternal and fertility effects (6).
TD_{Lo} (13-21 day pregnant) oral rat, 23 mg kg^{-1} affects embryo/foetus included extra embryonic structures (7).
TD_{Lo} (1-28 day pregnant) intramuscular rabbit, 17 mg kg^{-1} caused abortion and development abnormalities to cardiovascular system (8).

Metabolism and toxicokinetics

Metabolised by hydroxylation to the 15-hydroxy derivative in the liver, then further hydroxylation occurs to yield the 1α,25-dihydroxy derivative, as well as the 24(*R*)25-dihydroxy derivatives in the kidneys (8).

Other effects

Other adverse effects (human)

Hypercalcaemia developed in 21 patients due to vitamin D poisoning. All patients had taken mg doses. Most patients showed symptoms of hypercalcaemia, however others had anorexia, nausea, vomiting, weight loss, headache, or renal impairment. Other symptoms were mental and included apathy, fatigue and confusion. Two patients died while intoxicated (4).
Oral human (9 months), 6 mg day^{-1} vitamin D_2 caused severe hyperglycaemia (9).
Excessive doses during pregnancy are suspected to cause retardation and congenital heart defects in children (10).

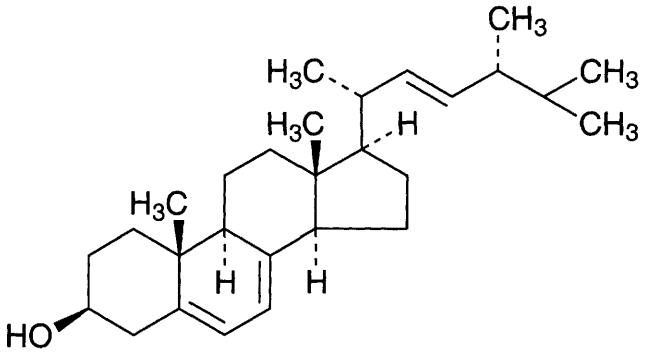
Other comments

The adverse effects of vitamin D metabolites and analogues on renal function is reported (11).
Active constituent in a number of commercial vitamin preparations, as well as in irradiated bread and milk.

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *Z. Gesamte Exp. Med.* 1950, **116**, 138.
3. Takahashi, O. *Toxicol. Lett.* 1993, **69**(3), 257-272.
4. Paterson, G. R. *Lancet* 1980, **1**, 1164.
5. Ornoy, A. et al *Arch. Pathol.* 1969, **87**, 563.
6. Nebel, L. et al *Israel J. Med. Sci.* 1966, **2**, 14.
7. Potrliege, P. R. *Arch. Pathol.* 1962, **73**, 371.
8. *Paediatr. Res.* 1979, **13**, 121.
9. Ulmann, A. et al *Nouv. Presse. Med.* 1981, **10**, 2965.
10. Dreisbach, R. H. *Handbook of Poisoning: Prevention, Diagnosis and Treatment* 11th ed., 1983, 494, Lange Medical Publications, CA, USA.
11. Karis, J. A. et al *Nephron.* 1981, **28**, 17

E43 ergosterol



$C_{28}H_{44}O$ **Mol. Wt.** 396.66 **CAS Registry No.** 57-87-4

Synonyms (3β,22*E*)-ergosta-5,7,22-trien-3-ol; ergosterin; provitamin D; provitamin D_2

EINECS No. 200-352-7

Uses Synthesis of vitamin D

Occurrence Isolated from *Candida*, and *Saccharomyces* spp. and other microorganisms.

Physical properties

M. Pt. 156-158°C **B. Pt.** 250°C at 0.1 mmHg

Solubility Water: miscible. Organic solvents: benzene, chloroform, diethyl ether, ethanol, light petroleum

Environmental fate

Abiotic removal

When irradiated with UV light converted into vitamin D_2 via lumisterol and tachysterol (1).

Genotoxicity

In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations negative (2).

Other effects

Other adverse effects (human)

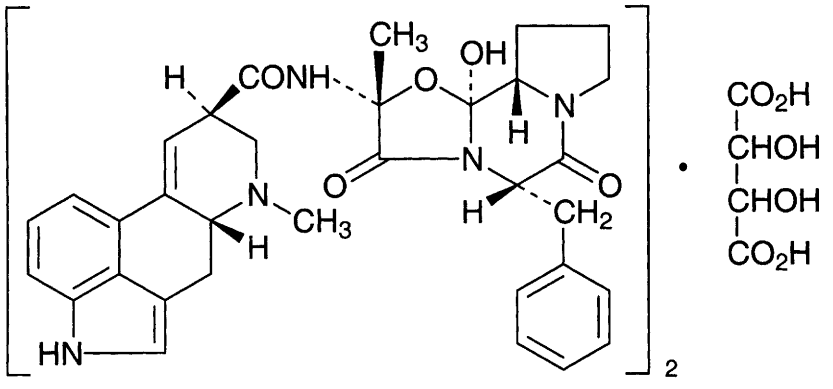
Some individuals exhibit hypertension. Changes in blood chemistry include elevated plasma calcium and non-protein nitrogen. Mobilisation of bone calcium contributes to hypercalcaemia and is responsible for osteoporosis (3).

Metastatic calcification has been reported in the cornea and conjunctiva in the form of band keratopathy, often accompanied by white flecks and crystal-like opacities in the bulbar conjunctiva (4).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. Rosenkranz, H. S. et al *Environ. Mol. Mutagen.* 1990, **16**(3), 149-177.
3. Gilman, A. G. et al (Eds) *Goodman and Gilmans' The Pharmacological Basis of Therapeutics* 6th ed., 1980, 1542, MacMillan, New York, NY, USA.
4. Grant, W. M. *Toxicology of the Eye* 2nd ed., 1974, 1083, Charles C. Thomas, Springfield, IL, USA

E44 ergotamine tartrate



$C_{70}H_{76}N_{10}O_{16}$ **Mol. Wt.** 1313.43 **CAS Registry No.** 379-79-3

Synonyms 12'-hydroxy-2'-methyl-5'α-(phenylmethyl)ergotamane-3',6',18-trione tartrate; [*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate 5'α-ergotamane-3',6',18-trione (2:1) salt; Ergomar; Ergotartrate; Ercal; Femergin; Medihaler Ergotamine

EINECS No. 206-835-9 **RTECS No.** KE 8225000

Uses Analgesic specifically for the treatment of migraine. Has been used as an oxytocin in veterinary medicine.

Physical properties

M. Pt. 190°C (decomp. 203°C)

Solubility Water: 2 g l^{-1}. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{Lo} oral mouse 300 mg kg^{-1} (1).

LD_{50} intravenous mouse, rat 62, 80 mg kg^{-1}, respectively (2).

LD_{50} subcutaneous cat 11 mg kg^{-1} (2).

TD_{Lo} intraperitoneal mouse 412 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Oral ♀ human (13 wk) 11 mg kg^{-1} intermittently caused blood pressure effects (4).

Oral human (26 wk) 3700 μg kg^{-1} intermittently caused gastro-intestinal and central nervous system effects (5).

Teratogenicity and reproductive effects

Oral administration of ergotamine tartrate to rabbit, rat, mouse, positive experimental teratogen (6).

Oral rat (6-15 day gestation) 100 mg kg^{-1} caused teratogenic effects (1).

Subcutaneous rat (5 days post-birth) 100 mg kg^{-1} caused reproductive effects (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (8).

In vitro human lymphocyte cells 100 μg l^{-1} induced chromosomal aberrations (9).

In vitro Chinese hamster ovary cells possessed mitodepressive and clastogenic activity (10).

In vitro Chinese hamster ovary cells sister chromatid exchanges positive (11).

Other effects

Other adverse effects (human)

Prolonged administration causes gangrene due to constrictions of the peripheral arterioles with consequent arrest of blood flow (12).

Other comments

Properties of ergotamine tartrate reviewed (6).
Uses and adverse effects reviewed (13).

References

1. *Teratology* 1973, **7**, 227.
2. Sax, N. I. et al *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
3. *Br. UK Patent Appl.* US Patent Office Science Library, Arlington, VA, USA.
4. *Postgraduate Med. J.* 1985, **61**, 461.
5. *Headache* 1978, **18**, 95.
6. *Dangerous Prop. Ind. Mater. Rep.* 1981, **1**(3), 65-66.
7. *Endocrinology* 1972, **90**, 285.
8. Dighe, R. et al *Teratog., Carcinog., Mutagen.* 1988, **8**(3), 169-174.
9. *Mutat. Res.* 1977, **48**, 205.
10. Dighe, R. P. et al *Biovigyanam* 1986, **12**(1), 86-88.
11. Zeiger, E. et al *Environ. Mutagen* 1987, **9**(Suppl. 9), 1-109.
12. *Pharmaceutical Codex* 11th ed., 1979, Pharmaceutical Press, London, UK.
13. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK

E45 erionite

$$(K_2, Na_2, Ca)MgAl_8Si_{28}O_{72}.\ 28H_2O$$

CAS Registry No. 66733-21-9

Synonyms hydrated potassium sodium calcium magnesium aluminium silicate
Uses Mineral specimen and chemical filter. Formerly used as a noble metal-impregnated catalyst in a hydrocarbon-cracking process. Also used to increase soil fertility and to control odours in livestock production. Not known to be currently mined or marketed for commercial purposes.
Occurrence Naturally occurring fibrous zeolite found notably in Durkee, Baker County, Oregon; Nevada, South Dakota and Arizona, USA, in the Faroe Islands and in the Cappadocia region of Turkey.

Physical properties

Specific gravity ≈ 2.0

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to animals and humans, IARC classification Group 1 (1).
Inhalation Fischer 344 rats (52 wk) 10 mg m^{-3} (respirable range), 7 hr day^{-1}, 5 day wk^{-1}. 27/28 exposed and 0/28 control animals developed pleural mesotheliomas (2).
Intraperitoneal ♂ mice (21 months), single dose of 10 or 30 mg fibrous erionite in 1 ml saline. 4/5 treated and 0/5 control mice developed malignant peritoneal tumours (3).

Intrapleural rats (weighing *c.* 150 g) 3 × 20 mg at one-month intervals. Of the animals that survived to 8 months or more, 39/40 treated ♂s, 43/48 treated ♀s, 0/25 ♂ controls and 0/25 ♀ controls developed pleural mesotheliomas (4).

Genotoxicity

C3H 10T1/2 cells (at concentrations of 100-200 μg ml^{-1}) and human A549 cells (at concentrations of 50-200 μg ml^{-1}), unscheduled DNA synthesis positive. Morphologically transformed foci were induced in C3H 10T1/2 cells at concentrations >10 μg ml^{-1} in the cell transformation assay (5).

Other effects

Other adverse effects (human)

A very high mortality from malignant mesothelioma was reported in three Turkish villages (Karain, Sarihidir, Tuzkoy) where there was erionite contamination in the soil, road dust and building stones and where exposure was from birth (6,7).

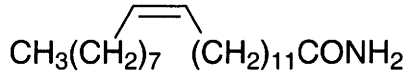
Other comments

Consists of white prismatic crystals in radiating groups. Not known to occur in other than fibrous form, in single needles or in clusters. The basic structure of erionite is the alumino-silicate tetrahedra with the oxygen shared between two tetrahedra. Six tetrahedra on each edge of the unit form part of a chain of indefinite length.
Carcinogenic risks to humans evaluated (1).
In vitro activities of pathogenic mineral dusts reviewed (8).

References

1. *IARC Monograph* 1987, **42**, 225-239.
2. Wagner, J. C. et al *Br. J. Cancer* 1985, **51**, 727-730.
3. Suzuki, Y. *Environ. Res.* 1982, **27**, 433-445.
4. Pylev, L. N. et al *Gig. Tr. Prof. Zabol.* 1986, **161**, 33-37.
5. Poole, A. et al *Br. J. Cancer* 1983, **47**, 697-705.
6. Baris, Y. I. et al *Thorax* 1978, **33** 181-192.
7. Baris, Y. I. et al *Lancet* 1981, **i**, 984-987.
8. Brown, R. C. et al *Toxicology* 1980, **17**(2), 143-147

E46 erucamide



$C_{22}H_{43}NO$ **Mol. Wt.** 337.59 **CAS Registry No.** 112-84-5

Synonyms (Z)-13-docosenamide; *cis*-13-docosenamide; erucyl amide; Armid E; Petrac Eramide; Polydis TR 131; Unislip 1753; Armoslip E

EINECS No. 204-009-2

Uses Antiblocking agent in polymers. Lubricant for polymer films. Solvent for waxes.

Physical properties

M. Pt. 78-81°C **Flash point** 74°C (closed cup) **Volatility** v.p. 1.28×10^{-6} mmHg at 25°C
Solubility Organic solvents: acetone, ethanol, isopropanol

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor 6310 indicated that environmental accumulation is likely (1).

Environmental fate

Degradation studies
Reported to undergo degradation by fungi (2).

Abiotic removal
Volatilisation from model river water, $t_{1/2}$ (calc.) 23 days (1).
Reaction with hydroxyl radicals in the atmosphere, $t_{1/2}$ (est.) 3.7 hr for reaction with ozone 2.1 hr (3).

Adsorption and retention
Estimated log K_{oc} 4.02 indicated strong adsorption to soil and sediments (1).

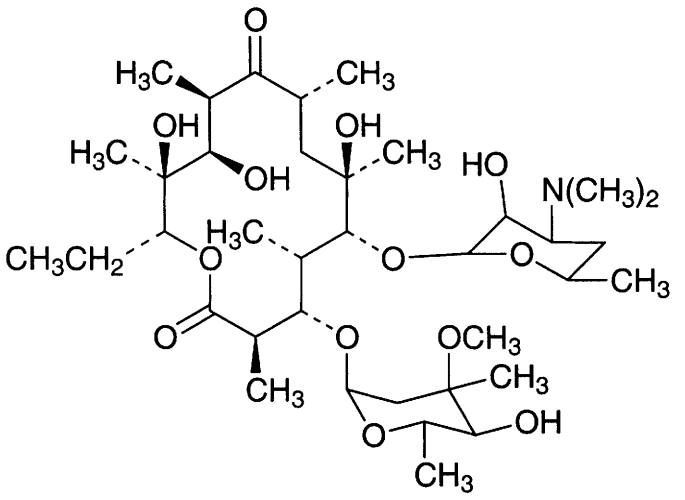
Legislation

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

1. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw Hill, New York, NY, USA.
2. Potts, J. E. *Kirk-Othmers Encyclopedia of Chemical Technology* 3rd ed., 1984, **Suppl.**, 631, John Wiley & Sons, New York, NY, USA.
3. Atkinson, R. *Environ. Sci. Chem.* 1988, **7**, 435-442.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E47 erythromycin



$C_{37}H_{67}NO_{13}$ **Mol. Wt.** 733.94 **CAS Registry No.** 114-07-8

Synonyms Abboticin; ERYC; Dotycin; Pantomicina; Robimycin; A/T/S; E-Mycin; Erthro; Ery Derm; Ery-Tab; Erythromid; Emgel

EINECS No. 204-040-1 **RTECS No.** KF 4375000

Uses Antibiotic.

Occurrence Produced by a strain of *Streptomyces erythreus*.

Physical properties

M. Pt. 135-140°C; resolidified m. pt. 190-193°C

Solubility Water: 2 g l^{-1}. Organic solvents: acetone, acetonitrile, chloroform, ethanol, ethyl acetate

Ecotoxicity

Invertebrate toxicity

Concentration of 80 mg l^{-1} erythromycin and formalin completely inhibited or reduced metamorphosis in *Penaeus stylirostris* exposed for 12 or 24 hr. Metamorphosis to protozoea is more susceptible to toxic effects than is naupliar survival. Toxic effects were not observed at 16 mg l^{-1} erythromycin and formalin (1).

70% of 40 anaerobic bacteria were resistant to erythromycin in 10% CO_2 and 30% in 5% CO_2 (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral hamster, rat 3000, 9000 mg kg^{-1}, respectively (3,4).

LD_{50} intraperitoneal mouse, guinea pig 410-460 mg kg^{-1} (4,5).

LD_{50} subcutaneous, intravenous rat, mouse 426-427 mg kg^{-1} (6,7).

LD_{50} subcutaneous mouse 1800 mg kg^{-1} (8).

Sub-acute and sub-chronic data

Administered by unknown route 200 mg day^{-1} for 7-10 days in a human, it had no toxic effects on liver function, on the formed elements of the blood or an urinary clinical chemistry (9).

Teratogenicity and reproductive effects

Subcutaneous ♀ rat (6-10 day post birth) 50 mg kg^{-1} caused teratogenic and reproductive effects (10).

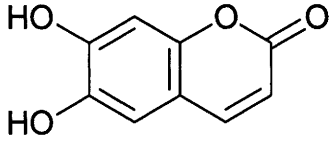
Other comments

Chemical, pharmacological, clinical applications and adverse interactions reviewed (11,12).
Interactions at the level of drug-metabolising enzymes discussed (13).
Action, uses and adverse effects reviewed (14).
Erythromycin inhibited 99% *Staphylococcus aureus* isolated from human skin (15).

References

1. Castille, F. L. et al *J. World Aquacult. Soc.* 1986, **17**(1-4), 13-18.
2. Jensen, J. E. et al *Acta Pathol., Microbiol. Immunol. Scand., Sect. B* 1987, **95B**(1), 65-73.
3. *Arch. Malad. Prof. Med. Trav. Secur. Soc.* 1978, **39**, 259.
4. *J. Am. Pharm. Assoc.* 1952, **41**, 555.
5. Sax, N. I. et al *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
6. *Compilation of LD_{50} Values of New Drugs* 1975, **1**, 115.
7. *Antibiot. Chemother. (Basel) 1954-70* 1952, **2**, 281.
8. Umezawa, H. et al (Eds.) *Index of Antibiotics from Actinomycetes* 1967, University of Tokyo Press, Tokyo, Japan.
9. Kolwas, Z. et al *Czas. Stomatol.* 1987, **40**(4), 231-235 (*Chem. Abstr.* **108**, 266q).
10. *Osaka-Shiritsu Daigaku Igaku Zasshi* 1965, **14**, 107.
11. Fernandes, P. B. *Antimicrob. Newsl.* 1987, **4**(4), 25-34.
12. Brittain, D. C. *Med. Clin. North Am.* 1987, **71**(6), 1147-1154.
13. Mansuy, D. *Int. Congr. Ser. – Excerpta Med.*, 1987, **734**, 19-28.
14. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
15. Hugbo, P. G. et al *Microbios Lett.* 1986, **33**(130), 71-73

E48 esculetin



$C_9H_6O_4$ **Mol. Wt.** 178.14 **CAS Registry No.** 305-01-1

Synonyms 6,7-dihydroxy-2*H*-1-benzopyran-2-one; 6,7-dihydroxycoumarin

EINECS No. 206-161-5 **RTECS No.** GN 6382500

Uses Analgesic and anti-inflammatory drug. In filters for absorption of UV light.
Occurrence Occurs in a variety of plants. Metabolite of coumarin.

Physical properties

M. Pt. 271-273°C
Solubility Water: dilute alkalis. Organic solvents: ethanol, glacial acetic acid

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 1500 mg kg^{-1} (1).

Teratogenicity and reproductive effects
EC_{50} (1 min) rat sperm motility 18 mg l^{-1} (2).

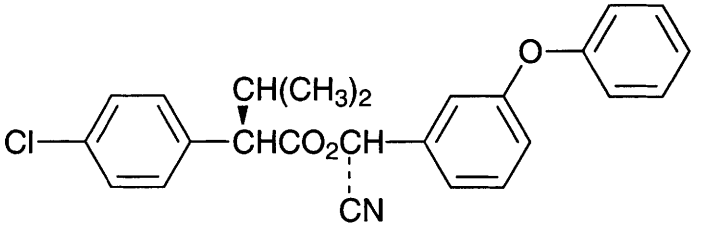
Irritancy
Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (3).

Sensitisation
Caused contact sensitisation in guinea pigs in assessment by Freund's complete adjuvant technique (4).

References

1. *Nippon Yakurigaku Zasshi* 1968, **64**, 714.
2. Pardeep Kumar, G. et al *Contraception* 1989, **39**(5), 531.
3. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1532, Sigma-Aldrich, Milwaukee, WI, USA.
4. Hausen, B. M. et al *Contact Dermatitis* 1986, **15**(5), 289-294

E49 esfenvalerate



$C_{25}H_{22}ClNO_3$ **Mol. Wt.** 419.91 **CAS Registry No.** 66230-04-4

Synonyms (*S*)-α-cyano-3-phenoxybenzyl-(*S*)-2-(4-chlorophenyl) isovalerate; [*S*-(*R*,*R*)]-cyano(3-phenoxyphenyl) methyl 4-chloro-α-(1-methylethyl)-, benzeneacetate; fenvalerate α; (*S*-*S*)-fenvalerate; Asana; Halmark; Sumi-alpha; Sumicidin Aα; Sumi-gold; Sumi-alfa; Sumigard

RTECS No. CY 1576367

Uses Acaricide and insecticide.

Physical properties

M. Pt. 59-60.2°C **B. Pt.** 151-167°C (technical) **Specific gravity** 1.163 at 23°C with respect to water at 23°C
Partition coefficient log P_{ow} 6.22 at 25°C (1) **Volatility** v.p. 2.63×10^{-7} mmHg at 20°C
Solubility Water: 0.002 mg l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, chloroform, dimethyl sulfoxide, ethyl cellosolve, *n*-hexane, kerosene, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 690 ng l^{-1} extremely toxic to aquatic animals (1,2).

Invertebrate toxicity
0.25 mg l^{-1} (6 doses at 2 wk intervals) reduced *Daphnia* populations from 250-400 animals l^{-1} to <100 animals l^{-1} (3).

Bioaccumulation
Fathead minnows accumulated 65.6 μg kg^{-1} (body weight) in 24 hr from a nominal aquatic concentration of 0.21 μg l^{-1}. Depuration was to 22.1 μg kg^{-1} after 8 days (4).
Macrophytes, *Chara* sp. and *Potamogeton natans* accumulated 90.7 ng g^{-1} in 24 hr from an aquatic concentration of 0.86 ng l^{-1} (4).

Environmental fate

Abiotic removal

Undergoes oxidative photodegradation in soil, hydration of the cyano group and ether cleavage at the alcohol moiety being the dominant reactions (5).

Adsorption and retention

Sediment absorption showed an uptake of 46.1 ng g^{-1} of organic sedimentary carbon from 0.5 μg l^{-1} in 24 hr. This increased to 140 ng kg^{-1} after 64 days, but the aquatic concentration was not constant (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail 381 mg kg^{-1} (2).
LD_{50} oral rat 75-88 mg kg^{-1} (2).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1,2).
LD_{50} dermal rat >6000 mg kg^{-1} (2).

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, inadequate evidence of carcinogenicity to animals, IARC classification group 3 (6).
Oral rat (6 wk) 500 mg kg^{-1} diet, 2 wk after single intraperitoneal administration of 200 mg kg^{-1} *N*-nitrosodiethylamine. Prominent neurological signs and moderate growth retardation were observed. No modifying potential by *N*-nitrosodiethylamine-induced liver carcinogenesis was observed, in contrast to positive controls (7).

Metabolism and toxicokinetics

Following oral administration of ^{14}C-labelled esfenvalerate to rats and mice, radioactivity was rapidly and almost completely excreted in the urine and faeces. Metabolism involved oxidation at the 2- and 3-positions of the acid moiety and the 2'- and 4'-phenoxy positions of the alcohol ester cleavage, and conjugation with glucuronic acid, sulfuric acid, glycine and taurine. Radiolabel did not cross the placenta from maternal blood to the foetuses of rats (8,9).

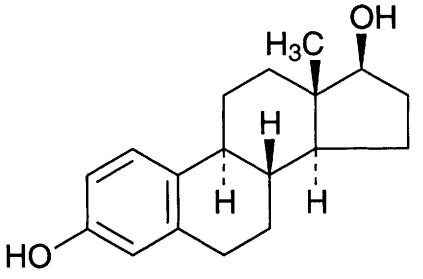
Legislation

US maximum residue in foods for esfenvalerate and fenvalerate 0.05 ppm (10).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).
Partition coefficient exceeds EC limit of 3.0.
WHO Toxicity Class II (13).
EPA Toxicity Class II (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Fairchild, J. F. et al *Environ. Toxicol. Chem.* 1992, **11**(1), 115-129.
4. Heinis, L. J. et al *Environ. Toxicol. Chem.* 1992, **11**(1), 11-25.
5. Katagi, T. *J. Agric. Food Chem.* 1991, **39**(7), 1351-1356.
6. *IARC Monograph* 1991, **53**, 309-328.
7. Hagiwara, A. et al *Cancer Lett. (Shannon, Irel.)* 1990, **54**(1-2), 67-73.
8. Isobe, N. et al *Nippon Noyaku Gakkaishi* 1990, **15**(2), 159-168 (Eng.) (*Chem. Abstr.* **115**, 84758g).
9. Shiba, K. et al *Nippon Noyaku Gakkaishi* 1990, **15**(2), 169-174 (Eng.) (*Chem. Abstr.* **115**, 84757f).
10. *Fed. Reg.* 1990, **55**(125), USEPA, 26440-26442.
11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
13. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

E50 estradiol



$C_{18}H_{24}O_2$ **Mol. Wt.** 272.39 **CAS Registry No.** 50-28-2

Synonyms dihydroxyestrin; β-estradiol; 3,17-epihydroxyestratriene; (17β)-estra-1,3,5(10)-triene-3,17-diol; oestradiol; 17β-oestradiol; Diogyn; Diogynets; Estrace; Menorest

EINECS No. 200-023-8 **RTECS No.** KG 2975000

Uses Treatment of symptoms of the climacteric, particularly for vasomotor and psychological disturbances.
Occurrence Naturally occurring oestrogenic hormone in mammals.

Physical properties

M. Pt. 178-179°C
Solubility Water: almost insoluble. Organic solvents: acetone, chloroform, 1,4-dioxane, diethyl ether, ethanol

Environmental fate

Abiotic removal
39% degradation occurred in drinking water containing up to 0.94 ng l^{-1} after 10 days (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (2).
Oral mouse (24 months), 0, 0.1, 1.0 or 5.0 mg kg^{-1} diet induced mammary tumours in 4/47, 0/35, 6/36 and 8/48 animals, respectively, after 52 wk. Other malignant tumours which occurred were: 1 adenoma of the cervix; 1 osteosarcoma of the cranium in the 0.1 mg kg^{-1} group; 2 adenocarcinomas of the uterus; 3 adenocarcinomas of the cervix; and 1 adenocarcinoma of the uterus. No such tumours occurred in controls (3).
Subcutaneous mouse (12 months), 80 μg $animal^{-1}$ 2 × wk^{-1} for 6 months did not cause an increase in the incidence of mammary tumours compared with controls. An increased incidence of lymphosarcomas (28% in intact, 47% in ovariectomised, 10% in controls) was reported. These occurred between 3-10 months while the first occurred in controls in 12 months (4).
Subcutaneous implantation of 20 mg to ♂ hamsters induced kidney tumours in 75% of animals (period of experiment not stated) (5).
Subcutaneous implant, castrated ♂ mouse (2 yr), 0, 1, 2.5, 5, 10 or 100 μg $animal^{-1}$. The incidences of mammary tumours were 11/33, 11/31, 23/27, 24/27, 27/27 and 23/24, with latent periods of 515, 675, 270, 145, 185 and 175 days, respectively (6).
Injection ♀ mouse (73 weeks), 0.1, 5 or 2.5 μg $animal^{-1}$ for first 5 days of life. ≈50% of the animals were ovariectomised at 16-17 weeks of age. All mice that received the two higher doses and 37/42 low-dose mice developed vaginal cornification. Vaginal epithelial downgrowths and hyperplastic vaginal lesions resembling epidermoid carcinoma developed in a dose-dependent manner after 64-73 wk, with lower incidence in ovariectomised mice. The mean ovarian weights of all the intact treated animals were more than twice those of

controls. Epithelial downgrowths occurred in 5/10 intact controls but no hyperplastic lesions were seen (7).
β-Estradiol, estriol and orestrone were administered subcutaneously to intact ♂ rats before treatment with 7,12-dimethylbenz[*a*]anthracene or procarbazine as 1-2% pellets weighing 5-7 mg each. No mammary cancers occurred up to 370 days in untreated controls or estrogen-treated rats. Higher doses of β-estradiol had an inhibitory effect on carcinogen-induced tumour development (8).

Teratogenicity and reproductive effects

Injection mouse (14 days), 1 μg day^{-1} for 7 days caused a reduction in testicular weight (9).
Subcutaneous mouse, 50 μg on days 15 or 17 of gestation caused irreversible cornification or stratification of the vaginal epithelium which were seen at birth. At 3 months of age corpora lutea were absent in 4/12 animals treated on day-17 and 5/6 animals treated on day-15 (10).

Metabolism and toxicokinetics

Metabolised *in vitro* with cell lysates containing cytochrome P_{450} to give 2-hydroxy and 4-hydroxy metabolites. Further metabolism to uncharacterised products was also reported (11).
Reported to be rapidly absorbed from the nasal cavity in rats. Bioavailability was 50%, 71% and 34% for doses of 5, 10 and 20 μg rat^{-1}, respectively. Following intraduodenal administration, 2-5% bioavailability was observed for the same doses. Partial oxidation to estrone was identified following nasal administration, whereas greater oxidation occurred following intraduodenal administration (12).
The metabolic clearance rate in ♀ rhesus monkeys infused continuously with β-estradiol was 52.8 l day^{-1} kg^{-1} on day-14 of the menstrual cycle, 31.1 l day^{-1} kg^{-1} on day-9 and 35.5 l day^{-1} kg^{-1} on day 23. There was no change in the ratio of free and albumin-bound β-estradiol on those three days of the cycle (13).
Exists in equilibrium with estrone in the blood pool of these oestrogens (14).
Following topical application of 10 μg (on 2 cm area skin), 18% permeated through mouse skin *in vitro*. Permeation was accompanied by limited cutaneous first-pass metabolism. Metabolites identified were estrone and estriol (15).
Metabolism in rats and humans involves 2-hydroxylation, 16α-hydroxylation and 16α-oxygenation. Glucuronides of the various metabolites are excreted in the bile. Differences in the metabolism of oestrogens by humans and rats lie mostly in the type of conjugation (16-19).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (20,21).
Escherichia coli SOS-chromotest positive (22).
In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (23).
In vitro Chinese hamster ovary cells, sister chromatid exchanges positive (24).
In vitro human embryonic fibroblasts and renal epithelial cells, chromosomal aberrations positive (25).
In vivo mouse sperm, induction of micronuclei positive (26).
In vivo mouse bone marrow, chromosome aberrations negative (27).

Other effects

Any other adverse effects

Intramuscular rat and quail, 23 mg kg^{-1} induced renal lesions in the quail but not in rats (28).
Ovariectomised rats were administered 0.13 ng day^{-1} for 8 days by infusion into the femur trabecular bone. Ovariectomy caused a 50% reduction in trabecular bone volume, a 3-fold increase in relative resorption surfaces, a 2-fold increase in osteoclast number, a 9-fold increase in osteoblast number and an 8-fold increase in relative osteoid surface. Infusion with β-estradiol restored the trabecular bone volume, decreased the osteoclast number and the relative resorption surface to control levels, and further increased osteoblast number and the relative osteoid surface. Thus β-estradiol acted locally to inhibit bone resorption and stimulate bone formation (29).
In vitro investigations on cultured rat hippocampal interneurons indicate that estradiol decreases GABAergic inhibition in the hippocampus causing increased excitatory drive on pyrimidal cells, thus possibly providing a mechanism for the formation of new dendritic spines (30).

Adult ♂ rats were injected daily with 50 µg estradiol, estradiol plus testosterone propionate (25 mg every 3 days), or estradiol plus human menopausal gonadotrophin (equivalent to 25 iu FSH plus 25 iu LH) for 15 days. The results showed that estradiol treatment of the seminiferous epithelium elicited an apoptosis pattern different from that reported to be caused by gonadotrophin or testosterone withdrawal, suggesting a possible role for estradiol in modulating germ-cell death in the adult rabbit testis (31).

Other comments

Use, occurrence, analysis, physical properties, carcinogenicity, teratogenicity, metabolism and mutagenicity of β-estradiol and its esters reviewed (32).

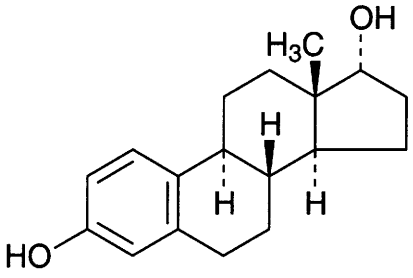
Has been reported to occur as contaminant in some drinking water samples (32,1).

Oestrogens are persistent in the environment. They have been reported to occur in sewage effluent used for irrigation in Tel Aviv, Israel at concentrations of 24-48 ng l^{-1} (33).

References

1. Rurainski, R. D. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1977, **118**(6).
2. *IARC Monograph* 1987, **Suppl. 7**, 280-281.
3. Higham, B. et al *J. Environ. Pathol. Toxicol.* 1977, **1**, 1-30.
4. Gardner, W. V. et al *Cancer Res.* 1944, **4**, 73-87.
5. Liehr, J. G. et al *Chem.-Biol. Interact.* 1986, **59**(2), 173-184.
6. Rudali, G. et al *Biomedicine* 1978, **29**, 45-46.
7. Kimura, T. et al *J. Natl. Cancer Inst.* 1967, **39**, 75-83.
8. Lemon, H. M. et al *Cancer Res.* 1975, **35**, 1341-1353.
9. Ono, Y. et al *Kyoto-furitsu Ika Daigaku Zasshi* 1987, **96**(9), 759-764 (Japan.) (*Chem. Abstr.* **107**, 229372y).
10. Kimura, T. *Endocrinol. Jpn.* 1975, **22**, 497-502.
11. Aoyama, T. et al *Endocrinology (Baltimore)* 1990, **126**(6), 3101-3106.
12. Bawashi-Nassar, R. N. et al *Drug Metab. Dispos.* 1989, **17**(3), 248-254.
13. Longcope, C. et al *Biol. Reprod.* 1988, **39**(3), 561-565.
14. Longcope, C. et al *J. Steroid Biochem.* 1990, **35**(5), 601-605.
15. Kao, J. et al *J. Pharmacol. Exp. Ther.* 1987, **241**(2), 482-487.
16. Bartke, A. et al *Steroids* 1971, **18**, 303-311.
17. Balt, H. M. *Pharmacol. Ther.* 1979, **4**, 155-181.
18. Williams, K. I. H. *Steroids* 1970, **15**, 105-111.
19. Breuer, H. et al *Adv. Biosci.* 1968, **3**, 71-79.
20. Lang, R. et al *Mutat. Res.* 1979, **67**, 361-365.
21. Ingerowski, G. H. et al *Mutat. Res.* 1981, **91**, 93-98.
22. Van Aswegan, C. H. et al *Clin. Physiol. Biochem.* 1989, **7**(1), 34-39.
23. Althaus, F. R. et al *Cancer Res.* 1982, **42**, 3010-3015.
24. Kochhar, T. S. *Experientia* 1988, **44**(1), 62-63.
25. Lycette, R. R. et al *N. Z. Med. J.* 1970, **72**, 114-117.
26. Pylkkanen, L. et al *Mutat. Res.* 1991, **261**(3), 181-191.
27. Malkova, J. et al *Neoplasma* 1977, **24**, 277-284.
28. Kupsh, C. C. et al *Avian Pathol.* 1991, **20**(1), 25-34.
29. Takano-Yamamato, T. et al *Proc. Natl. Acad. Sci. USA* 1990, **87**(6), 2172-2176.
30. Murphy, D. D. et al *J. Neurosci.* 1998, **18**(7), 2550-2559.
31. Blanco-Rodriguez, J. et al *J. Reprod. Fertil.* 1997, **110**(1), 61-70.
32. *IARC Monograph* 1979, **21**, 279-326.
33. Shore, L. S. et al *Bull. Environ. Contam. Toxicol.* 1993, **51**, 361-366

E51 α-estradiol



$C_{18}H_{24}O_2$ **Mol. Wt.** 272.39 **CAS Registry No.** 57-91-0

Synonyms 3,17-dihydroxyestratriene; epiestradiol; 17α-estradiol; (17α)-estra-1,3,5(10)-triene-3,17-diol; 17α-estradiol

RTECS No. KG 3750000

Occurrence Metabolite of estradiol.

Physical properties

M. Pt. 216-219°C

Solubility Water: alkaline solution. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1. Evaluation applies to the oestrogen group of chemicals as a whole and not necessarily to all individual chemicals within the group (1). Oral rat, 0.02 g kg^{-1} via diet antagonised the carcinogenic effects of feeding 0.6 g kg^{-1} *p*-dimethylamino-azobenzene on the livers of the animals. Moderate inhibition was observed, although the introduction of a hydroxyl group at 16α or of a methyl group at 17α potentiated the effect of 17α-estradiol (2).

Teratogenicity and reproductive effects

Injection mouse (14 days), 1 μg day^{-1} for 7 days caused an increase in testicular weight and in sperm counts (3).

Genotoxicity

In vitro human fibroblasts, unscheduled DNA synthesis negative (4).

Other effects

Any other adverse effects

Implants on either side of the brain in ovariectomised rats lowered food intake and body weight but did not affect water intake. The study concluded that the effects of oestrogens on ingestive and reproductive behaviours were organised separately within the brain (5).

Ovariectomised rats were administered 6.5 ng day^{-1} for 8 days by infusion into the femur trabecular bone. Ovariectomy caused a 50% reduction in trabecular bone volume, a 3-fold increase in relative resorption surfaces, a 2-fold increase in osteoclast number, a 9-fold increase in osteoblast number and an 8-fold increase in relative osteoid surface. Infusion with α-estradiol slightly increased the osteoblast number and osteoid surface. Its potency was 1/100 that of β-estradiol (6).

Other comments

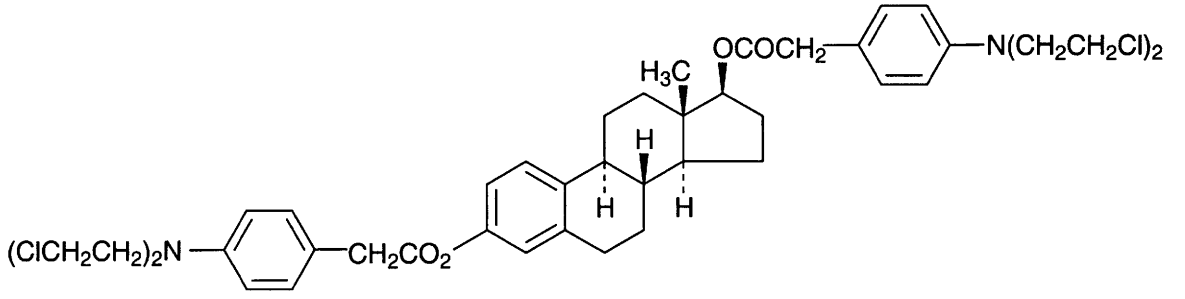
High-dose oestrogen therapy has been used effectively in the treatment of human breast cancer (7).

Sex hormones and Sjogren's syndrome reviewed (8).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 280-281.
2. Lacassagne, A. et al *C. R. Seances Sci., Ser. D Acad. Sci.* 1968, **267**(1), 137-140.
3. Ono, Y. et al *Kyoto-furitsu Ika Daigaku Zasshi* 1987, **96**(9), 759-764 (Japan.) (*Chem Abstr.* **107**, 229372y).
4. Allred, L. E. et al *J. Toxicol. Environ. Health* 1982, **10**(1), 143-156.
5. Butera, P. C. et al *Physiol. Behav.* 1990, **47**(6), 1291-1293.
6. Takano-Yamamoto, T. et al *Proc. Natl. Acad. Sci. USA* 1990, **87**(6), 2172-2176.
7. Reddel, R. R. et al *Cancer Res.* 1987, **47**(20), 5323-5329
8. Sullivan, D.A. *J. Rheumatol., Suppl.* 1997, **50**, 17-32

E52 estradiol mustard



$C_{42}H_{50}Cl_4N_2O_4$ **Mol. Wt.** 788.68 **CAS Registry No.** 22966-79-6

Synonyms (17β)-estra-1,3,5,(10)-triene-3,17-diol, bis{4-[bis(2-chloroethyl)amino]benzeneacetate}; estra-1,3,5(10)-triene-3,17β-diol, bis{4-[bis(2-chloroethylamino)phenyl]}acetate

RTECS No. KG 7300000

Uses Chemotherapeutic agent.

Physical properties

M. Pt. 40-65°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (1).

National Toxicology Program tested rats and mice via gavage. Evidence for carcinogenicity in ♂ and ♀ rats negative, in ♂ and ♀ mice positive (2).

Oral mouse (1 yr) 2340, 4680 mg kg^{-1} fed intermittently caused carcinogenic effects (3).

Reported as a carcinogen affecting ♂ and ♀ mice at multiple sites (4,5).

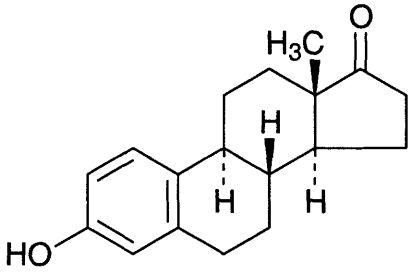
Intraperitoneal mouse (8 wk) 480 mg kg^{-1} intermittently caused a significant increase in the incidence of tumours (6).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 72.
2. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-059, NIEHS, Research Triangle Park, NC, USA.

3. *Natl. Cancer Inst. Carcinog. Tech. Rep. Ser. No. NCI-CG-TR-59* 1978, Research Triangle Park, NC, USA.
4. Ashby, J. et al *Mutat. Res.* 1991, **257**, 229-306.
5. Benigni, R. *Mutat. Res.* 1990, **244**(1), 79-91.
6. *Cancer Res.* 1973, **33**, 3069

E53 estrone



$C_{18}H_{22}O_2$ **Mol. Wt.** 270.37 **CAS Registry No.** 53-16-7

Synonyms E_1; 1,3,5-estratrien-3-ol-17-one; folliculin; follicular hormone; 3-hydroxyestra-1,3,5(10)-trien-17-one; ketohydroxyestrin; oestrone theelin; Tokokin; Menformon A

EINECS No. 200-164-5 **RTECS No.** KG 8575000

Uses In the treatment of symptoms occurring during or after the climacteric and after ovariectomy, for dysfunctional uterine bleeding, the treatment of prostatic carcinoma and for ♀ hypogonadism and primary ovarian failure.

Occurrence Metabolite of β-estradiol. Occurs in the urine of pregnant women and mammals, in the follicular liquor of many animals and in the human placenta. Occurs in the pollen grains of the date palm (1).

Physical properties

M. Pt. 258-260°C (99+% purity)

Solubility Water: 30 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, chloroform, 1,4-dioxane, ethanol, fixed oils, pyridine

Ecotoxicity

Toxicity to other species

Subcutaneous ♀toad, 0.1 mg wkly initiated hepatocellular carcinoma (4% of animals after 14 wk). When administered immediately after wkly administration of 3 mg *N*-nitrosodimethylamine the incidence of hepatocellular carcinomas was not affected, although the time lag before carcinoma appearance was reduced (2).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (3).

Oral castrated ♂ mouse (2 yr) 0, 0.06, 0.6 or 6.0 μg day^{-1} for life caused a dose-related increase in the incidence of mammary tumours (4).

Injection rat, 50-200 μg $animal^{-1}$ day^{-1} (total dose 30-40 mg) resulted in mammary cancers in 6/6 castrated ♂ rats and 4/5 ovariectomised ♀ rats. A lower incidence was found in intact animals. Induction time ranged from 31-83 wk (5).

Subcutaneous implant ♂ hamster, 20 mg pellets induced malignant kidney tumours in 7/8 intact hamsters and 10/10 castrates. No kidney tumours were seen in 61 intact or 60 castrated controls (6).
Subcutaneous implant rat, 10 mg pellets containing 90% estrone and 10% cholesterol. Pellets were implanted for 10-53 wks or more in groups of animals 3, 8, 12 or 38 wk of age. An increased incidence of adrenal carcinomas, mammary carcinomas and pituitary tumours was observed in all treated groups of both sexes. The incidence of mammary adenomas was increased in treated ♂ and ♀ rats up to 1 yr, but was lower than that in controls thereafter (7).
β-Estradiol, estriol or estrone were administered subcutaneously to intact ♀ rats 48 hr before treatment with 7,12-dimethylbenz[*a*]anthracene or procarbazine as 1-20% pellets weighing 5-7 mg each. No mammary tumours occurred up to 370 days in oestrogen-treated rats. Pellets containing 10% estrone had an inhibitory effect on carcinogen-induced tumour development (8).

Teratogenicity and reproductive effects
Injection rat, 1 μg animal^{-1} on day-3 of gestation had no embryonic or teratogenic effects (9).
Subcutaneous rat, single injection of 1-140 μg animal^{-1} at different times of gestation between days 1-10. Termination of pregnancy (100%) was achieved by administration of 20 μg on days 1 and 2, by 40 μg on day-3, by 80 μg on day-4 and by 50 μg on day-5. 140 μg given between days 6-10 decreased the number of implantations, increased the number of dead foetuses and abnormal growth, and spacing of foetuses (10).

Metabolism and toxicokinetics
Following infusion into ♀ rhesus monkeys 29.2% was converted into β-estradiol as measured in the blood, and 77.4% as measured in the urine. Following infusion of β-estradiol 21.5% was converted into estrone as measured in the blood, and 7.7% as measured in the urine. Thus, interconversion occurs in pools which are in equilibrium with the blood pool of these oestrogens (11).
Estrone was rapidly taken up by isolated perfused rat and guinea pig liver to yield ≥10 metabolites excreted in the bile. Sulfated metabolites appeared and reached a peak concentration after ~10 min. These were partly converted into sulfoglucuronides and partly hydrolysed to be reconjugated as glucuronides (12).
Following topical application of 10 μg (on 2 cm^2 area skin) 10.6% permeated through mouse skin *in vitro*. The extent of cutaneous first pass metabolism was extensive. Metabolites identified were estradiol and estriol (13).

Genotoxicity

In vitro Chinese hamster ovary cells, sister chromatid exchanges positive (14).
In vitro Chinese hamster V79 lung cells, with metabolic activation gene mutation negative (15).
In vitro Chinese hamster Don (22;XY) cells, induction of aneuploidy positive, a dose-response relationship could not be established (16).

Other comments

Use, occurrence, physical properties, analysis, carcinogenicity, teratogenicity and metabolism of estrone and estrone benzoate reviewed (1).
Metabolism in human breast tissue reviewed (17).

References

1. *IARC Monograph* 1979, **21**, 343-362.
2. Sakr, S. A. et al *Arch. Geschwulstforsch.* 1989, **59**(1), 7-10.
3. *IARC Monograph* 1987, **Suppl. 7**, 280-281.
4. Rudali, G. et al *Biomedicine* 1978, **29**, 45-46.
5. Geschickter, C. F. et al *Arch. Pathol.* 1942, **33**, 334-356.
6. Kirkman, H. *Natl. Cancer Inst. Monogr.* 1959, **1**, 59-75.
7. Noble, R. L. *Cancer Res.* 1977, **37**, 1929-1933.
8. Lemon, H. M. *Cancer Res.* 1975, **35**, 1341-1353.
9. Dickmann, Z. *J. Reprod. Fertil.* 1973, **32**, 65-69.
10. Haddad, V. et al *Int. J. Fertil.* 1969, **14**, 56-63.
11. Longcope, C. et al *J. Steroid Biochem.* 1990, **35**(5), 601-605.

12. Roy, A. B. et al *Xenobiotica* 1987, **17**(11), 1299-1313.
13. Kao, J. et al *J. Pharmacol. Exp. Ther.* 1987, **241**(2), 482-487.
14. Kochhar, T. S. *Experientia* 1988, **44**(1), 62-63.
15. Drevon, C. et al *Mutat. Res.* 1981, **89**, 83-90.
16. Wheeler, W. J. et al *Mutat. Res.* 1986, **171**(1), 31-41.
17. James, V. H. T. et al *Ann. N. Y. Acad. Sci.* 1990, **595**, 227-235

E54 etacelasil

$CH_3OCH_2CH_2OSi(CH_2CH_2Cl)(OCH_2CH_2OCH_3)OCH_2CH_2OCH_3$

$C_{11}H_{25}ClO_6Si$ **Mol. Wt.** 316.85 **CAS Registry No.** 37894-46-5

Synonyms 2-chloroethyltris(2-methoxyethoxy)silane; 6-(2-chloroethyl)-6-(2-methoxyethoxy)-2,5,7,10-tetraoxa-6-silaundecane; Alsol

EINECS No. 253-704-7 **RTECS No.** VV 2140000

Uses Growth regulator. Abscission agent which loosens fruit because of its ethylene-releasing activity.

Physical properties

B. Pt. 85°C at 0.001 mmHg **Specific gravity** 1.10 at 20°C **Volatility** v.p. 2.03×10^{-6} mmHg at 20°C
Solubility Water: 25 g l^{-1} at 20°C. Organic solvents: miscible with benzene, dichloromethane, hexane, methanol, *n*-octanol

Occupational exposure

Supply classification toxic
Risk phrases May cause harm to the unborn child – Harmful if swallowed – Harmful: danger of serious damage to health by prolonged exposure if swallowed (R61, R22, R48/22)
Safety phrases Avoid exposure – obtain special instructions before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, crucian carp, bluegill sunfish >100 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2066 mg kg^{-1} (1,2).
LC_{50} (4 hr) inhalation rat >3.7 mg l^{-1} air (1,2).
LD_{50} dermal rat >3100 mg kg^{-1} (1,2).

Sub-acute and sub-chronic data
Oral rat (90 day) 20 mg kg^{-1} day^{-1}, dog 10 mg kg^{-1} day^{-1}. No adverse effects were recorded (1,2).

Irritancy
Slight irritant to rabbit skin. Non irritant to rabbit eye (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class III (5).

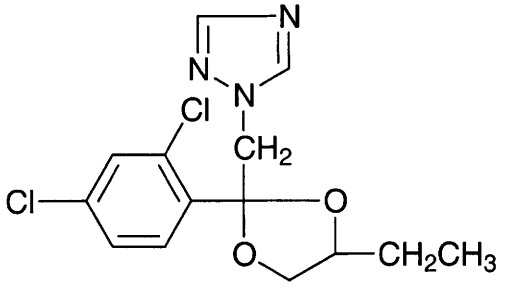
Other comments

Non-toxic to birds (1,2).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

E55 etaconazole



$C_{14}H_{15}Cl_2N_3O_2$ **Mol. Wt.** 328.20 **CAS Registry No.** 60207-93-4

Synonyms 1-[2-(2,4-dichlorophenyl)-4-ethyl-1,3-dioxolan-2-yl]methyl-1*H*-1,2,4-triazole

EINECS No. 262-107-0 **RTECS No.** XZ 4610000

Uses Superseded fungicide.

Physical properties

M. Pt. 75-93°C **Specific gravity** 1.40 at 20°C **Volatility** v.p. 2.3×10^{-7} mmHg at 20°C

Solubility Water: 80 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, *n*-hexane, methanol, propan-2-ol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, carp 2.5-4.0 mg l^{-1} (1)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1343 mg kg^{-1} (1).

LD_{50} dermal rat >3100 mg kg^{-1} (1).

Irritancy

Slight irritant to rabbit skin and eyes (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
WHO Toxicity Class III (4).

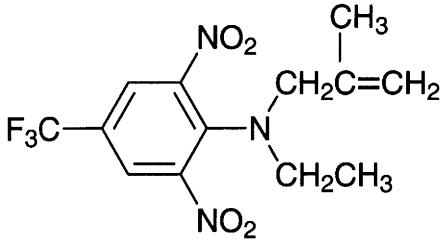
Other comments

The use of etaconazole as a fungicide has now been superseded (5).

References

1. *The Pesticide Manual* 7th ed., 1983, British Crop Protection Council, Farnham, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
5. *The Pesticide Manual* 9th ed., 1991, British Crop Protection Council, Farnham, UK

E56 ethalfluralin



$C_{13}H_{14}F_3N_3O_4$ **Mol. Wt.** 333.27 **CAS Registry No.** 55283-68-6

Synonyms *N*-ethyl-*N*-(2-methyl-2-propenyl)-2,6-dinitro-4-(trifluoromethyl)benzenamine; *N*-ethyl-*N*-α,α,α-trifluoro-*N*-(2-methylallyl)-2,6-dinitro-*p*-toluidine; *N*-ethyl-*N*-methylallyl-4-trifluoromethyl-2,6-dinitroaniline; Sonalan; Sonalen; Buvilan; Edge

EINECS No. 259-564-3 **RTECS No.** XU 6200000

Uses Pre-emergent herbicide.

Physical properties

M. Pt. 54-57°C **B. Pt.** 256°C (decomp.) **Partition coefficient** log P_{ow} 5.114 at 25°C and pH 7
Volatility v.p. 8.8×10^{-5} mmHg at 25°C
Solubility Water: 0.3 mg l^{-1} at 25°C and pH 7. Organic solvents: acetone, acetonitrile, benzene, chloroform, hexane, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout 0.102, 0.136 μg l^{-1}, respectively (1).
LC_{50} (96 hr) goldfish 0.1 mg kg^{-1} (2).

Invertebrate toxicity
Not toxic to bees. Contact LD_{50} 5.5 mg bee^{-1} (2,1).

Environmental fate

Degradation studies
Microbial degradation occurs (3).

Abiotic removal
Photolytic degradation occurs (3).

Adsorption and retention
Strongly adsorbed on soil with negligible leaching, $t_{1/2}$ 25-46 days (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail, mallard duck >200 mg kg^{-1} (2,1).
LD_{50} oral rat >5 mg kg^{-1} (1).
LD_{50} oral dog, cat >200 mg kg^{-1} (2,1).
LD_{50} dermal rabbit >2000 mg kg^{-1} (2,1).

Carcinogenicity and chronic effects
Oral rat, mouse (2 yr) 100 mg kg^{-1} in diet caused no adverse effects (2,1).

Metabolism and toxicokinetics
Oral rat, 86% is excreted within 48 hr (64% in faeces, 22% in urine) and 95% within 7 days. Glucuronide conjugates have been found as metabolites in bile (2).

Irritancy
Mild irritant to rabbit skin and eyes (2,1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
Partition coefficient exceeds EC limit of 3.0.
WHO Toxicity Class Table 5 (6).

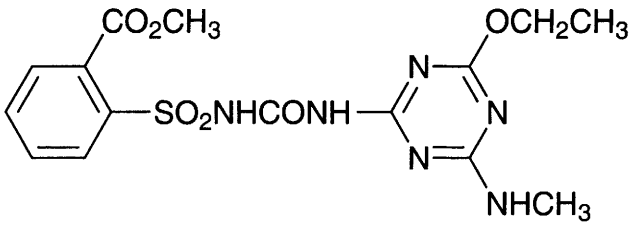
Other comments

Hazardous properties reviewed (7).
Metabolic pathways reviewed (8).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Hayden, B. J. et al *Bull. Environ. Contam. Toxicol.* 1983, **25**, 508.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
7. *Dangerous Prop. Ind. Mater. Rep.* 1988, **8**(3), 61-62.
8. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

E57 ethametsulfuron-methyl



$C_{15}H_{18}N_6O_6S$ **Mol. Wt.** 410.41 **CAS Registry No.** 97780-06-8

Synonyms methyl 2-[(4-ethoxy-6-methylamino-1,3,5-triazin-2-yl)carbamoylsulfamoyl]benzoate; methyl 2-[[[[[4-ethoxy-6-(methylamino)-1,3,5-triazin-2-yl]amino]carbonyl]amino]sulfonyl]benzoate; Muster

RTECS No. DG 9886000

Uses Herbicide.

Physical properties

M. Pt. 194°C **Specific gravity** 1.6 **Partition coefficient** log P_{ow} 0.89 (pH 7), (1)
Volatility v.p. 0.733 pPa at 25°C
Solubility Water: 50 mg l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, ethanol, methanol, ethyl acetate, methylene chloride

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout >600 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* 34 mg l^{-1} (1).
Contact LD_{50} (14 days) earthworm >1000 mg kg^{-1} soil (1).
Acute toxicity to honeybees >12.5 μg bee^{-1} (1).

Environmental fate

Anaerobic effects
Anaerobic DT_{50} 2-9 months, depending on sediment pH (1).

Degradation studies
Under laboratory conditions soil half-life was found to be 9 weeks and three major metabolites were identified (no further information given). Aquatic half-life was 2-9 months, depending on the sediment pH (1).

Abiotic removal
Photolysis is not a major degradation pathway but in soil photolysis studies sunlight accelerated degradation three-fold compared with dark controls (1).

Adsorption and retention
Mobility ranges from very mobile in sandy loam soil to very low mobility in loam soil (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail, mallard duck >2250 mg kg^{-1} (1).
LD_{50} oral rat, rabbit >11000, >5000 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation rat >5.7 mg l^{-1} (1).

Sub-acute and sub-chronic data
LD_{50} (5 days) oral bobwhite quail, mallard duck >5620 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects
No-observable-effect level (90 days) rats, mice 5000 ppm; (1 yr) rats, dogs 500, 3000 ppm, respectively; (18 months) mice 5000 ppm (1).

Teratogenicity and reproductive effects
Non-teratogenic in rats and rabbits (1).

Metabolism and toxicokinetics
Rapidly metabolised and excreted in urine and faeces following administration to rats. Half-lives for excretion range from 12 hr in ♂ rats to 21-26 hr in ♀ rats. Five days after dosing at the highest level <0.2% of the dose remained in tissues (1).

Irritancy
Non-irritating to skin, slightly irritating to eyes of rabbits (1).

Sensitisation
Non-sensitising to guinea-pig skin (1).

Genotoxicity

Non-mutagenic in rats (1).

Legislation

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (2). Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (3).

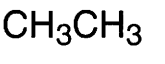
Other comments

Metabolic pathways reviewed (4).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations*, 1991, HMSO, London, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

E58 ethane



C_2H_6 **Mol. Wt.** 30.07 **CAS Registry No.** 74-84-0

Synonyms bimethyl; dimethyl; methylmethane; ethyl hydride

EINECS No. 200-814-8 **RTECS No.** KH 3800000

Uses Manufacture of chlorinated derivatives. Refrigerant in some two-stage refrigeration systems where low temperatures are produced, and as a fuel gas.

Occurrence Constituent of natural gas (about 99%).
Man-made sources include diesel and petrol engines.

Physical properties

M. Pt. –172°C **B. Pt.** –88°C **Flash point** –130°C **Specific gravity** 0.572 at 108°C with respect to water at 4°C
Volatility v.den. 1.04
Solubility Water: 47 mg l^{-1} at 20°C. Organic solvents: ethanol

Occupational exposure

UN No. 1035 (compressed)

UN No. 1961 (refrigerated liquid) **HAZCHEM Code** 2PE (compressed) **HAZCHEM Code** 2WE (refrigerated liquid) **Conveyance classification** flammable gas
Supply classification extremely flammable
Risk phrases Extremely flammable (R12)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Environmental fate

Nitrification inhibition
Inhibits nitrification in the soil by inhibiting the monooxygenase enzyme responsible for oxidation of ammonia by chemoautotrophic nitrifying microorganisms such as *Nitrosomonas europaea* (1).

Degradation studies
Ammonia monooxygenase of *Nitrosomonas europaea* catalyses the oxidation of ethane to alcohol in the presence of NH_4^+ (2).
BOD^{25}_{35} 2.45 mg l^{-1}, ThOD 3.73 mg l^{-1} O_2 (3).
A thermophilic methane-oxidising bacteria, H-2 (type 1), oxidised ethane to ethylene oxide (4).

Mammalian & avian toxicity

Metabolism and toxicokinetics
Labelled ^{14}C-ethane inhalation rat (8 hr) resulted in 50% radioactivity being recovered as carbon dioxide and 1% radioactivity was recovered in the urine (5).

Other effects

Other adverse effects (human)
Narcotic at high concentrations (6).

Other comments

Irrigation and rains increased the ethane content in soils, showing that it is formed in the soil and does not emanate from deep down. In non-flooded soils, ethane content was higher than in natural gas, suggesting ethane evolved from topsoil without involvement of high temperature or pressure. Thus it is a microbial process to balance atmospheric hydrocarbons (7).
Flammable asphyxiant (6).
Reviews on human health effects, experimental toxicity and physico-chemical effects listed (8).

References

1. McCarty, G. W. et al *Biol. Fertil. Soils* 1991, **11**(3), 231-233.
2. Hyman, M. R. et al *Appl. Environ. Microbiol.* 1988, **54**(12), 3187-3190.

3. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold, New York, NY, USA.
4. Imai, T. et al *Appl. Environ. Microbiol.* 1986, **52**(6), 1403-1406.
5. Daugherty, M. S. et al *Drug Metab. Dispos.* 1988, **16**(5), 666-671.
6. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
7. Orlov, D. S. et al *Pochvovedenie* 1987, (6), 89-94 (Russ.) (*Chem. Abstr.* **107**, 114794v).
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E59 ethanedithiol

$$HSCH_2CH_2SH$$

$C_2H_6S_2$ **Mol. Wt.** 94.20 **CAS Registry No.** 540-63-6

Synonyms 1,2-ethanedithiol; dithioethylene glycol; ethylene dimercaptan; dithioglycol; ethylene dithioglycol; ethylenedithiol; ethyl hydropersulfide

EINECS No. 208-752-3 **RTECS No.** KI 3325000

Uses Intermediate in organic synthesis.

Physical properties

B. Pt. 144-146°C **Flash point** 44°C (closed cup) **Specific gravity** 1.123 at 23.5°C with respect to water at 4°C
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 342 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 50 mg kg^{-1} (2).
LD_{50} intravenous mouse 56 mg kg^{-1} (3).

Other effects

Other adverse effects (human)
Inhalation of ethanedithiol may cause severe headache and nausea (4).

References

1. *Drug Chem. Toxicol. (1977)* 1980, **3**, 249.
2. *Eur. J. Med. Chem.* 1982, **17**, 235.
3. *U.S. Army Armament Res. Dev. Command Report* No. NX02101, Chemical Systems Laboratory, NIOSH Exchange Chemicals.
4. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

E60 ethanethiol

CH_3CH_2SH

C_2H_6S **Mol. Wt.** 62.14 **CAS Registry No.** 75-08-1

Synonyms ethyl mercaptan; ethyl hydrosulfide; ethyl sulfhydrate; ethyl thioalcohol; thioethanol

EINECS No. 200-837-3 **RTECS No.** KI 9625000

Uses Chemical synthesis. Corrosion inhibitor. Olfactory warning for natural gas.

Occurrence Found in vinous fermentation. Found in urine of rabbits after ingestion of cabbage.

Physical properties

M. Pt. –147°C **B. Pt.** 35°C **Flash point** <–18°C (closed cup) **Specific gravity** 0.839 at 20°C with respect to water at 4°C **Volatility** v.p. 400 mmHg at 20°C ; v.den. 2.14

Solubility Water: 6760 mg l^{-1} at 20°C. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 0.5 ppm (1.3 mg m^{-3})

FR-VME 0.5 ppm (1 mg m^{-3})

UK-LTEL 0.5 ppm (1.3 mg m^{-3}) **UK-STEL** 2 ppm (5.2 mg m^{-3})

US-TWA 0.5 ppm (1.3 mg m^{-3})

UN No. 2363 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid

Supply classification highly flammable, harmful

Risk phrases Highly flammable – Harmful by inhalation (R11, R20)

Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Avoid contact with the eyes (S2, S16, S25)

Environmental fate

Degradation studies

Metabolised by *Corynebacterium, Flavobacterium, Streptomyces* and *Thermoactinomycetes* spp. in a process used to deodorise cattle faeces (1).

Metabolised by the green alga *Chlorella fusca* (2).

Metabolised by the methanogenic bacteria *Methanococcus, Methanobacterium, Methanobrevibacter* and *Methanosarcina* spp. (3).

Abiotic removal

Completely removed from gas by contact with sodium hypochlorite solution. The optimum condition for concentrations ≤33 mg m^{-3} were 1500 mg l^{-1} sodium hypochlorite at pH 7.95-9.90 and 25°C (4).

Removal from alkanes effected by adsorption onto Na_x zeolite (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1960 mg kg^{-1} (6).

LC_{50} (4 hr) inhalation rat 4420 ppm (7).

LD_{50} intraperitoneal rat 450 mg kg^{-1} (7).

Metabolism and toxicokinetics

Rapidly absorbed and excreted, metabolism in guinea pigs and dogs is largely to the sulfate, probably via a sulfonic intermediate (8).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye for 24 hr caused moderate irritation (6).

Other effects

Other adverse effects (human)
Inhalation by human volunteers of 10 mg m^{-3}, 3 hr day^{-1}, 5-10 days showed minimal effects such as a rise in olfactory threshold and altered taste reaction to bitter and sweet substances. All complained of periodic nausea, irritation of the mucous membranes, lips, mouth and nose, and a sensation of fatigue (9).

Other comments

Physical properties, safety precautions and toxicity reviewed (9).
Reviews on toxicity listed (10).
Autoignition temperature 298°C.

References

1. Ohta, Y. et al *Biol. Wastes* 1988, **24**(3), 227-240.
2. Krauss, F. et al *J. Gen. Microbiol.* 1987, **133**(5), 1209-1219.
3. Rajagopal, B. S. et al *Curr. Microbiol.* 1986, **14**(3), 137-144.
4. Shikjokova, T. V. et al *Zh. Prikl. Khim.* 1986, **59**(11), 2462-2466 (Russ.) (*Chem. Abstr.* **106**, 55126h).
5. Alfanas'ev Y. M. et al *Gazov. Prom-st.* 1987, (1), 36-37 (Russ.) (*Chem. Abstr.* **108**, 40706q).
6. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 166, Prague, Czechoslovakia.
7. *Am. Ind. Hyg. Assoc. J.* 1958, **19**, 171.
8. *Chemical Safety Data Sheets* 1992, **5**, 123-126, The Royal Society of Chemistry, London, UK.
9. *Documentation of Threshold Limit Values* 4th ed., 1980, 189, ACGIH, Cincinnati, OH, USA.
10. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E61 ethanol

$$CH_3CH_2OH$$

C_2H_6O **Mol. Wt.** 46.07 **CAS Registry No.** 64-17-5

Synonyms ethyl alcohol; absolute alcohol; ethyl hydrate; ethyl hydroxide

EINECS No. 200-578-6 **RTECS No.** KQ 6300000

Uses Antiseptic. Solvent and dehydratory agent, alcoholic beverages. Manufacture of denatured alcohol, pharmaceuticals, perfumery. Intermediate in organic synthesis.

Physical properties

M. Pt. –114.1°C **B. Pt.** 78.5°C **Flash point** 13°C (closed cup) **Specific gravity** 0.789 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.30 **Volatility** v.p. 43 mmHg at 20°C ; v.den. 1.6
Solubility Water: miscible with water Organic solvents: acetone, benzene, diethyl ether, dimethyl sulfoxide

Occupational exposure

DE-MAK 500 ppm (960 mg m^{-3})
FR-VME 1000 ppm (1900 mg m^{-3}) **FR-VLE** 5000 ppm (9500 mg m^{-3})

SE-LEVL 500 ppm (1000 mg m^{-3}) **SE-STEL** 1000 ppm (1900 mg m^{-3})
UK-LTEL 1000 ppm (1920 mg m^{-3})
US-TWA 1000 ppm (1880 mg m^{-3})

UN No. 1170 **HAZCHEM Code** 2[illegible] **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container tightly closed – Keep away from sources of ignition – No smoking (S2, S7, S16)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) fingerling trout 11.2 g l^{-1} (1).
LC_{50} (1, 24, 48, 72, 96 hr) fathead minnow >18-13.4 g l^{-1} (2).
LC_{50} (24 hr) creek chub >7 g l^{-1} (3).
LC_{50} (7 day) guppy 11 g l^{-1} (2).

Invertebrate toxicity
EC_{50} (5, 30 min) *Photobacterium phosphoreum* 34.9 g l^{-1} Microtox test (4).
Cell multiplication inhibition test *Pseudomonas putida* 6500 mg l^{-1}, *Microcystis aeruginosa* 1450 mg l^{-1}, *Scenedesmus quadricauda* 5000 mg l^{-1}, *Entosiphon sulcatum* 65 mg l^{-1} (5,6).
EC_{50} (4, 12 days) embryo grass shrimps *Palaemonetes pugio* 12.07, 3.63 g l^{-1}, respectively (7).

Environmental fate

Nitrification inhibition
50% inhibition of NH_3 oxidation in *Nitrosomonas* sp. at 4100 mg l^{-1} (8).

Degradation studies
Anaerobic lagoon 208, 352, 769 mg COD day^{-1} l^{-1} influent 80, 270, 270 mg l^{-1} effluent 35, 120, 13 mg l^{-1}, respectively (9).
Activated sludge after 6, 12, 24 hr gave 12.9%, 25.9%, 37.3% of ThOD, respectively (10).
BOD^{20}_5 1.58 mg l^{-1} O_2 at 10 mg l^{-1} using unadapted sewage, no lag period. BOD^{20}_{20} 1.78 mg l^{-1} at 10 mg l^{-1} using unadapted sewage (11).
BOD_5 0.93-1.67 mg l^{-1} O_2 and COD 1.99-2.11 mg l^{-1} O_2 (12).
ThOD 2.10 mg l^{-1} O_2 (13).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 3450, 7060 mg kg^{-1}, respectively (14,15).
LC_{50} (10 hr) inhalation rat 20,000 ppm (16).
LC_{50} (4 hr) inhalation mouse 39,000 mg m^{-3} (17).
LD_{50} intravenous rat 1440 mg kg^{-1} (18).
LD_{50} intravenous mouse 1973 mg kg^{-1} (19).
LD_{50} intraperitoneal rat 3750 mg kg^{-1} (20).

Sub-acute and sub-chronic data
Oral woman (12 wk) 256 g kg^{-1} caused central nervous system effects (21).
Oral rat (12 day) 6600 mg kg^{-1} day^{-1} total dose, administered at 2-hr intervals, or condensed exposure to 6600 mg kg^{-1} day^{-1} concentrated in a 4-day period. Induced microencephaly and delays in balancing ability and coordinated hindlimb movements (22).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity of alcoholic beverages in humans, inadequate evidence for carcinogenicity of ethanol or alcoholic beverages in animals, IARC classification for alcoholic beverages group 1 (23).
Gavage mouse (50 wk) 320 mg kg^{-1}, no evidence of tumorigenic activity (24).

Teratogenicity and reproductive effects

Oral rat (day-13 gestation) 4000 mg kg^{-1} caused teratogenic effects (25).

Oral pig-tailed macaque 300-4100 mg kg^{-1} wk^{-1} gave peak plasma concentrations of ethanol 2.4-55 mg l^{-1}. An increased rate of spontaneous abortion was related to exposure at ≥1800 mg kg^{-1} (20.5 mg l^{-1}) and pregnancy failure in days 1-30 gestation increased at doses >2500 mg kg^{-1}. Wkly exposure to ethanol in this nonhuman primate is comparable to available data on humans (26).

Oral rat (day 7-20 of gestation) 5, 10, 20, 40% (v/v) ethanol in drinking water and food caused a significant inhibition of maternal body weight gain during gestation in 20% group, with prolonged gestation length. Incidence of dams with total litter loss increased significantly in 40% group. Retarded growth of ♂ pups was observed in all groups. ♂ pups in 20% group were significantly inferior in the multiple T-maze water escape learning test (27).

Metabolism and toxicokinetics

Oral rat (day-20 gestation) 2000 mg kg^{-1} gave maximum ethanol concentration in blood and liver of mother and foetus at 2 hr, with higher concentrations in amniotic fluid at 4-8 hr (28).

♂ human oral, intravenous administration at 100, 400 mg kg^{-1}, a lower blood level occurs under oral administration due to metabolism during absorption (29).

Metabolism of ethanol is mediated by alcohol dehydrogenase, catalase and the microsomal ethanol-oxidising enzyme system. Microsomal induction leads to interaction of ethanol with drugs, hepatotoxic agents, steroids, vitamins and an increased activation of mutagens/carcinogens (30).

Irritancy

Dermal rabbit 400 mg (open) caused mild irritation (31).

Dermal rabbit (24 hr) 500 mg caused severe irritation and 100 g instilled into rabbit eye (24 hr) caused moderate irritation (15).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (32).

Escherichia coli WP25 (λ) microscreen assay negative, limited negative (33).

Escherichia coli CHY832, SA431 replicative killing mutatest positive (34).

Escherichia coli PQ37 SOS chromotest negative (35).

In vitro mouse lymphoma L5178Y tk^+/tk^- with and without metabolic activation negative (36).

In vitro human fibroblast cells, chromosomal aberrations positive (37).

In vitro ♀ human lymphocyte cells, sister chromatid exchanges negative (38).

In vitro human lymphoid cell lines did not exert a clastogenic effect alone, but clastogenic potential increased when ethanol was added concurrently with mutagens with a dose 0.5-1.0%. High doses of ethanol inhibit DNA and chromosome repair systems, supporting epidemiological evidence that ethanol may have cocarcinogenic properties (39).

In vitro ♂ mouse lymphocytes, sister chromatid exchange positive (40).

In vivo ♂ mouse (10 wk), 20% ethanol induced sister chromatid exchange in spermatogonia and chromosome dissociation in spermatocytes (41).

Differential response to environmental ethanol among 2nd-chromosome arrangements in experimental populations of *Drosophila buzzatii* positive (42).

In *Drosophila melanogaster*, the numbers of progeny reduced and induced teratogenic effects induced (43).

Drosophila melanogaster larvae in media containing 0, 4, 8, 14% ethanol, malformation reported, commonly of legs and wings in 10% emerging adults at the highest dose levels (44).

Vicia faba, Hordeum vulgare, Secale cereale sister chromatid exchange positive (45).

Other effects

Other adverse effects (human)

Human foetal hepatic cell line (WRL-68) cells (which do not express alcohol dehydrogenase or cytochrome P450 activity) were exposed for 120 min to 200 mM ethanol. No cell deaths or morphological alterations were observed by light microscopy. Lipid peroxidation values, measured as malondialdehyde production, were 127% compared

with control cell values and studies on cell proliferation, cell adhesion capacity, neutral red incorporation into lysosomes, glutathione content, protein sulfhydryl compounds, lipid peroxidation, inner mitochondrial membrane integrity, lactate dehydrogenase activity and ultrastructural alterations indicated that ethanol produced damage at the cellular level (46).

No increased incidence of liver or pancreatic diseases or marked reduction in work performance observed following regular medical surveillance of workers exposed to ethanol (47).

Children exposed to alcohol throughout pregnancy showed deficits in the ability to concentrate and showed behavioural problems. Hyperactivity and impulsive behaviour were not evident (48).

In vitro human hepatoblastoma cells exposed to 80 mM ethanol showed a threefold increase in length of mitochondria, proliferation, vesiculation and dilatation of the smooth endoplasmic reticulum. Cell viability (assessed by metabolism of methylxanthine dye) decreased to 68% of the control. Succinate dehydrogenase activity in cells treated for 24 hr decreased to 80% of control values (49).

Other comments

Induced small amounts of cytochrome P_{450} in *Saccharomyces cerevisiae* under conditions in which it is not normally detectable (42).

Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology and environmental effects listed (50).

Effects of alcohol consumption reviewed (24).

Absorption and metabolism of ethanol in organs reviewed (51).

The biochemical, molecular and immunological mechanisms suggested to explain the epidemiological observations regarding ethanol abuse and cancer are reviewed (52).

Ethanol absorption rates by skin and mucous membranes, effects on the central nervous system and ethanol-related problems in the workplace reviewed (53).

Epidemological and experimental evidence supporting the cocarcinogenic action of ethanol reviewed. Various pathogenetic mechanisms by which ethanol may enhance carcinogenesis discussed (54,55).

Alcohol and human cancer reviewed (56).

Ethanol effects on carcinogen activation and detoxication andof O^6-methylguanine transferase inhibition by ethanol reviewed (57).

Alcoholism and cirrhosis of the liver reviewed (58).

Risk factors, pathogenesis, clinical features, prognosis and treatment of alcoholic hepatitis discussed (59).

The mutagenicity of ethanol and its metabolite in humans and laboratory animals reviewed (60).

Pharmacokinetics reviewed (61).

The characterisation, mechanisms and preventative diagnosis on ethanol-induced teratogenicity reviewed (62-64).

The action, uses and adverse effects of ethanol reviewed (65).

The cytotoxic effects of ethanol on cultured human hepatocytes and fibroblasts is reduced by the presence of pyruvate. This may be related to the activity of the tricarboxylic acid cycle (66).

References

1. Majewski, H. S. et al *Water Res.* 1978, **13**, 217-221.
2. Matton, V. R. et al *EPA Report No. EPA-600/3-76-097* 1976, Washington, DC, USA.
3. Gillette, L. A. et al *Sewage Ind. Wastes* 1952, **24**(11), 1397-1401.
4. Kaiser, K. L. E. *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
5. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9).
6. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
7. Rayburn, J.R. et al *Arch. Environ. Contam. Toxicol.* 1997, **33**(2), 217-221.
8. Hooper, A. et al *J. Bacteriol.* 1967, **93**, 1309.
9. Hovious, J. C et al *J. Water Pollut. Control Fed.* 1973, **45**(1).
10. Gerhold, R. M. et al *J. Water Pollut. Control Fed.* 1966, **38**(4), 562.
11. Young, R. H. J. et al *J. Water Pollut. Control Fed.* 1968, **40**, 8.
12. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold, New York, NY, USA.
13. Price, K. S. et al *J. Water Pollut. Control Fed.* 1974, **46**, 1.

14. *Toxicol. Appl. Pharmacol.* 1970, **16**, 718.
15. Sax, N. I. et al *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
16. *Raw Material Data Handbook* 1974, Lehigh University, Bethlehem, PA, USA.
17. *Gig. Tr. Prof. Zabol.* 1982, **26**(8).
18. *Toxicol. Appl. Pharmacol.* 1971, **18**, 60.
19. *Handbook of Toxicology* 1956, **1**, 128.
20. *Environ. Health Perspect.* 1985, **61**, 321.
21. *J. Am. Med. Assoc.* 1977, **238**, 2143.
22. West, J. R. et al *Alcohol Alcohol.* 1987, **22**(Suppl.1) (Adv. Biomed. Alcohol. Res.) 461-465.
23. *IARC Monograph* 1988, **44**, 15-378.
24. *Cancer Lett. (Shannon, Irel.)* 1981, **13**, 345.
25. *Cytol. Genet. (Engl. Transl.)* 1981, **15**, 23.
26. Clarren, S. K. et al *Teratology* 1987, **35**(3), 355-366.
27. Yamamoto, Y. et al *Kinki Daigaku Igaku Zasshi* 1986, **11**(4), 493-506 (Japan.) (*Chem. Abstr.* **107**, 91622w).
28. Hayashi, M. *Arukoru Kenkyu to Yakubutsu Izon* 1991, **26**(2), 89-95.
29. Ueno, Y. et al *Arukoru Kenkyu to Yakubutsu Izon* 1990, **25**(2), 103-105.
30. Lieber, C. S. et al *Mutat. Res.* 1987, **186**(3), 201-233.
31. *Union Carbide Data Sheet* 1970, Union Carbide Corp, New York, NY, USA.
32. Khudolei, V. V. et al *Arch. Geschwulstforsch.* 1987, **57**(6), 453-462.
33. Rossman, T. G. et al *Mutat. Res.* 1991, **260**(4), 349-367.
34. Gordon, A. J. E. et al *Mutat. Res.* 1987, **190**(4), 253-258.
35. von der Hude, W. et al *Mutat. Res.* 1988, **203**(2), 81-94.
36. Wangenheim, J. et al *Mutagenesis* 1988, **3**(3), 193-205.
37. McMarrow, L. E. *Ann. N. Y. Acad. Sci.* 1991, 625 (Mol. Cell. Mech. Alcohol. Anesth.), 830-831.
38. Shim, J. S. et al *Mutat. Res.* 1989, **224**(4), 511-515.
39. Hsu, T. C. et al *Anticancer Res.* 1991, **11**(3), 1097-1101.
40. Hirai, M. et al *Arukoru Kenkyu to Yakubutsu Izon* 1988, **23**(3), 223-233.
41. Hirai, M. et al *Arukoru Kenkyu to Yakubutsu Izon* 1988, **23**(3), 243-251.
42. Blatiak, A. et al *J. Gen. Microbiol.* 1987, **133**(4), 1053-1059.
43. Xu, W. et al *Yichuan* 1988, **10**(4), 23-25 (Ch.) (*Chem. Abstr.* 1989, **111**, 2509g).
44. Ranganathan, S. et al *Teratology* 1987, **36**(1), 45-49.
45. Zhang, Z. et al *Mutat. Res.* 1991, **261**(1), 69-73.
46. Olivares, I. P. *Toxicology* 1997, **120**(2), 133-144.
47. Lun, A. et al *Z. Klin. Med.* 1990, **45**(20), 1817-1820 (Ger.) (*Chem. Abstr.* **114**, 68278z).
48. Brown, R. T. et al *Neurotoxicol. Teratol.* 1991, **13**(4), 369-375.
49. Cameron, R. G. et al *Toxicol. In Vitro* 1998, **12**(2), 111-122.
50. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
51. Erkomaishvili, A. I. *Soobshch. Akad. Nauk Gruz* 1991, **142**(1), 181-184 (Russ.) (*Chem. Abstr.* **115**, 225510j).
52. Garro, A. J. et al *Annu. Rev. Pharmacol. Toxicol.* 1990, **30**, 219-249.
53. Forney, R. B. *Clin. Chem. (Winston-Salem, NC)* 1987, **33**(11B), 82B-86B.
54. Farinati, F. et al *Ital. J. Gastroenterol.* 1988, **20**(6), 322-330.
55. Seitz, H. K. et al *Annu. Rev. Nutr.* 1988, **8**, 99-119.
56. Driver, H. E. et al *Anticancer Res.* 1987, **7**(3A), 309-320.
57. Garro, A. J. et al *Alcohol: Clin. Exp. Res.* 1986, **10**(6, Suppl.), 735-775.
58. Lieber, C. S. *N. Engl. J. Med.* 1988, **319**(25), 1639-1650.
59. Sherlock, S. *Alcohol Alcohol.* 1990, **25**(2-3), 189-196.
60. Obe, G. et al *Mutat. Res.* 1987, **186**(3), 177-200.
61. Holford, N. H. G. *Clin. Pharmacokinet.* 1987, **13**(5), 273-292.
62. Hoyseth, K. S. et al *Life Sci.* 1989, **44**(10), 643-649.
63. Graham, J. M. *Int. Congr. Ser. – Excerpta Med.* 1986, **689**(Interuterine Life) 383-388.
64. Randall, C. L. *Alcohol Alcohol.* 1987, **22**(Suppl. 1) (Adv. Biomed. Alcohol Res.) 125-132.
65. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
66. Fukaya, K. et al *Arch. Toxicol.* 1997, **71**(10), 651-654

E62 ethanolamine

$HOCH_2CH_2NH_2$

C_2H_7NO **Mol. Wt.** 61.08 **CAS Registry No.** 141-43-5

Synonyms 2-aminoethanol; monoethanolamine; 2-hydroxyethylamine; β-aminoethyl alcohol; Amietol

EINECS No. 205-483-3 **RTECS No.** KJ 5775000

Uses In syntheses and formulations of pharmaceuticals, polishes, toiletries and agricultural products. Used to remove CO_2 and H_2S from natural and other gases.

Physical properties

M. Pt. 10.3°C **B. Pt.** 170.8°C **Flash point** 90.5°C **Specific gravity** 1.0117 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} -1.31 (1) **Volatility** v.p. 0.4 mmHg at 20°C ; v.den. 2.11
Solubility Water: miscible. Organic solvents: chloroform; miscible with acetone, methanol

Occupational exposure

DE-MAK 2 ppm (5.1 mg m^{-3})
FR-VME 3 ppm (8 mg m^{-3})
JP-OEL 3 ppm (7.5 mg m^{-3})
SE-LEVL 3 ppm (8 mg m^{-3}) **SE-STEL** 6 ppm (15 mg m^{-3})
UK-LTEL 3 ppm (7.6 mg m^{-3}) **UK-STEL** 6 ppm (15 mg m^{-3})
US-TWA 3 ppm (7.5 mg m^{-3}) **US-STEL** 6 ppm (15 mg m^{-3})

UN No. 2491 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification harmful
Risk phrases Harmful by inhalation – Irritating to eyes, respiratory system and skin (R20, R36/37/38)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 190 mg l^{-1} (2).
LC_{50} (96 hr) goldfish 170 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 13.7 ppm Microtox test (3).
Cell multiplication inhibition test *Pseudomonas putida* 6.3 mg l^{-1} (4).
LOEC *Microcystis aeruginosa* 1.6 mg l^{-1} (5).
LOEC *Scenedesmus quadricauda* 0.75 mg l^{-1} (4).

Environmental fate

Nitrification inhibition
50% inhibition of NH_3 oxidation in *Nitrosomonas* spp. at 12.2 g l^{-1} (6).
16% inhibition of NH_3 oxidation in *Nitrosomonas* spp. at 1100 mg l^{-1} (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1720 mg kg^{-1} (8).
LD_{50} dermal rabbit 1000 mg kg^{-1} (9).
LD_{50} intraperitoneal rat 981 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Maximum daily no-effect-level in an oral 90-day study in rats was 0.32 g kg^{-1}. In inhalation studies, dogs, rats and guinea pigs survived 12-25 ppm for 90 days; some mortality occurred in 24-30 days in dogs exposed to 100 ppm, and in rodents exposed to 66-75 ppm. Skin irritation and lethargy occurred at 5-12 ppm (11).

Teratogenicity and reproductive effects

In pregnant rats, the compound induced a dose-dependent increase in foetal deaths, malformations and retarded growth (12).

Pregnant Sprague-Dawley rats and New Zealand White rabbits were exposed dermally to 0, 10, 25 or 75 mg kg^{-1} day^{-1} of monoethanolamine for 6 hr day^{-1} on days 6-15 of gestation for rats or days 6-18 for rabbits. A further group of rats was exposed to 225 mg kg^{-1} day^{-1}. There was increased skin irritation/lesions in rats at the 225 mg level and in rabbits at the 75 mg level, and decreased maternal body wt. gain. However, there was no evidence of developmental or foetal toxicity at any of the doses tested. NOEL maternal toxicity 75 and 10 mg kg^{-1} day^{-1} in rats and rabbits, respectively (13).

Irritancy

Instillation into rabbit eye caused severe injury (11).

Genotoxicity

Salmonella typhimurium TA98, T100, TA1535, TA1537 with and without metabolic activation negative (14).
Weak inducer of chromosome breaks in human lymphocytes (15).

Other effects

Any other adverse effects

The compound inhibits acetylcholinesterase *in vitro* at concentrations similar to tissue concentrations achieved by fatal doses in the rat (10).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicity, epidemiology, workplace experience and environmental effects listed (16,17).

References

1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983 Van Nostrand Reinhold, New York, USA.
2. *Shell Industrie Chemicalien gids* 1975, Shell Chemie.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J Can.* 1991, **26**(3), 361-431.
4. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
5. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **11**(a).
6. Hooper, A. et al *J. Bacteriol.* 1973, **115**, 480.
7. Hocken M. R. et al *J. Water Pollut. Control Fed.* 1977.
8. *Toxicol. Appl. Pharmacol.* 1977, **42**, 4176.
9. *Union Carbide Data Sheet* 1972, Union Carbide Corp, New York, USA.
10. Hartung, R. et al *Toxicol. Appl. Pharmacol.* 1968, **12**, 486.
11. Clayton, G. D. (Eds.) *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, **2A, 2B**, John Wiley & Sons, New York, NY, USA.
12. Mankes, R. F. *Teratog. Carcinog. Mutagen.* 1986, **6**(5), 403-417.
13. Liberacki, A. B. et al *Fundam. Appl. Toxicol.* 1996, **31**(1), 117-123.
14. Mortelmans, K. et al *Environ. Mol. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
15. Arutyunyan, R. M. et al *Tsitol. Genet.* 1987, **21**(6), 450.
16. Smyth, H. F. *J. Ind Hyg. Toxicol.* 1941, **23**, 259.
17. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E63 ethephon

$$ClCH_2CH_2P(O)(OH)_2$$

$C_2H_6ClO_3P$ **Mol. Wt.** 144.49 **CAS Registry No.** 16672-87-0

Synonyms 2-chloroethylphosphonic acid; β-chloroethylphosphonic acid; phosphonic acid, 2-chloroethyl-; Camposan; Chloroethephon; Ethrel; Florel; Agritrel; Arvest; Bromoflor; Direfon; Hero; Ibis; Prep

EINECS No. 240-718-3 **RTECS No.** SZ 7100000

Uses Plant growth regulator. Cotton defoliant.

Physical properties

M. Pt. 74-75°C **Volatility** v.p. $<7.52 \times 10^{-8}$ mmHg

Solubility Water: 1 kg l^{-1}. Organic solvents: acetone, ethanol, ethylene glycol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, rainbow trout 300-350 mg l^{-1} (1).

Environmental fate

Abiotic removal

In soil rapidly undergoes degradation to phosphoric acid, ethylene and chloride ions (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4230 mg kg^{-1} (1).

LD_{50} dermal rabbit 5730 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LC_{50} (8 day) mallard duck >10,000 mg kg^{-1} diet (3).

Carcinogenicity and chronic effects

In 2-yr feeding trials, rats receiving ≤3000 mg kg^{-1} diet showed no increase in carcinomas (3).

Irritancy

Topically applied ethephon 0.5% solution irritated rabbit eyes; (repeated application) 20% solution skin irritant (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (5).

Other effects

Other adverse effects (human)

0.5 g of 2% powder ingested in a suicide attempt caused severe epigastria and abdominal pain, vomiting, diarrhoea and reduction in cholinesterase activity (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

ADI 0.05 mg kg^{-1} body weight (3).
WHO Toxicity Class Table 5 (8).

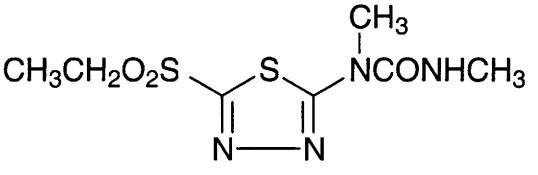
Other comments

When applied to barley for lodging control, ethephon also promotes tillering. Induction of tiller growth may be a result of inhibition of upper stem elongation by ethephon rather than a direct response of the buds to the compound (9,10).
Metabolic pathways reviewed (11).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Kanda, M. et al *Ann. Rep. Jpn. Inst. Rural Med.* 1974, **3**, 50.
3. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
4. Grabliauskiene, M. *Primen. Fiziol. Akt. Veshchestv. Sadovod. Mater. Simp.* 1972, **2**, 145-151, (Russ.) (*Chem. Abstr.* **84**, 174800k).
5. Moriya, M. et al *Mutat. Res.* 1983, **116**, 185-216.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
9. Foster, K. R. et al *Crop Sci.* 1992, **32**(6), 1345-1352.
10. Foster, K. R. et al *Curr. Plant Sci. Biotechnol. Agric.* 1992, **13**, 823-834.
11. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

E64 ethidimuron



$C_7H_{12}N_4O_3S_2$ **Mol. Wt.** 264.33 **CAS Registry No.** 30043-49-3

Synonyms urea, *N*-[5-(ethylsulfonyl)-1,3,4-thiadiazol-2-yl]-*N*,*N*'-dimethyl; Ustilan; 1-[5-ethyl sulfonyl-1,3,4-thiadiazol-2-yl]-*N*,*N*'-dimethylurea

EINECS No. 250-010-6 **RTECS No.** YT 0150000

Uses Suspended herbicide.

Physical properties

M. Pt. 156°C **Volatility** v.p. 7.52×10^{-9} mmHg at 20°C
Solubility Water: 3 g l^{-1} at 20°C. Organic solvents: propan-2-ol, dichloromethane

Occupational exposure

Supply classification irritant, dangerous to the environment
Risk phrases May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R43, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin – Wear suitable gloves – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S24, S37, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) golden orfe >1 g l^{-1}, goldfish 400-500 mg l^{-1}, carp 200-300 mg l^{-1} (1).

Environmental fate

Degradation studies

1 yr after application to soil at 5 g ha^{-1}, effects were seen on sunflower (at 13-16th leaf phase) and maize (9th-10th leaf phase) (2).

$t_{1/2}$ in soil of 3-4 months has been reported with breakdown to 3-(5-ethylsulfonyl-1,3, 4-thiadiazol-2-yl)-1-methylurea (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral Japanese quail, canary 300-1000 mg kg^{-1} (3).

LD_{50} oral rat, mouse >2.5 g kg^{-1} (3).

LD_{50} dermal rat >1 g kg^{-1} (3).

Sub-acute and sub-chronic data

Oral rats (90 day) in diet, showed a no-effect level of >1 kg^{-1} (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

WHO Toxicity Class Table 5 (6).

Other comments

Food contaminant. Water pollutant.

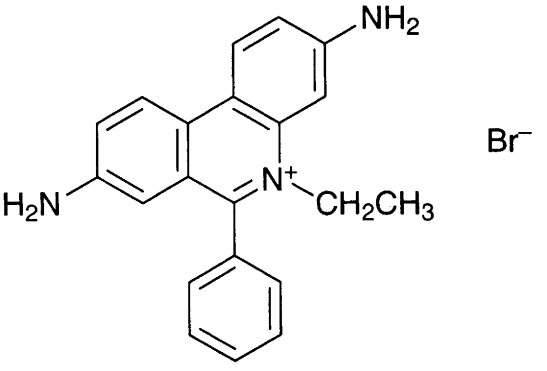
The compound is not harmful to bees (3).

Decomposes on distillation.

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Koleva, A. et al *Fiziol. Rast. (Sofia)* 1990, **16**(3), 51-57.
3. *The Pesticide Manual* 9th ed., 1991 British Crop Protection Council, Farnham, UK.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

E65 ethidium bromide



$C_{21}H_{20}BrN_3$ **Mol. Wt.** 394.31 **CAS Registry No.** 1239-45-8

Synonyms homidium bromide; 3,8-diamino-5-ethyl-6-phenylphenanthridinium bromide; Dromalic; 2,7-diamino-10-ethyl-9-phenylphenanthridinium bromide; RD 1572

EINECS No. 214-984-6 **RTECS No.** SF 7950000

Uses Staining agent used in sequence determination of nucleic acids. Veterinary trypanocide.

Physical properties

M. Pt. 260-262°C (decomp.)
Solubility Water: 5%. Organic solvents: chloroform

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 1.6 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} subcutaneous mouse 110 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 20 mg kg^{-1} (3).

Irritancy
Irritating to the skin, eyes, mucous membranes and upper respiratory tract (species unspecified) (4).

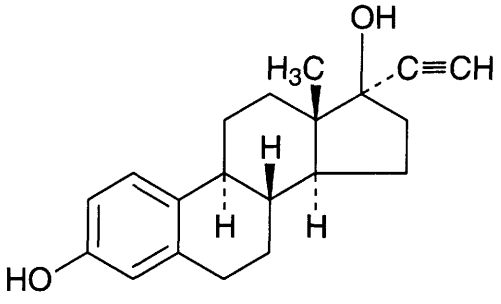
Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (5).
Saccharomyces cerevisiae meiotic chromosomal malsegregation positive (6).
Drosophila melanogaster wing-spot somatic mutation and recombination test positive (7).
In vitro Chinese hamster ovary cells HGPRT forward mutation assay with and without metabolic activation negative (8).
In vitro DNA unwinding assay using L1210 DNA topoisomerase positive (9).
In vitro Chinese hamster bone marrow cells, with and without metabolic activation chromosome aberrations negative (8).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. *Ann. Trop. Med. Parasitol.* 1952, **46**, 285.
3. *Cancer Res.* 1974, **34**, 2699.
4. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1549, Sigma-Aldrich, Milwaukee, WI, USA.
5. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
6. Sora, S. et al *Mutat. Res.* 1988, **201**(2), 375-384.
7. Graf, U. et al *Environ. Mol. Mutagen.* 1990, **16**(3), 225-237.
8. Oberly, T. J. et al *Environ. Mol. Mutagen.* 1990, **16**(4), 260-270.
9. Pommier, Y. et al *Nucleic Acids Res.* 1987, **15**(16), 6713-6731

E66 ethinyloestradiol



$C_{20}H_{24}O_2$ **Mol. Wt.** 296.41 **CAS Registry No.** 57-63-6

Synonyms ethynyloestradiol; (17α)-19-norpregna-1,3,5(10)-trien-20-yne-3,17-diol; Estinyl

EINECS No. 200-342-2 **RTECS No.** RC 8925000

Uses Oestrogen. Used in combination with progestogen as oral contraceptive for human use. In treatment of menopausal and post-menopausal symptoms and other oestrogen-deficiency states. Veterinary medicine as an oestrogen (1).

Physical properties

M. Pt. 182-184°C (141-146°C, hemihydrate)
Solubility Organic solvents: acetone, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1.7, >5 g kg^{-1}, respectively (2,3).
In rat and mouse toxic symptoms include salivation, lachrymation and reduced motor activity, with deaths usually occurring within 24 hr (4).

Sub-acute and sub-chronic data

Rats exposed to the compound neonatally (postnatal days 1-5) initially showed increased uterine weight and luminal epithelium hypertrophy, however by day-11, uterine weights decreased. Toxicity exhibited by altered prepubertal uterine gland development (5).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (6).

The compound has been studied in rats, mice, dogs and monkeys, tumorigenic activity reported in the first two species (7).
Oral mice (80 wk), unspecified concentration in diet, caused an increase in incidence of pituitary tumours and malignant mammary tumours in both ♀ and ♂. There was also, in ♀, an increase in malignant tumours of uterus and cervix (8).
Rats receiving the compound in diet for 104 wk demonstrated increased incidence of benign liver-cell tumours in ♂ and ♀ and malignant liver-cell tumours in ♀ (8).
In rats, a dose-response relationship in promotion of diethylnitrosamine hepatocarcinogenesis was seen in the dose range 16-90 μg day^{-1} for 30 wk (9).
At high doses, the compound both initiates and promotes development of γ-glutamyltranspeptidase positive foci in ♀ rats (10).

Teratogenicity and reproductive effects
Mice receiving 3-30 μg orally on day-1 of pregnancy showed teratogenic effects while doses ≥100 μg terminated pregnancies in all mice studied (11).
Rats receiving 5-500 μg kg^{-1} orally on first two days of pregnancy caused some pregnancies to terminate, but no abnormalities (12).
Oral hamsters, 2.5 mg single dose administered three days before mating caused lower pregnancy rates and increased resorptions (13).

Metabolism and toxicokinetics
Compound is rapidly and effectively absorbed from mammalian small intestine, but is subject to some first-pass metabolism in the gut wall (14).
The main metabolic pathway is aromatic 2-hydroxylation, in human, baboon and rat. In rabbit, a large amount of 'ring-D-homoannulated' metabolites are found (6,15,16).
Only slowly metabolised in the liver, excretion is mainly via urine with some metabolites in faeces (1).
Sulfation and glucuronidation occur (17).
Sulfation occurs in cytosolic fraction and glucuronidation in microsomal fractions of hepatic and extrahepatic human tissues (18).
The pharmacokinetics of the compound in humans, when administered with progesterones, has been reported in detail (19).

Genotoxicity

Salmonella typhimurium G46 and *Escherichia coli* K12 with and without metabolic activation negative (20).
Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (21).
Mouse dominant lethal mutations negative (22).

Other effects

Other adverse effects (human)
Interactions have been reported with antituberculous agents and vitamin C, resulting in enzyme induction (1).
Adverse effects are generally those shared with other oestrogens and include cardiovascular effects and effects on the blood lipid profile (1).

Any other adverse effects
The compound can influence hepatic cholesterol and lipoprotein metabolism (23).

Other comments

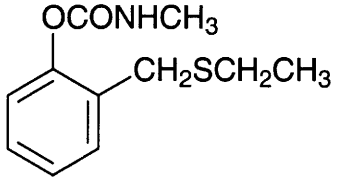
Suspected environmental endocrine disruptor (24).
Ethinylestradiol, originating from pharmaceutical use, and alkylphenol-polyethoxylates, originating from the biodegradation of surfactants and detergents during sewage treatment, have been suggested as the two most likely sources of oestrogenic substances present in sewage effluent (25).
Concentrations in sewage effluents, reservoirs, rivers and potable water in South East England were <20 ng l^{-1} (26).

Human metabolism reviewed (27).
Environmental signalling and endocrine disruption reviewed (28).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
2. Brotherton, J. *Sex Hormone Pharmacology* 1976, Academic Press, London, UK.
3. Goldenthal, E. I. *Toxicol. Appl. Pharmacol.* 1971, **18**, 185.
4. Makino, M. et al *Yakuri to Chiryo* 1990, **18**(7), 2583-2589.
5. Branham, W. S. *Toxicology* 1988, **51**(2-3), 201-212.
6. *IARC Monograph* 1987, **Suppl. 7**, 280-286.
7. *IARC Monograph* 1979, **21**, 233-255.
8. *Committee on Safety of Medicines* 1972, HMSO, London, UK.
9. Campen, D. et al *J. Toxicol. Environ. Health* 1990, **29**(3), 257-268.
10. Ghia, M. et al *Cancer Lett. (Shannon, Irel.)* 1989, **46**(3), 195-202.
11. Yanagimachi, R. et al *Fertil. Steril.* 1968, **19**, 787-801.
12. Yasuda, Y. et al *Am. J. Obstet. Gynecol.* 1977, **127**, 832-836.
13. Davis, B. K. et al *Acta Endocrinol.* 1972, **70**, 582-590.
14. Back, D. J. et al *Br. J. Clin. Pharmacol.* 1982, **13**, 325-330.
15. Abdel-Aziz, M. T. et al *Steroids* 1969, **13**, 809-820.
16. Bolt, H. M. *Pharm. Ther.* 1979, **4**, 155-181.
17. Pacifici, G. M. et al *J. Steroid Biochem.* 1988, **31**(3), 345-349.
18. Pacifici, G. M. et al *Colloq. INSERM* 1988, **173**, 321-324.
19. Jung-Hoffmann, et al *Contraception* 1989, **40**(3), 299-312.
20. Kraemer, M. et al *Naunyn Schmiedeberg's Arch. Pharmacol.* 1974, **284**, R46.
21. Zeiger, E. *Environ. Mol. Mutagen.* 1988, **11**, 1-157.
22. Badr, F. M. et al *Mutat. Res.* 1974, **26**, 529-534.
23. Erickson, S. et al *J. Lipid Res.* 1989, **30**(11), 1763-1771.
24. *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* 1997, EPA/630/R-96/012, Risk Assessment Forum, US Environmental Agency, Washington, DC 20460, USA.
25. Purdom, C.E. et al *Chem. Ecol.* 1994, **8**, 275-285.
26. Aherne, G. W. *J. Pharm. Pharmacol.* 1989, **41**(10), 735-736.
27. Guengerich, F. P. *Life Sci.* 1990, **47**(22), 1981-1988.
28. Cheek, A. O. *Environ. Health Perspect. Suppl.* 1998, **106**(1), 5-10

E67 ethiofencarb



$C_{11}H_{15}NO_2S$ **Mol. Wt.** 225.31 **CAS Registry No.** 29973-13-5

Synonyms 2-[(ethylthio)methyl]phenol, methylcarbamate; 2-(ethylthio)methylphenyl *N*-methylcarbamate; Bay-hox 1901; Croneton; Etocarb

EINECS No. 249-981-9 **RTECS No.** FC 2628000

Uses Soil and foliar insecticide, specific against aphids.

Physical properties

M. Pt. 33.4°C **B. Pt.** Decomp. on distillation. **Specific gravity** 1.231 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.04 **Volatility** v.p. 9.78×10^{-5} mmHg
Solubility Water: 1.8 g l^{-1} at 20°C. Organic solvents: dichloromethane, propanol, toluene

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, golden orfe 12.8, 61.8 mg l^{-1} (1).

Bioaccumulation
Unchanged ethiofencarb with its sulfoxide and sulfone metabolites and phenolic derivatives can be extracted from lettuce exposed to ethiofencarb (2).
When applied to land furrows, biological activity in foliage against *Myzus persicae* persisted in potato for 9 wk (3).

Environmental fate

Degradation studies
Plant metabolites included a sulfoxide and a sulfone (4).

Abiotic removal
Rate of photodegradation in water increased in the presence of humic substances (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral Japanese quail, canary 100-155 mg kg^{-1} (1).
LD_{50} oral hen 1 g kg^{-1} (1).
LD_{50} oral rat 200 mg kg^{-1} (6).
LC_{50} (4 hr) inhalation rat >0.25 mg l^{-1} (4).
LD_{50} dermal rabbit 2.5 g kg^{-1} (7).

Carcinogenicity and chronic effects
Rat (2 yr) in diet showed a no-effect level of 330 mg kg^{-1} diet (1).

Teratogenicity and reproductive effects
Oral pregnant ♀ rats 0.01 mg kg^{-1} day^{-1} was the maximum non-toxic dose to embryos, and 0.043 mg kg^{-1} day^{-1} was the minimum embryotoxic dose. Oral ♂ rats, 0.02 mg kg^{-1} day^{-1} was the maximum dose having a positive effect (8).
Spermatogenesis of intact rats of different growths and F_1 progeny were subjected to gonadotoxic action of ethiofencarb. Gonadotoxic action led to increased changes in sex cells, including polynuclear formation and a reduction in the total number of cells of spermatogenesis-related tissues and, primarily, the mononuclear cells (9).

Metabolism and toxicokinetics
Urine collected from rats dosed orally contains phenol sulfoxide and phenol sulfone (10).

Irritancy
Non-irritating to skin and eyes (species unspecified) (10).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive; TA1535 negative. Test strain AG26Z without metabolic activation positive (11).

Other effects

Any other adverse effects

Cholinesterase inhibitor and thus affects the nervous system of a variety of species (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (12).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).
WHO Toxicity Class II (14).
EPA Toxicity Class II (formulation) (1).
ADI 0.1 mg kg^{-1} body weight (1).
Tolerable daily intake (TDI) (human) 0.1 mg kg^{-1} (1).

Other comments

Food contaminant. Water pollutant.

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Cabras, P. et al *J. Chromatogr.* 1989, **462**, 430-431.
3. Woodford, J. A. al *Test Agrochem. Cultiv.* 1985, **6**, 24-25.
4. *Gig Sanit.* 1984, **49**(10), 23.
5. Jensen-Korte, U. et al *Sci. Total Environ.* 1987, **62**, 335-340.
6. *Farm Chemicals Handbook* 1983, C64, Meister Publishing, Willoughby, OH, USA.
7. *Mezhdunar. Kniga* 1984, **49**(10), 23.
8. Gritsevskaya, I. L. *Gig. Sanit.* 1988, **6**, 86-88 (Russ.) (*Chem. Abstr.* **109**, 87896n).
9. Ivanov, Y. V. *Gig. Tr. Prof. Zabol.* 1989, **3**, 54-55 (Russ.) (*Chem. Abstr.* **111**, 128458h).
10. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
11. Andreeva, I. V. *Gig. Sanit.* 1990, **1**, 59-62 (Russ.) (*Chem. Abstr.* **112**, No. 153499a).
12. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
13. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
14. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

E68 ethion

$$(CH_3CH_2O)_2P(S)SCH_2SP(S)(OCH_2CH_3)_2$$

$C_9H_{22}O_4P_2S_4$ **Mol. Wt.** 384.48 **CAS Registry No.** 563-12-2

Synonyms Ethopaz; phosphorodithioic acid, *S,S*-methylene, *O,O,O',O'*-tetraethyl ester; methylene-*S,S'*-bis(*O,O*-diethyldithiophosphate); ethyl methylene phosphorodithioate; Rodocid; Nialate; Cekuetion; Cethion; DEF; Ethanox; Hylemox; Moracap; Probeltion; Rhodacide; Solethion

EINECS No. 209-242-3 **RTECS No.** TE 4550000

Uses Insecticide. Non-systemic acaricide

Physical properties

M. Pt. −12°C to −13°C **B. Pt.** 164-165°C at 0.3 mmHg **Specific gravity** 1.220 at 20°C with respect to water at 4°C **Volatility** v.p. 1.5×10^{-6} mmHg at 25°C

Solubility Water: 2 ppm at 25°C. Organic solvents: acetone, chloroform, xylene

Occupational exposure

FR-VME 0.4 mg m^{-3}
US-TWA 0.4 mg m^{-3}
Supply classification toxic
Risk phrases Harmful in contact with skin – Toxic if swallowed (R21, R25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the eyes – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S25, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, cutthroat trout 220-720 μg l^{-1} (1).
LC_{50} (96 hr) scud 2-9 μg l^{-1} (2).

Environmental fate

Degradation studies
When applied to soil at an initial concentration of 10 ppm, sterile soil retained 50% for more than 24 wk, while non-sterile soil retained 5% for more than 24 wk (3).
Degradation in surface and groundwater is temperature dependent (4).

Abiotic removal
10 μg g l^{-1} of polluted river water in a sealed container was exposed to light, 50% remained at 8 wk (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral blackbird 45-58 mg kg^{-1} (6).
LD_{50} oral starling 304 mg kg^{-1} (6).
LD_{50} oral ♂ rat 54, ♀ 27 mg kg^{-1} (7).
LD_{50} dermal ♂ rat 245 mg, ♀ 62 mg kg^{-1} (7).

Sub-acute and sub-chronic data
Oral ♀ rat 300 ppm for 28 days in diet, showed no effect on growth. Cholinesterase activities were inhibited at doses >10 ppm (8).

Carcinogenicity and chronic effects
A 2-yr feeding study in which rats received the compound in diet established a no-effect level of 0.3 mg kg^{-1} day^{-1}. In dogs, the figure was 0.05 mg kg^{-1} day^{-1} (9).

Metabolism and toxicokinetics
Metabolised by oxidation to phosphorothioate followed by dealkylation and hydrolysis (10).
When administered to laying hens orally at 5 mg as ^{14}C-ethion, 69% was eliminiated in faeces. Highest levels were found in liver and kidney, lower levels in heart and brain. In eggs, higher levels found in yolk than in the white (11).
When administered to goats intravenously, residues from ^{14}C-ethion were detected in liver, kidney, fat and plasma 4 wk later. At 8 wk urinary metabolites were identified, 55% of dose was eliminated in urine within 2 wk and 27% in faeces (12).

Other effects

Any other adverse effects
A cholinesterase inhibitor, affecting the nervous systems in a variety of species. Subcutaneous doses of >400 mg kg^{-1} in atropinised chickens caused paralysis of leg muscles (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (13).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).
EPA Toxicity Class II (formulation) (9).
WHO Toxicity Class II (15).
ADI 0.002 mg kg^{-1} body weight (9).

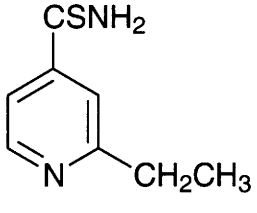
Other comments

Food contaminant. Water and air pollutant.
Compound is toxic to bees (10).
Toxicity reviewed (16).

References

1. *Fish Pesticide Research Lab.* 1971, Bureau of Sport Fish and Wildlife, Columbia, USA.
2. Sanders, H. O. *Fish Pesticide Res. Lab.* 1972, Bureau of Sport Fish and Wildlife, Columbia, USA.
3. Miles, J. R. W. *Bull. Environ. Contam. Toxicol.* 1979, **22**, 312-318.
4. Frank R. et al *Bull. Environ. Contam. Toxicol.* 1991, **47**(3), 371-380.
5. Eichelberger, J. W. *Environ. Sci. Technol.* 1971, **5**(6), 541-544.
6. Schafer, E. W. *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
7. Gaines, T. B. *Toxicol. Appl. Pharmacol.* 1969, **14**, 515.
8. *The Pesticide Manual* 1st ed., 1968, British Crop Protection Council, Farnham, UK.
9. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
10. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
11. Mosha, R. D. *Bull. Environ. Contam. Toxicol.* 1990, **45**(3), 375-381.
12. Mosha, R. D. *Pharmacol. Toxicol.* 1991, **69**(1), 34-37.
13. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
14. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
15. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
16. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(1), 9-37

E69 ethionamide



$C_8H_{10}N_2S$ **Mol. Wt.** 166.25 **CAS Registry No.** 536-33-4

Synonyms 2-ethyl-4-pyridinecarbothioamide; 2-ethylthioisonicotinamide; Aetina; Iridocin; Trescatyl; Trecator-SC

EINECS No. 208-628-9 **RTECS No.** NS 0350000

Uses Antibacterial (tuberculostatic).

Physical properties

M. Pt. 164-166°C (decomp.)
Solubility Organic solvents: hot acetone, pyridine

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1320 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 470 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 1350 mg kg^{-1} (2).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (3).
♂ and ♀ rats and mice receiving the compound in a National Toxicology Program test showed no evidence of carcinogenicity (4).
Oral mice (50 wk) 0.1 mg of 2% solution showed evidence of tumorigenic activity. Tumours of the thyroid were seen, and some papillary and epidermoid carcinomas (5).

Teratogenicity and reproductive effects
Oral, subcutaneous pregnant rat 54 and 270 mg kg^{-1}, respectively, on days 6-14 of pregnancy induced skeletal malformations in offspring (2).
Oral rabbit 13.5 and 27 mg kg^{-1} on day-14 of pregnancy caused no foetal malformations (2).

Metabolism and toxicokinetics
An oral dose of 1 g to humans gave peak plasma levels of 200 μg ml^{-3} at 3 hr (6).
Three metabolic pathways are known to exist, with metabolites excreted in urine. The thioketone group was hydrolysed to give ethylpyridine-4-carboxamide and the free carboxylic acid. The pyridinium *N*-atom was methylated, followed by hydroxylation at the 6-carbon atom to give *N*-methyl-2-ethylpyrid-6-one-4-thiocarboxamide. Sulfoxide was also produced (7-9).
S-oxidation by rat liver microsomes is mainly mediated by flavin-containing monoxygenases, but there may be cytochrome P_{450} involvement (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (11,12).

Other effects

Other adverse effects (human)
Toxic hepatitis has been associated with use of the compound and is accompanied by elevated levels of liver enzymes in plasma (13,14).

Any other adverse effects
Oral rat 100 mg kg^{-1} caused hepatotoxic and lipoperoxidation-enhancing effects. There were increases in serum alanine and aspartate aminotransferases along with an increase in conjugated dienes and malondialdehyde in liver, heart, lungs and kidney (15).

Other comments

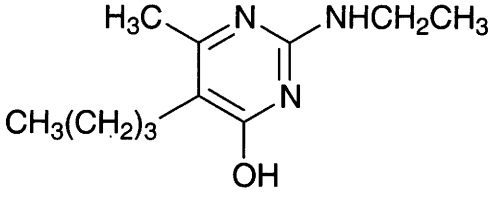
Active orally in man in doses from 250 mg twice daily (16).
Carcinogenicity and adverse health effects reviewed (17).

References

1. *Drugs in Japan, Ethical Drugs* 6th ed., 1982.
2. Dluzniewski, A. et al *Diss. Pharm. Pharmacol.* 1971, **23**, 383-392.

3. *IARC Monograph* 1987, **Suppl. 7**, 63.
4. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-046, NIEHS, Research Triangle Park, NC, USA.
5. Biancifiori, C. et al *Lav. Ist. Anat. Istol. Patol., Univ. Studi Perugia.* 1964, **24**, 145-166.
6. Goodman, Gilman, (Eds.) *The Pharmacological Basis of Therapeutics*, 5th ed., 1975, 1212-1213, Macmillan, New York, NY, USA.
7. Bieder, A. et al *Therapie* 1964, **19**(8), 897-907.
8. Bieder, A. et al *Ann. Pharm. Fr.* 1966, **24**, 493-500.
9. Ritter, W. *Prax. Pneumol.* 1973, **27**, 145.
10. Ruse, M. J. et al *Biochem. Soc. Trans.* 1991, **19**(2), 233S.
11. Zeiger, E. *Cancer Res.* 1987, **47**(5), 1287-1296.
12. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
13. Phillips, et al *Am. Rev. Respir. Dis.* 1963, **87**, 896-322.
14. Simon, E. et al *Scand. J. Respir. Dis.* 1969, **50**, 314-322.
15. Slivka, Y. I. *Probl. Tuberk.* 1987, **8**, 67-69 (Russ.) (*Chem. Abstr.* **108**, 15860c).
16. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
17. *IARC Monograph* 1983, **13**, 77

E70 ethirimol



$C_{11}H_{19}N_3O$ **Mol. Wt.** 209.29 **CAS Registry No.** 23947-60-6

Synonyms 4(*1H*)-pyrimidone, 5-butyl-2-(ethylamino)-6-methyl-; 2-(ethylamino)-4-methyl-5-*n*-butyl-6-hydroxypyrimidine; Milcurb; Milgo:PP149; ETH 560; Milstem

EINECS No. 245-949-3 **RTECS No.** UW 7380000

Uses Fungicide.

Physical properties

M. Pt. 159-160°C (phase change at 140°C) **Specific gravity** 1.21 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.3 at pH 7 and 20°C **Volatility** v.p. 2.0×10^{-6} mmHg at 25°C
Solubility Water: 150 mg l^{-1} at pH 7.3 and 20°C. Organic solvents: acetone, chloroform, ethanol, trichloroethylene

Occupational exposure

Supply classification harmful
Risk phrases Harmful in contact with skin (R21)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity
LC_{60} (96 hr) brown trout (fingerlings) 20 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} oral bees 1.6 mg bee^{-1} (2).

Environmental fate

Degradation studies

$t_{1/2}$ 3 days in plants (2).

$t_{1/2}$ 1 wk to 20 wk in soil, depending on conditions (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral cat, rat, rabbit 1-4 g kg^{-1} (3,4).

LD_{50} dermal rat 1 g kg^{-1} (1).

LD_{50} intravenous mouse 8 mg kg^{-1} (3).

Carcinogenicity and chronic effects

2-yr feeding trials in dogs established a no-effect level of 30 mg kg^{-1} (1).

2-yr feeding trials in rats established a no-effect level of 200 mg kg^{-1} diet (2).

Metabolism and toxicokinetics

After oral administration to rats, metabolised by hydroxylation of the butyl group (2).

Irritancy

Non-irritant to rabbit skin (2).

Mild irritant to rabbit eyes (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (5).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

WHO Toxicity Class Table 5 (7).

EPA Toxicity Class IV (formulation) (1).

Other comments

Soil and water pollutant.

Metabolism and mode of action reviewed (8).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Bebbington, R. M. et al *Chem. Ind. (London)* 1969, **42**, 1512.
4. Frear, E. H. (Ed.) *Pesticide Index* 1976, **5**, 106.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
8. Calderbank, A. *Acta Phytol. Pathol.* 1971, **6**, 355

E71 ethoate-methyl

$$CH_3CH_2NHC(O)CH_2SP(S)(OCH_3)_2$$

$C_6H_{14}NO_3PS_2$ **Mol. Wt.** 243.29 **CAS Registry No.** 116-01-8

Synonyms phosphorodithioic acid, *S*-[2-(ethylamino)-2-oxoethyl] *O,O*-dimethyl ester; *S*-(*N*-ethylcarbamoylmethyl) *O,O*-dimethyl phosphorodithioate; dimethoate ethyl; American Cyanamid 18706B/77; 2-dimethoxyphosphinothioylthio-*N*-ethylacetamide

EINECS No. 204-121-1 **RTECS No.** TE 0960000

Uses Superseded insecticide and acaricide.

Physical properties

M. Pt. 67-68°C **Specific gravity** 1.164 at 70°C

Solubility Water: 8.5 g l^{-1} at 26°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, olive oil, xylene

Occupational exposure

Supply classification harmful

Risk phrases Harmful in contact with skin and if swallowed (R21/22)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 125-350 mg kg^{-1}, respectively (1,2).

LD_{50} dermal rat 2 g kg^{-1} (1).

LD_{50} intramuscular rat 250 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Oral rat (50 day) 300 ppm diet caused no toxic symptoms (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

River water pollutant. Contaminant in drinking water.

Compound is an inhibitor of cholinesterase and thus affects the nervous systems of a variety of species (unspecified) (1,2).

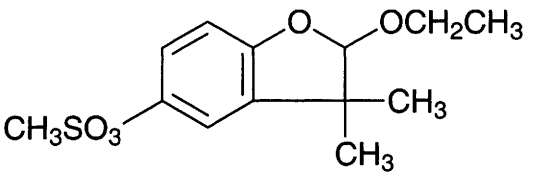
Biological activity reviewed (7).

References

1. *World Rev. Pest Control* 1970, **9**, 119.
2. *Special Publication of Entomological Society of America* 1974.
3. *Farmaco, Ed. Sci.* 1966, **21**, 443.
4. *The Pesticide Manual* 4th ed., 1974, 249, British Crop Protection Council, Farnham, UK.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.

6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. Haas, A. *Actual. Chim.* 1987, (5), 183-188

E72 ethofumesate



$C_{13}H_{18}O_5S$ **Mol. Wt.** 286.35 **CAS Registry No.** 26225-79-6

Synonyms 2-ethoxy-2,3-dihydro-3,3-dimethyl-5-benzofuranol, methanesulfonate; (2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl) methanesulfonate; Nortron; Tramat; NC 8438; Agrijet; Barclay Keeper; Boxer; Fumesin; Kemiron; Nortron; Prograss; Sabel; Tempest

EINECS No. 247-525-3 **RTECS No.** DF 7716500

Uses Pre- and post-emergence herbicide.

Physical properties

M. Pt. 70-72°C **Specific gravity** 1.14 **Partition coefficient** log P_{ow} 2.7 **Volatility** v.p. 6.45×10^{-7} mmHg at 25°C
Solubility Water: 50 mg l^{-1} at 25°C. Organic solvents: acetone, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) guppy 15 mg l^{-1} (1).
LC_{50} (96 hr) rainbow trout, bluegill sunfish, 11.91-20.2, 12.37-21.2 mg l^{-1}, respectively (1).

Invertebrate toxicity
Treatment inhibited growth and respiration of leached soil microorganisms. Does not affect oligotrophs but affects saprophytes (2).
No effect on honey bees by contact or orally 0.016 mg bee^{-1} (1).

Environmental fate

Degradation studies
Soil degradation $t_{1/2}$ >5 wk under moist warm conditions; under dry and cold conditions >14 wk (3).
Plants metabolised the compound to the 2-hydroxy and 2-oxo- derivatives (3).

Mammalian & avian toxicity

Acute data
LD_{50} mallard duck, bobwhite quail >3552, >8743 mg kg^{-1}, respectively (1).
LD_{50} oral rat >6.4 g kg^{-1} (4).
LD_{50} dermal rat 1.4 g kg^{-1} (1).

Sub-acute and sub-chronic data
LD_{50} (8 day) oral bobwhite quail, mallard duck >839, >1082 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects
2-yr feeding trials in rats yielded a no-effect level of >1 g kg^{-1} diet (1).

Irritancy
Mild skin irritant (species unspecified) (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
WHO Toxicity Class Table 5 (7).

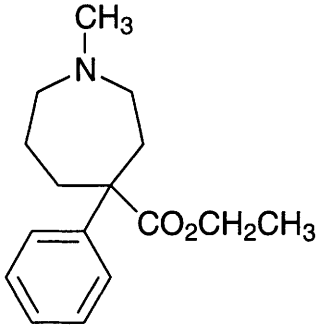
Other comments

Soil and groundwater pollutant.
The compound potentiates the toxicity of dinitroaniline herbicides to plants such as sugar beet (8).
Metabolic pathways reviewed (9).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Tyvryakanova, G. K. et *Agrokhimiya* 1987, **4**, 93-97 (Russ.) (*Chem. Abstr.* **107**, 2316j).
3. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
4. Lewis, R. J. (Ed.) *Registry Toxic Effects of Chemical Substances* 1979, 50.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
8. Warn J. E. *J. Am. Soc. Sugar Beet Technol.* 1987, **24**(1), 57.
9. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

E73 ethoheptazine



$C_{16}H_{23}NO_2$ **Mol. Wt.** 261.36 **CAS Registry No.** 77-15-6

Synonyms hexahydro-1-methyl-4-phenyl-1*H*-azepine-4-carboxylic acid, ethyl ester; 4-carbethoxy-1-methyl-4-phenylhexamethylenimine; ethyl heptazine; Wy-401; Zactane

EINECS No. 201-007-3 **RTECS No.** CM 2800000

Uses Analgesic for mild to moderate pain in humans, usually given orally in conjunction with a non-steroidal anti-inflammatory analgesic.

Physical properties

B. Pt. 133-134°C at 1 mmHg **Specific gravity** 1.038 at 26°C with respect to water at 4°C

Mammalian & avian toxicity

Metabolism and toxicokinetics

Compound can be detected in urine of humans after oral dosing (1).

Other effects

Other adverse effects (human)

Compound has a pethidine-like action affecting the central nervous system (2).

Other comments

Compound is one of those with potential for abuse by athletes (1).
Usually used as the citrate salt.

References

1. Caldwell, R. et al *Ann. Clin. Biochem.* 1989, **28**(5), 430-443.
2. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK

E74 ethoprophos

$$(CH_3CH_2CH_2S)_2P(O)OCH_2CH_3$$

$C_8H_{19}O_2PS_2$ **Mol. Wt.** 242.34 **CAS Registry No.** 13194-48-4

Synonyms *O*-ethyl-*S*,*S*-dipropyl phosphorodithioate; Prophos; Mocap; Ethoprop; Hellacap; Mucap; Sanimul

EINECS No. 236-152-1 **RTECS No.** TE 4025000

Uses Non-systemic insecticide. Nematocide.

Physical properties

B. Pt. 86-91°C at 0.2 mmHg **Specific gravity** 1.094 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.59 **Volatility** v.p. 3.5×10^{-4} mmHg at 26°C
Solubility Water: 700 mg l^{-1} at 20°C. Organic solvents: acetone, cyclohexane, diethyl ether, ethanol, xylene

Occupational exposure

Supply classification very toxic
Risk phrases Toxic if swallowed – Very toxic in contact with skin (R25, R27)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37/39, S45)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) goldfish, rainbow trout 13.6-13.8 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish 2.07 mg l^{-1} (1).

Invertebrate toxicity

When applied to turfgrass, a single application reduced earthworm population by 60-99% with effects lasting ≥20 wk. Rate of incorporation of humus into soil by surviving worms was also reduced (2).

Environmental fate

Degradation studies

$t_{1/2}$ in humic soil (pH 4.5) ≈87 days; in sandy loam soil (pH 7.2-7.3) $t_{1/2}$ 14-28 days (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral blackbird, chicken, starling, mallard duck 4.2-12.6 mg kg^{-1} (4-6).
LD_{50} dermal mallard duck 10.6 mg kg^{-1} (5).
LD_{50} oral rat, rabbit 34-55 mg kg^{-1} (1,4).
LD_{50} dermal rabbit 60 mg kg^{-1} (7).

Sub-acute and sub-chronic data

Chicks fed 50-200 ppm in diet for ≤3 wk. Only those groups receiving 50 ppm showed no fatalities. Plasma cholinesterase activity was inhibited 95% and weight loss was observed (4).
In a 90-day feeding trial no pathological or histological changes were observed in dogs receiving 100 mg kg^{-1} diet, although cholinesterase levels were inhibited (1).

Metabolism and toxicokinetics

Can be absorbed through skin (5,8).
Metabolic rate in rats depends on the capacity of carboxyesterase hydrolysis and the ability of metabolites to penetrate tissue, including the brain (9).

Other effects

Any other adverse effects

The compound inhibits cholinesterase activity and thus affects the nervous systems of a variety of species (unspecified) (4,5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
Partition coefficient exceeds EC limit of 3.0.
WHO Toxicity Class Ia (12).
EPA Toxicity Class II (formulation) (1).
ADI 0.0003 mg kg^{-1} body weight (1).

Other comments

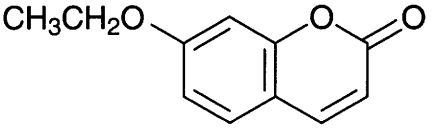
Land and water pollutant.
Growth of *Agrobacterium tumefaciens* was slightly inhibited by concentrations of 5 ppm. Growth of *Pseudomonas selanacearum*, *Azobacterichrococcum* and *Rhizobium japonicum* was stimulated by concentrations of 150 and 300 ppm (13).
Not toxic to bees (14).
Potency is 0.33 × that of ethyl parathion (8).
Metabolism reviewed (15).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.

2. Potter, D. A. *J. Econ. Entomol.* 1990, **83**(6), 2362-2369.
3. Smelt, J. H. et al *Pestic. Sci.* 1977, **8**, 147.
4. Sherman, M. et al *Toxicol. Appl. Pharmacol.* 1967, **11**, 49.
5. Hudson, R. H. *Toxicol. Appl. Pharmacol.* 1979, **49**, 451.
6. Schafer, E. W. *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
7. *World Rev. Pest Control* 1970, **9**, 119.
8. Knaak, J. B. et al *Bull. Environ. Contam. Toxicol.* 1987, **38**(5), 834-839.
9. Ershova, E. A. et al *Vestn. Akad. Med. Nauk SSSR* 1988, (5), 53-39 (Russ.) (*Chem. Abstr.* **109**, 144270e).
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
13. Ahmed, A. H. *Alexandria Sci. Exch.* 1990, **11**(4), 47-59.
14. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
15. Iqbal, Z. M. et al *Biochem. Pharmacol.* 1972, **21**, 1569

E75 7-ethoxycoumarin



$C_{11}H_{10}O_3$ **Mol. Wt.** 190.20 **CAS Registry No.** 31005-02-4

Synonyms 7-ethoxy-2*H*-1-benzopyran-2-one

EINECS No. 250-429-4

Uses Substrate for fluorometric assay of microsomal monooxygenase activity.

Physical properties

M. Pt. 88-90°C

Mammalian & avian toxicity

Metabolism and toxicokinetics

Metabolised in perfused rat intestinal epithelial cells, undergoing cytochrome P_{450}-dependent oxidative deethylation yielding 7-hydroxycoumarin, which then forms the glucuronide and sulfate conjugates. In the liver, sulfate conjugation predominates (1).

References

1. Albers, R. et al *Toxicol. Appl. Pharmacol.* 1991, **109**(3), 507-513

E76 2-ethoxyethanol

$$CH_3CH_2OCH_2CH_2OH$$

$C_4H_{10}O_2$ **Mol. Wt.** 90.12 **CAS Registry No.** 110-80-5

Synonyms ethylene glycol monoethyl ether; Cellosolve; Emkanol; 2-ethoxyethyl alcohol; ethyl cellosolve; ethylene glycol ethyl ether; glycol monoethyl ether; Oxitol; Soliviol; EGEE; EE Solvent; Ethyl Icinol; Polysolv EE

EINECS No. 203-804-1 **RTECS No.** KK 8050000

Uses Antifreeze. Catalyst. Solvent. Photographic developer. Fuel additive. Intermediate in organic synthesis.

Physical properties

M. Pt. –90°C **B. Pt.** 135°C **Flash point** 44°C **Specific gravity** 0.9310 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} –0.153 (1) **Volatility** v.p. 3.8 mmHg at 20°C ; v.den. 3.10
Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (19 mg m^{-3}) (sum of ether and acetate)
FR-VME 5 ppm (19 mg m^{-3})
JP-OEL 5 ppm (18 mg m^{-3})
SE-LEVL 5 ppm (19 mg m^{-3}) **SE-STEL** 10 ppm (40 mg m^{-3})
UK-LTEL MEL 10 ppm (37 mg m^{-3})
US-TWA 5 ppm (18 mg m^{-3})

UN No. 1171 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid
Supply classification toxic
Risk phrases May impair fertility – May cause harm to the unborn child – Flammable – Harmful by inhalation, in contact with skin and if swallowed (R60, R61, R10, R20/21/22)
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
LC_{50} (7 day) guppy 16,400 mg l^{-1} (2).
LC_{50} (24 hr) goldfish 5400 mg l^{-1} (3).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 430 ppm Microtox test (4).

Environmental fate

Degradation studies
Degraded anaerobically by the bacteria *Acetobacterium malicum* and *Pelobacter venetianus* isolated from freshwater sediments. Fermentation products were acetate and ethanol (5).
BOD_5 adapted sewage seed 65% ThOD; unadapted sewage seed 53 % ThOD (6).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere $t_{1/2}$ 11.4 hr (calc.) (7).
Adsorption onto activated carbon 63 mg g^{-1} carbon (8).

Adsorption and retention
K_{ow} 20.9 indicates that 2-ethoxyethanol will not bind strongly to soil and sediments (9).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2125-2450 mg kg^{-1} (10,11).
LC_{50} (7 hr) inhalation rat, mouse 1800-2000 ppm (12,13).
LD_{50} dermal rat, rabbit 3300, 3900 mg kg^{-1}, respectively (13,14).
LD_{50} intravenous rat 2400 mg kg^{-1} (13).
LD_{50} intraperitoneal mouse, rat 1700, 2800 mg kg^{-1}, respectively (15,16).

Teratogenicity and reproductive effects

Inhalation rat (7-13 or 14-20 days gestation) 900 ppm 7 hr day^{-1}, no offspring survived. Exposure to 200 ppm 7 hr day^{-1} caused ≈34% neonatal deaths. Prenatal exposure to 100 ppm caused behavioural and neurochemical alterations in offspring of rats (17).
Gavage ♂ rat (6 wk) 936 mg kg^{-1} day^{-1} on 5 day wk^{-1} caused testicular atrophy with decreased sperm count and sperm motility, and abnormal sperm morphology (18).
Intraperitoneal rat, 50 mg kg^{-1} on day 7-17 of gestation caused a reduction in maternal weight gain and 100% foetal mortality (19).

Metabolism and toxicokinetics

Following administration of ^{14}C-labelled 2-ethoxyethanol in drinking water at doses of 180-2600 mg l^{-1}, <5% was exhaled unmetabolised, 25-40% was eliminated as ethoxyacetic acid and 18% as ethylene glycol in the urine and 20% was exhaled as carbon dioxide (20).

Irritancy

Dermal rabbit 50 mg caused mild irritation and 50 mg instilled into rabbit eye caused moderate irritation (durations unspecified) (21).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1538 with and without metabolic activation negative (22).
Drosophila melanogaster sex-linked recessive lethal assay negative (22).
In vitro Chinese hamster ovary cells, sister chromatid exchanges without metabolic activation and chromosomal aberrations positive only without activation (23).

Legislation

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (24).

Other comments

Residues have been isolated from natural waters (25).
Environmental fate reviewed (25).
Reviews on experimental toxicology and human health effects listed (26).

References

1. Hansch, C. et al *Log P and Parameter Database: A Tool for the Quantitative Prediction of Bioactivity* 1983, Comtex Scientific Corporation, New York, NY, USA.
2. Konemann, W. H. *Quantitative Structure-Activity Relationships for Kinetics and Toxicity of Aquatic Pollutants and their Mixtures in Fish 1979*, Univ. Utrecht, Netherlands.
3. Lipnick, R. L. et al *Xenobiotica* 1987, **17**(8), 1011-1025.
4. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
5. Tanaka, K. et al *Arch. Microbiol.* 1988, **149**(3), 181-187.
6. Bridie, A. L. et al *Water Res.* 1979, **13**, 627-630.
7. *GEMS: Graphical Exposure Modeling System. Fate of Atmospheric Pollutants* 1986, US EPA Office of Toxic Substances, Washington, DC, USA.
8. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.

9. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods. Environmental Behaviour of Organic Pollutants* 1982, McGraw-Hill, New York, NY, USA.
10. *Gig. Tr. Prof. Zabol.* 1988, **32**(3), 48.
11. *Kodak Company Report* 1982, MSDS-10, 170A.
12. *J. Ind. Hyg. Toxicol.* 1943, **25**, 157.
13. *Raw Material Data Handbook: Organic solvents* 1974, **1**, 54, National Association of Printing Ink Research Institute, Bethlehem, PA, USA.
14. *Toxicologist* 1984, **4**, 180.
15. *Fed. Am. Soc. Exp. Biol: Fed. Proc.* 1947, **6**, 342.
16. *Arzneim.-Forsch.* 1971, **21**, 880.
17. *Neurotoxicology* 1981, **2**, 231.
18. Oudiz, D. et al *Toxicol. Appl. Pharmacol.* 1986, **84**(3), 576-583.
19. Wicknamaratne, G. A. de S. *Teratogen., Carcinogen., Mutagen.* 1987, **7**(1), 73-83.
20. Medinsky, M. A. et al *Toxicol. Appl. Pharmacol.* 1990, **102**(3), 443-455.
21. *Union Carbide Data Sheet* 1966, Union Carbide Corporation, New York, NY, USA.
22. McGregor, D. B. *Environ. Health Perspect.* 1984, **57**, 97-103.
23. Galloway, S. M. et al *Environ. Mol. Mutagen.* 1987, **10**(Suppl.10), 1-175.
24. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
25. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, **2**, 258-262, Lewis Publishers, Chelsea, MI, USA.
26. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E77 2-(2-ethoxyethoxy)ethanol acetate

$$CH_3CH_2O(CH_2)_2O(CH_2)_2C(O_2)CH_3$$

$C_8H_{16}O_4$ **Mol. Wt.** 176.21 **CAS Registry No.** 112-15-2

Synonyms carbitol acetate; diethylene glycol monoethyl ether acetate

EINECS No. 203-940-1 **RTECS No.** KK 8925000

Uses Solvent.

Physical properties

M. Pt. –25°C **B. Pt.** 218-219°C (98% purity) **Flash point** 95°C (open cup) (98% purity)
Specific gravity 1.0114 at 20°C with respect to water at 20°C **Volatility** v.p. 0.05 mmHg at 20°C ; v.den. 6.07
Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol, vegetable oil

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, rat 4, 11 g kg^{-1}, respectively (1,2).
LD_{50} dermal rat, rabbit 8, 15 g kg^{-1}, respectively (1,3).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation (1).
500 mg instilled into rabbit eye caused moderate irritation, 125 mg caused mild irritation (3).

Legislation

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

Reviews on experimental toxicology and human health effects listed (5).

References

1. *Union Carbide Data Sheet* 1965, Union Carbide Corporation, New York, NY, USA.
2. *J. Ind. Hyg. Toxicol.* 1941, **23**, 259.
3. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data Sheets* 2nd ed., 1988, **1**, 1556, Sigma-Aldrich, Milwaukee, WI, USA.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E78 1-ethoxyethyl acetate

$$CH_3CH_2OCH(O_2CCH_3)CH_3$$

$C_6H_{12}O_3$ **Mol. Wt.** 132.16 **CAS Registry No.** 1608-72-6

Synonyms 1-ethoxy-1-ethanol acetate

EINECS No. 216-537-0

Other comments

Role of atmospheric oxidation has been discussed (1).

References

1. Hartmann, D. L. *Commun. Eur. Communities* EUR10832 *Phys. Chem. Behaviour Atmos. Pollut.* 1987, 223-235

E79 2-ethoxyethyl acetate

$$C_2H_5OCH_2CH_2(O)OCCH_3$$

$C_6H_{12}O_3$ **Mol. Wt.** 132.16 **CAS Registry No.** 111-15-9

Synonyms ethylene glycol monoethyl ether acetate; 2-ethoxyethanol acetate; cellosolve acetate; β-ethoxyethyl acetate; ethyl cellosolve acetate; *O*-ethylglycol acetate; oxitol acetate; ethyl glycol acetate; Poly-solv EE acetate

EINECS No. 203-839-2 **RTECS No.** KK 8225000

Uses Absorbent for carbon dioxide. Catalyst. Solvent. Automobile lacquers.

Physical properties

M. Pt. -62°C **B. Pt.** 152-156°C **Flash point** 56°C (open cup) **Specific gravity** 0.9748 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 0.65 (1) **Volatility** v.p. 1.2 mmHg at 20°C ; v.den. 4.72 **Solubility** Water: 230 g l^{-1} at 20°C (2). Organic solvents: acetone, diethyl ether, ethanol, olive oil

Occupational exposure

DE-MAK 5 ppm (27 mg m^{-3}) (sum of ether and acetate)
FR-VME 5 ppm (27 mg m^{-3})
JP-OEL 5 ppm (27 mg m^{-3})
SE-LEVL 5 ppm (30 mg m^{-3}) **SE-STEL** 10 ppm (50 mg m^{-3})
UK-LTEL MEL 10 ppm (55 mg m^{-3})
US-TWA 5 ppm (27 mg m^{-3})

UN No. 1172 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid
Supply classification toxic
Risk phrases May impair fertility – May cause harm to the unborn child – Harmful by inhalation, in contact with skin and if swallowed (R60, R61, R20/21/22)
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
LC_{50} (24 hr) goldfish 160 mg l^{-1} (1).
LC_{50} (24, 48, 96 hr) fathead minnow 44, 43.5, 42.2 mg l^{-1}, respectively (3).

Bioaccumulation
Calculated bioconcentration factor 0.6 indicates that environmental accumulation is unlikely (4).

Environmental fate

Degradation studies
BOD_5 41% ThOD (5).

Abiotic removal
Volatilisation from model river water, $t_{1/2}$ 34 days, and from model pond water, $t_{1/2}$ 1 yr (4,6).
92% removal from wastewater by treatment with UV irradiation and hydrogen peroxide (7).
Reaction with photochemically produced hydroxyl radicals, $t_{1/2}$ (est.) ≈29 hr (8).
Adsorption by activated carbon 132 mg g^{-1} carbon (9).

Adsorption and retention
Calculated K_{oc} 5 indicates that adsorption onto soil and sediments will not occur (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, rat 1950, 2900 mg kg^{-1}, respectively (10,11).
LC_{50} (8 hr) inhalation rat 12,100 mg m^{-3} (12).
LD_{50} dermal rabbit 10,500 mg kg^{-1} (13).
LD_{50} intraperitoneal mouse 1420 mg kg^{-1} (14).
Acute toxic effect in rats and rabbits after oral administration was severe haematuria. Dermal exposure mainly induced a marked decrease in white blood cells. Inhalation exposure produced kidney injury, necrosis and glomerular injury (10).

Teratogenicity and reproductive effects
Inhalation rat, 600 ppm for 7 hr day^{-1} on day 7-15 of gestation, induced complete resorption of litters. 390 ppm reduced foetal weights and induced skeletal and cardiovascular defects (15).
Oral mouse, administration at sub-acute levels 5 day wk^{-1} for 5 wk caused testicular atrophy and leucopenia (16).

Metabolism and toxicokinetics
The urinary metabolite following inhalation exposure of human volunteers was ethoxyacetic acid, $t_{1/2}$ 23 hr (17).

Irritancy

Dermal rabbit 490 mg caused mild irritation and 40 mg instilled into rabbit eye caused moderate irritation (duration unspecified) (13).

Other effects

Other adverse effects (human)

The menstrual histories were obtained for 52 women exposed to 2-ethoxyethyl acetate in the liquid crystal display manufacturing industry and 55 non-exposed controls. Individual exposures were monitored during the entire 8-hr shift using passive dosimeters and by start- and end-of-shift urine analysis. The workers were exposed to a mean time-weighted average of 0.51 ppm of the glycol ether. No significant differences were observed between the exposed and control subjects for duration of each menstual cycle, days of the menses and amount of flow (18).

Legislation

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (19).

Other comments

Toxicity reviews cited (20).

Autoignition temperature 379°C.

References

1. Lipnick, R. L. et al *Xenobiotica* 1987, **17**(8), 1011-1025.
2. *Environmental Properties of Chemicals* Research Report 91, 658-662 Ministry of the Environment, 1990, VAPK-Publishing, Helsinki, Finland.
3. Holcombe, G. W. et al *Environ. Pollut., Ser. A* 1984, **35**, 367-381.
4. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
5. Bridie, A. L. et al *Water Res.* 1979, **13**, 627-630.
6. *EXAMS II Computer Simulation* 1987, USEPA, Washington DC, USA.
7. Hirose, M. et al *Jpn. Kokai Tokkyo Koho JP. 62,262,792, [87,262,792] (Cl. CO2 F1/72)* 1987, (Iwasaki Electric Co Ltd; NEC Environmental Engineering Ltd).
8. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
9. Guisti, D. M. et al *J. Water Pollut. Control. Fed.* 1974, **46**(5), 947-965.
10. Truhaut, R. et al *Toxicol. Appl. Pharmacol.* 1979, **25**(1), 117.
11. *USEPA 8EHQ-0682- 0450* 1982, Office of Pesticides and Toxic Substances, Washington DC, USA.
12. *Am. Ind. Hyg. Assoc. J.* 1959, **20**, 364.
13. *Union Carbide Data Sheet* 1967, Union Carbide Corp., New York, NY, USA.
14. *Shell Chemical Co. Report* 1961, 2.
15. Nelson, B. K. et al *Environ. Health Perspect.* 1984, **57**, 261-271.
16. Nagaro, K. et al *Sangyo Igaku* 1979, **21**(1), A29.
17. Groeseneken, D. et al *Br. J. Ind. Med.* 1987, **44**(7), 488-493.
18. Chia, S. E. et al *Am. J. Ind. Med.* 1997, **31**(2), 248-152.
19. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
20. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E80 2-ethoxyethyl ether

$$CH_3CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_3$$

$C_8H_{18}O_3$ **Mol. Wt.** 162.23 **CAS Registry No.** 112-36-7

Synonyms bis(2-ethoxyethyl) ether; diethylene glycol diethyl ether; 1,1'-oxybis(2-ethoxyethane); diethyl carbitol; ethyl diglyme; 3,6,9-trioxaundecane

EINECS No. 203-963-7 **RTECS No.** KN 3339000

Uses Solvent.

Physical properties

M. Pt. –44.3°C **B. Pt.** 180-189°C **Flash point** 71°C (open cup) (99+% purity) **Specific gravity** 0.9082 at 20°C with respect to water at 20°C **Volatility** v.p. 0.5 mmHg at 25°C ; v.den. 5.6
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies
BOD_{10} 0.10 mg l^{-1} O_2 for standard dilute sewage (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4970 mg kg^{-1} (2).
LD_{50} oral guinea pig 1850 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Inhalation rat, 400 ppm 7 hr day^{-1} for 17 days caused restlessness. Autopsy revealed normal organs (4).

Teratogenicity and reproductive effects
Gavage rabbit, 0, 50, 200 or 400 mg kg^{-1} $days^{-1}$ on days 6-19 of gestation. Maternal toxicity and reduced ♀ foetal weight was observed for the high dose (5).
Gavage mouse 3000 mg kg^{-1} on days 6-13 of gestation reduced maternal weight gain, but had no effect on the offspring (6).

Irritancy
50 mg instilled into rabbit eye caused moderate irritation (exposure not specified) (2).

Other effects

Any other adverse effects
Intraduodenal injection of 1 ml kg^{-1} rats stimulated choleresis (7).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

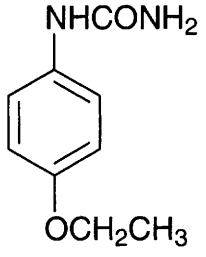
Autoignition temperature 205°C

References

1. Mills, E. J. et al *Proc. 8th Purdue Ind. Waste Conf.* 1953, 492.
2. *Union Carbide Data Sheet* 25 April 1958.

3. Smyth, H. F. et al *J. Ind. Hyg. Toxicol.* 1941, **23**, 259.
4. Cage, J. C. *Br. J. Ind. Med.* 1970, **27**.
5. Sleet, R. et al *Report* 1987, RTI-184, NTP-88018, Research Triangle Park, NC, USA.
6. Hardin, B. D. et al *Teratog., Carcinog., Mutagen.* 1987, **7**, 29-48.
7. Crose, G. et al *Boll. – Soc. Ital. Biol. Sper.* 1973, **49**(11), 653.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E81 4-ethoxyphenylurea



$C_9H_{12}N_2O_2$ **Mol. Wt.** 180.21 **CAS Registry No.** 150-69-6

Synonyms *p*-phenetolcarbamide; *p*-phenetylurea; Dulcin; Sucrol; Valzin

RTECS No. YT 2275000

Uses Non-nutritive sweetener (about 250 times as sweet as cane sugar).

Physical properties

M. Pt. 173-174°C

Solubility Water: 1.25 g l^{-1}. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat (adult) 3.2 g kg^{-1} (1).

LD_{50} oral rat (young) 4.9 g kg^{-1} (1).

LD_{Lo} oral dog 1 g kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rat, 0.5 g kg^{-1} body weight daily, lethal within several days to a few weeks (1,3).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (4).

Teratogenicity and reproductive effects

Intragastric mice (8-10 day gestation), 10-50 mg kg^{-1} body weight. No malformations were seen on 18-day foetuses. The offspring of mice treated on days 6-7 of pregnancy suffered retarded growth and in some cases death (5).

Metabolism and toxicokinetics

Rapidly absorbed following oral administration to rats. Highest concentrations are found in the liver, kidneys, brain and lungs. Tissue levels fall to one-tenth within 24 hr after dosing (6).

Rabbits dosed with 4-ethoxyphenylurea excreted 3% unchanged in the urine, 27% as the *N*-glucuronide, 40% (collectively) as *p*-hydroxyphenylurea and its *O*-sulfate and *O*-glucuronide, and a small amount of *p*-aminophenol (7).

Genotoxicity

4-Ethoxyphenylurea has tumorigenic potentialities and should not be used as a food additive (8).

Other effects

Other adverse effects (human)

Human volunteers (including diabetics) ingesting 0.1-0.6 g day^{-1} for a year suffered no adverse effects (9). Two deaths in children have been associated with the ingestion of 8-10g 4-ethoxyphenylurea. Doses of 20-40g caused dizziness, nausea, methaemoglobinaemia with cyanosis, hypotension, and, in one case, coronary disturbance (10).

Other comments

Carcinogenic risk to man reviewed (11).

References

1. Bekemeier, H. et al *Arzneim.-Forsch.* 1958, **8**, 150-151.
2. *Abdernalden's Handbuch der Biologischen Arbeitsmethoden*, Leipzig, Germany, 1935, **4**, 1345.
3. Lettre, H. et al *Naturwissenschaften* 1955, **42**, 217.
4. *IARC Monograph* 1987, **Suppl. 7**, 63.
5. Tanaka, R. *Japan. J. Publ. Hlth.* 1964, **11**, 909-915.
6. Agaki, M. et al *Chem. Pharm. Bull.* 1965, **13**, 1200-1206.
7. Agaki, M. et al *Chem. Pharm. Bull.* 1966, **14**, 1-9.
8. *Eleventh Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Tech. Rep. Ser. 383*, 1968, 13.
9. Rost, E. et al *Arb. Reichgesundh. Amte* 1926, **57**, 212-220.
10. Buhr, G. *Med. Klinik* 1948, **43**, 105-108.
11. *IARC Monograph* 1976, **12**, 97-105

E82 1-ethoxypropane

$$CH_3CH_2CH_2OCH_2CH_3$$

$C_5H_{12}O$ **Mol. Wt.** 88.15 **CAS Registry No.** 628-32-0

Synonyms ethyl propyl ether; propyl ethyl ether

EINECS No. 211-036-3 **RTECS No.** KO 0600000

Uses Solvent.

Physical properties

M. Pt. 79°C **B. Pt.** 64°C **Flash point** < -20°C **Specific gravity** 0.7386 at 20°C with respect to water at 4°C
Solubility Organic solvents: acetic acid, diethyl ether, ethanol

Occupational exposure

UN No. 2615 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LC_{50} (15 min) inhalation mouse 220 mg m^{-3} (1).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. *Anesthesiology* 1950, **11**, 455.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E83 2-ethoxypropane

$$(CH_3)_2CHOCH_2CH_3$$

$C_5H_{12}O$ **Mol. Wt.** 88.15 **CAS Registry No.** 625-54-7

Synonyms ethyl isopropyl ether; isopropyl ethyl ether

EINECS No. 210-900-7 **RTECS No.** KO 0250000

Occurrence Naturally, in leaf oil of plants.

Physical properties

B. Pt. 53-54°C **Specific gravity** 0.720 at 25°C with respect to water at 4°C

Solubility Water: miscible. Organic solvents: acetone, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LC_{50} (15 min) inhalation mouse 220 mg m^{-3} (1).

References

1. *Anesthesiology* 1950, **11**, 455

E84 1-ethoxy-2-propanol

$$H_3CH_2COCH_2CH(OH)CH_3$$

$C_5H_{12}O_2$ **Mol. Wt.** 104.15 **CAS Registry No.** 1569-02-4

EINECS No. 216-374-5 **RTECS No.** UB 5250000

Physical properties

B. Pt. 131°C at 760 mmHg **Specific gravity** 0.9028 at 20°C with respect to water at 4°C

Solubility Organic solvents: diethyl ether, ethanol

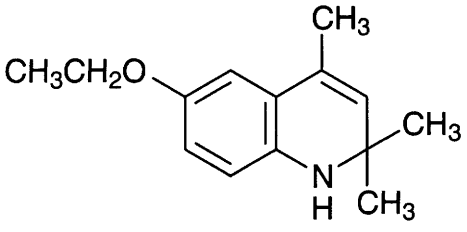
Other comments

Reviews on human health effects, environmental effects, experimental toxicity, ecotoxicology, exposure levels and hazard assessment listed (1).

References

1. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E85 ethoxyquin



$C_{14}H_{19}NO$ **Mol. Wt.** 217.31 **CAS Registry No.** 91-53-2

Synonyms 6-ethoxy-1,2-dihydro-2,2,4-trimethylquinoline; 1,2-dihydro-2,2,4-trimethyl-6-ethoxyquinoline; Niflex; Santoflex; Santoquin; Scam

EINECS No. 202-075-7 **RTECS No.** VB 8225000

Uses Antioxidant for foods and rubber products. Superseded plant growth regulator.

Physical properties

B. Pt. 118-123°C at 1 mmHg **Specific gravity** 1.030 at 25°C with respect to water at 25°C
Volatility v.den. 7.48

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin (S2, S24)

Ecotoxicity

Fish toxicity
No effect on growth was observed in rainbow trout fed for 20 wk on a diet containing ethoxyquin. Serum activity levels of glutamate-oxalacetate transaminase, lactate dehydrogenase and creatine kinase were all increased. The increase was attributed to tissue damage (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 800, 1920 mg kg^{-1}, respectively (2,3).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Oral mouse (10 wk) 0.25% diet caused a significant augmentation of primary immune response assayed by the Jerne haemolytic plaque technique (5).

Carcinogenicity and chronic effects
Newborn mouse tumourigenesis assay: 30 mg (total dose) injected subcutaneously into 24-hr-old mice. Statistically significant increase in lung tumours in ♀ reported after 1 yr (6).

Teratogenicity and reproductive effects
Oral rat, 125-500 mg kg^{-1} day^{-1} on day 6-15 of gestation caused no teratogenic effects (7).

Metabolism and toxicokinetics
Following oral administration of 0-5% of the hydrochloride in the diet of mice, tissue residue levels were monitored for 14 wk. The mean ethoxyquin residues ranged from 0.84-4.58 μg g^{-1} liver and 0.11-0.92 μg g^{-1} brain (8).
In rats, the major metabolic reaction identified was deethylation of ethoxyquin to produce 6-hydroxy-2,2,4-trimethyl-1,2-dihydroquinoline and 2,2,4-trimethylquinoline. Hydroxylation also occurred (9).

Sensitisation
Two cases of sensitivity reported in animal feed workers. Contact dermatitis attributed to the additives in animal feed (10).

Genotoxicity

Salmonella typhimurium TA1538 with and without metabolic activation negative (11-13).
Escherichia coli PQ 37 SOS Chromotest with and without metabolic activation negative (13).

Other effects

Any other adverse effects
Oral rat 0.5% (duration unspecified) caused severe kidney damage, renal calcification from renal papilla to pelvis. However, the treatment completely prevented the formation of aflatoxin B_1-induced preneoplastic liver lesions (14).
Doses of <150 ppm in diet of marmoset increased mortality. In rats, growth depression, pathological changes to kidney, liver and blood and death occurred (15).
Low chronic toxicity in rats, 0.2% in diet caused transient depression in growth rate. At autopsy damage was apparent in kidneys, liver and thyroid gland in ♂ only (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (17).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).
EPA Toxicity Class III (3).

Other comments

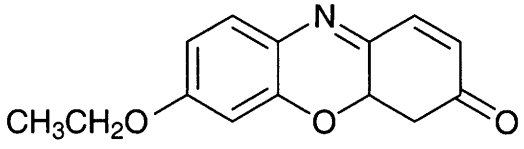
Metabolism reviewed (9,19).

References

1. Oberbach, H. *Fett. Wiss. Technol.* 1988, **90**(6), 226-230 (Ger.) (*Chem. Abstr.* **109**, 109247f).
2. *Rubber Chem. Technol.* 1972, **45**, 627.
3. *The Pesticide Manual* 9th ed., 1991, 350, British Crop Protection Council, Farnham, UK.
4. *NTIS Report AD277-689* Natl. Tech. Inf. Ser., Springfield, VA, USA.
5. Good, R. W. et al *J. Tenn. Acad. Sci.* 1989, **64**(4), 217-220.
6. Fuji, K. *Carcinogenesis (London)* 1991, **12**(8), 1409-1415.
7. Khera, K. S. *J. Environ. Sci. Health, Part B* 1979, **14B**(6), 563-578.

8. Kim, H. L. *J. Toxicol. Environ. Health* 1991, **33**(2), 229-236.
9. Skaare, J. V. *Xenobiotica* 1979, **9**, 640.
10. Burrows, D. *Br. J. Dermatol.* 1975, **92**(2), 167-170.
11. Yamaguchi, T. et al *Eisei Kagaku* 1991, **37**(1), 6-13 (Japan.) (*Chem. Abstr.* **115**, 2940y).
12. Klopman, G. et al *Mutat. Res.* 1990, **228**, 1-50.
13. von der Hude, W. et al *Mutat. Res.* 1988, **203**(2), 81-94.
14. Manson, M. M. et al *Carcinogenesis (London)* 1987, **8**(5), 723-728.
15. McIntosh, G. H. *Aust. Vet. J.* 1986, **63**(1), 385-386.
16. *Garner's Veterinary Toxicology* 3rd. ed., 1967, 287, Williams & Wilkins, Baltimore, MD, USA.
17. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
18. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
19. Wilson, R. H. et al *Agric. Food Chem.* 1959, **7**, 206

E86 7-ethoxyresorufin



$C_{14}H_{11}NO_3$ **Mol. Wt.** 241.25 **CAS Registry No.** 5725-91-7

Synonyms 7-ethoxy-3*H*-phenoxazin-3-one; 7-hydroxy-3*H*-phenoxazin-3-one, ethyl ether

Uses Redox indicator for titanometry and stannometry. Fluorometric substrate for cytochrome P_{450}-linked mixed function oxidase enzymes.

Physical properties

M. Pt. 225°C

Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Metabolism and toxicokinetics

Undergoes *O*-deethylation by cytochrome P_{450} isoenzymes of lung and liver microsomes (1,2).

References

1. von Bahr, C. et al *Microsomes Drug Oxid., Proc. Int. Symp., 6th 1984* 1985, 370-379.
2. Philpot, R. M. et al *Microsomes Drug Oxid., Proc. Int. Symp., 6th 1984* 1985, 248-255

E87 ethyl acetate

$$CH_3CO_2CH_2CH_3$$

$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 141-78-6

Synonyms acetic ether; ethyl ethanoate; vinegar naphtha; acetoxyethane

EINECS No. 205-500-4 **RTECS No.** AH 5425000

Uses Used in artificial fruit essences. As a solvent for nitrocellulose, varnishes, lacquers and in cleaning textiles. In the manufacture of photographic film, artificial silk and perfumes.

Physical properties

M. Pt. –83°C **B. Pt.** 76-77°C **Flash point** –4.4°C (closed cup) **Specific gravity** 0.900 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.73 **Volatility** v.p. 100 mmHg at 27°C ; v.den. 3.04
Solubility Water: 100 ml l^{-1} at 25°C. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 400 ppm (1500 mg m^{-3})
FR-VME 400 ppm (1400 mg m^{-3})
JP-OEL 200 ppm (720 mg m^{-3})
SE-LEVL 150 ppm (500 mg m^{-3}) **SE-STEL** 300 ppm (1100 mg m^{-3})
UK-LTEL 400 ppm (1460 mg m^{-3})
US-TWA 400 ppm (1440 mg m^{-3})

UN No. 1173 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Do not breathe vapour – Do not empty into drains – Take precautionary measures against static discharges (S2, S16, S23, S29, S33)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) common Indian catfish 212 mg l^{-1}. Lowering of hepatic glycogen, hyperglycaemia and hyperlacticaemia reported (1).
LC_{50} (96 hr) fathead minnow 230 mg l^{-1} (2).
In fish, ethyl acetate is metabolised by *in vivo* hydrolysis of carboxylic acid esters. Lethal properties of this class of compounds cannot be compared unless relative carboxylase esterase activities for the species are known (3).

Invertebrate toxicity
Cell multiplication inhibition test, *Pseudomonas putida* 650 mg l^{-1}, *Entosiphon sulcatum* 202 mg l^{-1} (4).

Toxicity to other species
LC_{50} (48 hr) Mexican axolotl 150 mg l^{-1} (5).

Environmental fate

Nitrification inhibition
Nitrosomonas growth inhibited by 50% at 18 g l^{-1} (6).

Anaerobic effects
96% utilisation occurred in an anaerobic reactor with a 20-day retention time (7).

Degradation studies

BOD_5 36-68% reduction in dissolved oxygen using sewage inoculum (8-11).

100% degradation occurred in 20 hr using activated sludge (12).

Abiotic removal

Photochemical reactivity, $t_{1/2}$ 2-8 days, variance depended on atmospheric conditions (13).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 11.3 mg kg^{-1} (14).

LC_{50} (8 hr) inhalation rat 1600 ppm (15).

LC_{Lo} (1 hr) inhalation mouse 31 mg m^{-3} (16).

♂ CFW albino mice were exposed to 0-8000 ppm acetate vapour for 20 min. Decrease in locomotor activity at the higher levels; LOEC 2000 ppm. High concentration also affected observed functional behaviour. Recovery was rapid (17).

LD_{50} intraperitoneal mouse 709 mg kg^{-1} (18).

Sub-acute and sub-chronic data

Inhalation rats, mice 10 and 43 mg m^{-3} for 90 days, increased numbers of leukocytes, decreased blood cholinesterase activity and liver mixed-function oxidase activity reported (19).

Teratogenicity and reproductive effects

Inhalation ♂ rat 2 × day^{-1} for 7 days caused a decrease in the weight of the testes and accessory reproductive organs, as well as reducing acid phosphatase activity in the prostate and plasma testosterone levels. Body weight was also decreased, as were spermatozoa levels in the epididymis (20).

Metabolism and toxicokinetics

The extent of metabolism of ethyl acetate inspired into the upper respiratory tract was measured as 40-65% in rats and 63-90% in hamsters (21).

Following exposure to 402 ppm for 4 hr, ethanol, as a metabolite, was measured in alveolar air at a concentration of 4.2 ppm (22).

Irritancy

Irritant to mucous membranes, especially eyes, buccal cavity and respiratory passage (23).

The skin on hands of workers exposed to ethyl acetate measured pH 6.6-8.4, compared with the pH 3-6 of controls. Dermatitis is reported to have developed on the hands of workers exposed to ethyl acetate (24).

Shows mild to moderate *in vitro* activity in the bovine corneal opacity assay for ocular irritancy (25).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (26).

Saccharomyces cerevisiae, increased aneuploidy frequency (27).

Chinese hamster V79 cells negative for micronuclei induction (28).

Vicia faba induced stimulation of mitotic index and chromosome aberrations in anaphase cells and micronuclei in interphase cells (29).

Other effects

Other adverse effects (human)

Increased levels of serum bile acids, indicative of early signs of liver failure, were found in a group of workers exposed to a mixture of organic solvents including ethyl acetate (30).

Any other adverse effects

Inhalation rat (4 hr), unspecified concentration caused leucopenia without any change in differential or red blood cell count (30).

Other comments

Human odour perception 0.6 mg m^{-3} (16).
Considered safe for use as a cosmetic ingredient (31).
Reviews on experimental toxicology, exposure and human health effects listed (32).

References

1. Gupta, A. B. et al *Ecotoxicol. Environ. Saf.* 1982, **6**(2), 166-170.
2. Brooke, L. T. et al *Acute Toxicities of Organic Chemicals to Fathead Minnows* 1984, 27, Center for Lake Superior Environmental Studies, Univ. of Wisconsin, WI, USA.
3. Kamlet, M. J. et al *Environ. Sci. Technol.* 1987, **21**, 149-155.
4. Bringmann, G. et al *Water Res.* 1980, **14**, 231.
5. Sloof, W. et al *Bull. Environ. Contam. Toxicol.* 1980, **24**, 439.
6. Clark, C. et al *J. Bact.* 1967, **93**, 1309.
7. Chou, W. L. et al *Biotech. Bioeng. Symp.* 1979, **8**, 391-414.
8. Price, K. S. et al *J. Water Pollut. Control Fed.* 1974, **46**, 63-77.
9. Ettinger, M. B. *Ind. Eng. Chem.* 1956, **48**, 256-259.
10. Young, R. H. F. et al *J. Water Pollut. Control Fed.* 1968, **40**, 354-368.
11. Heukelekian, H. et al *J. Water Pollut. Control Assoc.* 1955, **29**, 1040-1053.
12. Slave, T. et al *Rev. Chim.* 1974, **25**, 666-670.
13. Campbell, I. M. et al *Chem. Phys. Lett.* 1978, **53**, 385-389.
14. Smyth, H. F. et al. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
15. *Patty's Industrial Hygiene and Toxicology* 2nd ed., 1958-1963, Interscience Publishers, New York, NY, USA.
16. *Commun. Eur. Commun. Rep. Ethyl Acetate* 1988, European Atomic Energy Community, EUR11553.
17. Bowen, S. E. et al *Fundam. Appl. Toxicol.* 1997, **35**(2), 189-196.
18. Sax, N. I. *Dangerous Properties of Industrial Materials* 7th ed., 1989, Van Nostrand Reinhold, New York, NY, USA.
19. Solomin, G. I. et al *Kosm. Biol. Aviakosmicheskaya Med.* 1975, **9**(1), 40-44.
20. Yamada, K. *Biol. Pharm. Bull.* 1993, **16**(4), 425-427.
21. Morris, J. B. *Toxicol. Appl. Pharmacol.* 1990, **102**(2), 331-345.
22. Vangala, R. R. et al *Arch. Toxicol.* 1991, **14**(Recent Dev. Toxicol.: Trends, Methods Probl.), 259-262.
23. Gu, Z. et al *Weisheng Dulixue Zazhi* 1988, **2**(1), 1-4 (*Chem. Abstr.* **112**, 93613w).
24. Mirzoyan, I. M. *Vop. Gig. Tr. Profzabol. Mater. Nauch Konf.* 1971, 244-246, A. P. Filin (Ed.) (*Chem. Abstr.* **116**, 10900w).
25. Gautheron, P. et al *Fund. Appl. Toxicol.* 1992, **18**(3), 442-449.
26. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141.
27. Mayer, V. M. et al *Mutat. Res.* 1987, **187**(1), 31-35.
28. Franco, G. et al *Occup. Environ. Chem. Hazard* 1986, 173-177.
29. Gomez-Arroyo, S. et al *Cytologia (Tokyo)* 1986, **51**(1), 133-142.
30. Brondeau, M. T. et al *J. Appl. Toxicol.* 1990, **10**(2), 83-86.
31. *J. Am. Coll. Toxicol.* 1989, **8**(4), 681-705.
32. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E88 ethyl acetoacetate

$$CH_3C(O)CH_2CO_2CH_2CH_3$$

$C_6H_{10}O_3$ **Mol. Wt.** 130.14 **CAS Registry No.** 141-97-9

Synonyms acetoacetic ester; diacetic ether; ethyl acetyl acetate; ethyl 3-oxobutanoate; FEMA No.2415

EINECS No. 205-516-1 **RTECS No.** AK 5250000

Uses Organic synthesis. Cross-linking catalyst. Chelating agent. Solvent. Flavouring agent.
Occurrence Occurs in the strawberry.

Physical properties

M. Pt. –43°C **B. Pt.** 181°C **Flash point** 84°C **Specific gravity** 1.0261 at 20°C with respect to water at 20°C
Volatility v.p. 1 mmHg at 28.5°C ; v.den. 4.48
Solubility Water: ~ 3%. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, ethyl acetate

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, fathead minnow, rainbow trout 300-310 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (96 hr) *Daphnia magna* 230 mg l^{-1} (1).
EC_{50} (30 min) *Photobacterium phosphoreum* 320 ppm, Microtox test (2).
Toxicity threshold for *Pseudomonas putida, Scenedesmus quadricauda, Entosiphon sulcatum* 8-390 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 4000, 5100 mg kg^{-1}, respectively (4,5).

Irritancy
510 mg instilled into rabbit eye caused mild irritation (exposure not specified) (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

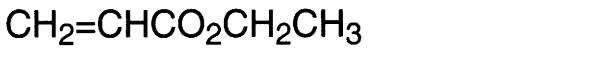
Other comments

At room temperature exists as mixture of the keto form (93%) and enol form (7%) (8).
Autoignition temperature 295°C.

References

1. Fielder, H. et al *Toxicol. Environ. Chem.* 1990, **28**(2-3), 167-188.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
4. Smyth, H. F. et al *J. Ind. Hyg. Toxicol.* 1949, **31**, 60.
5. *J. Pharm. Sci.* 1971, **60**, 1810.
6. *Union Carbide Data Sheet* 12 March 1969.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, 624, Van Nostrand Reinhold, New York, NY, USA

E89 ethyl acrylate



$C_5H_8O_2$ **Mol. Wt.** 100.12 **CAS Registry No.** 140-88-5
Synonyms ethoxycarbonylethylene; ethyl 2-propenoate
EINECS No. 205-438-8 **RTECS No.** AT 0700000
Uses Manufacture of copolymers used in surface coatings, textiles, paper and adhesives. Fragrance additive in cosmetics and foods.

Physical properties

M. Pt. -71.2°C **B. Pt.** 99.8°C **Flash point** 15.6°C (open cup) **Specific gravity** 0.9234 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.32 **Volatility** v.p. 29 mmHg at 20°C ; v.den. 3.5
Solubility Water: 20 g l^{-1} at 20°C. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (21 mg m^{-3})
FR-VME 5 ppm (20 mg m^{-3})
SE-LEVL 5 ppm (20 mg m^{-3}) **SE-STEL** 10 ppm (40 mg m^{-3})
UK-LTEL 5 ppm (21 mg m^{-3}) **UK-STEL** 15 ppm (62 mg m^{-3})
US-TWA 5 ppm (20 mg m^{-3}) **US-STEL** 15 ppm (61 mg m^{-3})

UN No. 1917 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid
Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful by inhalation, in contact with skin and if swallowed – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact (R11, R20/21/22, R36/37/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges – Wear suitable protective clothing and gloves (S2, S9, S16, S33, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (72 hr) goldfish 20 mg l^{-1} (1).

Environmental fate

Nitrification inhibition
IC_{50} (25 day) *Nitrosomonas* 47 mg l^{-1} (2).

Anaerobic effects
IC_{50} (50 day) methanogenic bacteria 130 mg l^{-1} (2).

Degradation studies
ThOD 1.92; COD 1.71 (3).
BOD_5: 28% reduction of ThOD in non-acclimated fresh water; 66% reduction in ThOD in acclimated fresh water; 11% reduction of ThOD in non-acclimated salt water (3).

Abiotic removal
Adsorption by activated carbon 157 mg g^{-1} carbon (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 1000, 2000 mg kg^{-1}, respectively (5-7).
LC_{50} (4 hr) inhalation rat, mouse, rabbit 1000-16,400 ppm (7,8).
LD_{50} dermal rabbit 1800-2000 mg kg^{-1} (6,7).
LD_{50} intraperitoneal rat, mouse, 450, 600 mg kg^{-1}, respectively (9,10).

Sub-acute and sub-chronic data
Gavage rat (2 wk) 20-200 mg kg^{-1} day^{-1} caused irritation and lesions in the forestomach, and a decrease in the total non-protein sulfhydryl content of the forestomach. No depletion of non-protein sulfhydryl was observed in the glandular stomach or liver (11).
Inhalation rat, mouse (3 day) 25, 75 or 225 ppm for 6 hr day^{-1}. The lower dose caused no adverse effects. Changes in the nasal turbinates were observed in the higher dose groups (12).

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, sufficient evidence of carcinogenicity to animals, IARC classification group 2B (13).

Gavage rat, mouse (2 yr) 100 or 200 mg kg^{-1} day^{-1} caused squamous cell carcinomas in the forestomach of ♂ and ♀ rats and mice, and squamous cell papillomas or carcinomas in the forestomach of ♂ and ♀ rats and mice (14).

Dermal ♂ mouse, 25 µl 3 × wk^{-1} for life did not cause any treatment-related tumours. The mean survival time of 408 days did not differ significantly from controls (15).

Inhalation rat, mouse (27 month) 100, 310 or 920 mg m^{-3} 6 hr day^{-1} for 5 day wk^{-1}. Body weight gain was reduced in all treated groups. In the high-dose animals treatment was discontinued after 6 months owing to a significant decrease in body weight gain. An increased incidence of thyroid follicular adenomas occurred in high-dose ♂ mice A dose-related increase in the incidence of non-neoplastic lesions of the olfactory mucosa was observed in all groups (16).

Teratogenicity and reproductive effects

Oral rat 0, 24, 50, 100, 200 or 400 mg kg^{-1} day^{-1} on day 6-16 of gestation. Maternal body weight was reduced in all treated groups. Resorptions were slightly increased with the three highest doses, but the number of live foetuses per litter was not significantly affected. The incidence of delayed ossification was increased in all treated groups (17).

Inhalation rat 0, 205 or 615 mg m^{-3} 6 hr day^{-1} on day-16 of gestation. Hypoplastic tail and associated skeletal defects were observed in three foetuses in 3/30 litters in the high-dose group. Maternal toxicity in the high-dose group was reflected in reduced food consumption and body weight gain (18).

Metabolism and toxicokinetics

Following oral administration to rats of 2,3-^{14}C-labelled substance, ≈50% radioactivity was eliminated within 24 hr, principally as carbon dioxide. Urinary metabolites included 3-hydroxypropanoic acid, and *N*-acetyl-*S*-(carboxyethyl)cysteine and its ethyl ester which are derived by GSH conjugation (19).

Irritancy

Dermal rabbit (24 hr) 10 mg caused mild irritation and exposure to 1200 ppm for 7 hr caused eye irritation (20).

Sensitisation

Sensitisation was reported in some patients in patch tests (21).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (14,22).

Drosophila melanogaster sex-linked recessive lethal assay negative (23).

In vitro Chinese hamster lung and ovary cells, chromosomal aberrations and sister chromatid exchanges without metabolic activation positive (24,25).

In vitro mouse lymphoma L5178Y tk^{+1}/tk^{-} positive (25).

In vivo mouse bone marrow, micronucleation and polychromaticity of erythrocytes positive (26).

Other comments

Physical properties, use, occurrence, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (27,28).

Toxicity reviewed (29).

References

1. Reinert, K. H. *Regul. Toxicol. Pharmacol.* 1987, **7**(4), 384-389.
2. Blum, D. J. et al *Res. J. Water Pollut. Control Fed.* 1991, **63**(3), 198-207.
3. Price, K. S. et al *J. Water Pollut. Control Fed.* 1974, **46**, 1.
4. Giusti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.
5. Tanii, H. et al *Toxicol. Lett.* 1982, **11**, 125-129.
6. Union Carbide Corp. *Toxicology Studies – Ethyl Acrylate* 1971, Industrial Medicine and Toxicology Dept., New York, NY, USA.

7. Pozzani, V. C. et al *J. Ind. Hyg. Toxicol.* 1949, **31**, 311-316.
8. Lomonova, G. V. et al *Gig. Tr. Prof. Zabol.* 1979, **9**, 55-56.
9. Paulet, G. et al *Arch. Mol. Prof.* 1975, **36**, 58-60.
10. Lawrence, W. H. et al *J. Dent. Res.* 1972, **51**, 526-535.
11. Frederick, C. B. et al *Toxicol. Pathol.* 1990, **18**(2), 247-256.
12. Miller, R. et al *19th Annu. S.O.T. Meeting, Washington*, USA, 1980.
13. *IARC Monograph* 1987, **Suppl. 7**, 63.
14. *National Toxicology Program Research and Testing Divison* 1986, Report No. TR-259, NIEHS, Research Triangle Park, NC, USA.
15. de Pass, L. R. et al *J. Toxicol. Environ. Health* 1984, **14**, 115-120.
16. Miller, R. R. et al *Drug Chem. Toxicol. (1977)* 1985, **8**, 1-42.
17. Pietrowicz, D. et al *Zwierzeta Lab.* 1980, **17**, 67-72.
18. Murray, J. S. et al *Toxicol. Appl. Pharmacol.* 1981, **60**, 106-111.
19. De Bethizy, J. D. et al *Fundam. Appl. Toxicol.* 1982, **8**(4), 549-561.
20. *J. Ind. Hyg. Toxicol.* 1949, **31**, 317.
21. Kanerva, L. et al *Contact Dermatitis* 1988, **18**(1), 10-15.
22. Waegemaekers, T. H. J. M. et al *Mutat. Res.* 1984, **137**, 95-102.
23. Valencia, R. et al *Environ. Mutagen.* 1985, **7**, 325-348.
24. Ishidate, M. et al (Ed.) *The Data Book of Chromosomal Aberration Tests In Vitro Chinese Hamster Fibroblasts/CHL Cells* 1983, 197, The Realize Inc., Tokyo, Japan.
25. Zeiger, E. et al *Environ. Mol. Mutagen.* 1990, **16**(Suppl. 18), 1-14.
26. Przybojewska, B. et al *Mutat. Res.* 1984, **135**, 189-191.
27. *IARC Monograph* 1986, **39**, 81-98.
28. *Chemical Safety Data Sheets* 1990, **1**, 89-92, The Royal Society of Chemistry, London, UK.
29. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E90 ethylamine

$CH_3CH_2NH_2$

C_2H_7N **Mol. Wt.** 45.08 **CAS Registry No.** 75-04-7

Synonyms ethanamine; aminoethane; 1-aminoethane; monoethylamine; EA

EINECS No. 200-834-7 **RTECS No.** KH 2100000

Uses Intermediate in organic synthesis. Plasticiser. Solvent.

Occurrence Decomposition product of amino acids. Residues have been identified in natural waters, soils, crops, dairy products and fish meat (1).

Physical properties

M. Pt. –81°C **B. Pt.** 16.6°C **Flash point** –16°C **Specific gravity** 0.683 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} –0.13 **Volatility** v.p. 400 mmHg at 20°C ; v.den. 1.56
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (9.4 mg m^{-3})
FR-VME 10 ppm (18 mg m^{-3}) **FR-VLE** 15 ppm (27 mg m^{-3})
JP-OEL 10 ppm (18 mg m^{-3})
SE-LEVL 10 ppm (18 mg m^{-3}) **SE-STEL** 15 ppm (30 mg m^{-3})
UK-LTEL 10 ppm (19 mg m^{-3})
US-TWA 5 ppm (9.2 mg m^{-3}) **US-STEL** 15 ppm (27.6 mg m^{-3})

UN No. 1036 **HAZCHEM Code** 2PE **Conveyance classification** flammable gas
Supply classification extremely flammable, irritant
Risk phrases Extremely flammable – Irritating to eyes and respiratory system (R12, R36/37)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Do not empty into drains (S2, S16, S26, S29)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) creek chub ≈40 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 31,200 ppm Microtox test (3).
Toxicity threshold for *Microcystis aeruginosa*, *Scenedesmus quadricauda* 1.3-2.3 mg l^{-1} and *Entosiphon sulcatum* 45 mg l^{-1} (4,5).
Toxicity treshold *Pseudomonas putida* 29 mg l^{-1} (5).

Bioaccumulation
Calculated bioconcentration factor <1 indicated that environmental accumulation is unlikely (6).

Environmental fate

Degradation studies
Arthrobacter P1 was able to utilise ethylamine as carbon and nitrogen source for growth (7).
Utilised as a nitrogen source by the filamentous fungus *Aspergillus versicolor*, but significant growth of the organism required other carbon substrates (8).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in water, $t_{1/2}$ (est.) 321 days, and in the atmosphere $t_{1/2}$ (est.) ≈8 hr (1).
Evaporation from model river water ecosystem, $t_{1/2}$ (est.) ≈2 days (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >100 mg kg^{-1} (9).
LD_{50} oral rat 400 mg kg^{-1} (10).
LC_{Lo} (4 hr) inhalation rat 3000 ppm (11).
LD_{50} dermal rabbit 390 mg kg^{-1} (11).
LD_{Lo} intravenous rabbit 350 mg kg^{-1} (12).

Metabolism and toxicokinetics
Readily absorbed from respiratory and gastro-intestinal tracts. When administered to humans, ≈32% was recovered in the urine (13).
Slowly oxidised by monoamine oxidase to form hydrogen peroxide and the corresponding aldehyde. Subsequently, the peroxide is removed by catalase and the aldehyde converted into the carboxylic acid by aldehyde oxidase (14).

Irritancy
Inhalation mouse (15 min) 150 ppm caused pulmonary irritation (15).
Dermal rabbit (24 hr) 500 mg caused mild irritation and 250 μg instilled into rabbit eye for 24 hr caused severe irritation (16).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (17).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Environmental fate of ethylamine reviewed (1,19).
Reviews on experimental toxicology and human health effects listed (20).
Untreated retort waters (containing ethylamine) were highly toxic to *Nitzschia closterium*, growth was inhibited by concentrations of 100 ppm of retort water in seawater (21).
Physico-chemical properties, toxicity, occupational exposure, hazards and legislation recommendations cited (22,23).

References

1. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, **2**, 234-239, Lewis Publishers, Chelsea, MI, USA.
2. Gillette, L. A. et al *Sewage Ind. Wastes* 1952, **24**(11), 1397-1401.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9).
5. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
6. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
7. de Boer, L. et al *Antonie van Leeuwenhock* 1989, **56**(3), 221-232.
8. Lindley, N. D. *Appl. Environ. Microbiol.* 1987, **53**(2), 246-248.
9. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
10. Smyth, H. F. et al *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
11. *Arch. Environ. Health* 1960, **1**, 343.
12. *Abdernalden's Handbuch der Biologischen Arbeitsmethoden* 1935, **4**, 1295, Leipzig, Germany.
13. Rechenberger, J. *Hoppe-Seyler's Z. Physiol. Chem.* 1984, **265**, 275-284.
14. Clayton, G. D. (Ed.) *Patty's Industrial Hygiene and Toxicology* 1981, **2B**, 3135-3173, John Wiley & Sons, New York, NY, USA.
15. Gagnaire, F. et al *J. Appl. Toxicol.* 1989, **9**(5), 301-304.
16. Marhold, J. V. *Prehled Prumyslove Toxikologie Organicke Latky* 1986, 429, Prague, Czechoslovakia.
17. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
18. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
19. Buhler, D. R. et al (Ed.) *Ethel Brownings Toxicity and Metabolism of Industrial Solvents* 2nd ed., 1990, **2**, 95-101, Elsevier, Amsterdam, Netherlands.
20. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
21. Mann, K. et al *Fuel* 1987, **6**(3), 404-407.
22. *Cah. Notes Doc.* 1990, **141**, 879-882 (Fr.) (*Chem. Abstr.* **114**, 233949d).
23. Bressa, G. *D. A., Dif. Ambientale* 1990, **14**(3), 30-31 (Ital.) (*Chem. Abstr.* **115**, 119237r)

E91 ethyl amyl ketone

$$CH_3(CH_2)_4C(O)CH_2CH_3$$

$C_8H_{16}O$ **Mol. Wt.** 128.21 **CAS Registry No.** 106-68-3

Synonyms 3-octanone; octan-3-one; amyl ethyl ketone; ethyl *n*-amyl ketone

EINECS No. 203-423-0 **RTECS No.** RH 1485000

Uses Solvent.

Occurrence Aroma component of plants. Occurs in dairy and meat products. Alarm pheromone in myrmicine ants.

Physical properties

M. Pt. -18.5°C **B. Pt.** 164-168°C **Flash point** 46°C (98+% purity) **Specific gravity** 0.822 at 20°C with respect to water at 20°C **Volatility** v.p. 2 mmHg at 25°C
Solubility Organic solvents: miscible with acetone, diethyl ether, soluble ethanol

Occupational exposure

SE-LEVL 25 ppm (130 mg m^{-3}) **SE-STEL** 50 ppm (250 mg m^{-3})
US-TWA 25 ppm (131 mg m^{-3})

UN No. 2271 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 406 mg kg^{-1} (1).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (2).

Sensitisation
Did not cause sensitisation in patch test on human volunteers (3).

Legislation

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

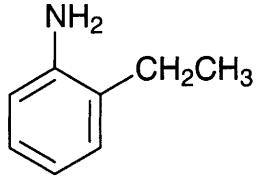
Other comments

Reviews on toxicity listed (5).

References

1. *Food Cosmet. Toxicol.* 1974, **12**, 715.
2. *Shell Chemical Co. Unpublished Report* 1961, 5, San Roman, CA, USA.
3. Opdyke, D. L. J. (Ed.) *Monographs on Fragrance Raw Materials* 1979, 346, Pergamon Press, New York, NY, USA.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E92 2-ethylaniline



$C_8H_{11}N$ **Mol. Wt.** 121.18 **CAS Registry No.** 578-54-1
Synonyms 2-ethylbenzenamine; *o*-ethylaniline
EINECS No. 209-424-2 **RTECS No.** BX 9800000
Uses Intermediate in chemical synthesis.

Physical properties

M. Pt. –44°C **B. Pt.** 210°C **Flash point** 91°C **Specific gravity** 0.983 at 25°C with respect to water at 25°C
Partition coefficient log P_{ow} 1.74 **Volatility** v.den. 4.17
Solubility Water: insoluble. Organic solvents: chloroform, diethyl ether, ethanol, toluene

Occupational exposure

UN No. 2273 **HAZCHEM Code** 3X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy 75 mg l^{-1} (1).

Invertebrate toxicity
IC_{50} (16 hr) *Escherichia coli* 4800 mg l^{-1} (2).
EC_{50} (24 hr) *Daphnia magna* 14-25 mg l^{-1} (3).

Environmental fate

Degradation studies
BOD_5 0.048 mg l^{-1} O_2 (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 750 mg kg^{-1} (5).
LD_{50} oral quail, starling >1000 mg kg^{-1} (4).
LD_{50} oral rat 1260 mg kg^{-1} (6).

Irritancy
Irritating to eyes, skin, mucous membranes and respiratory tract (species unspecified) (7).

Genotoxicity

In vitro primary rat hepatocytes DNA repair test negative (8).

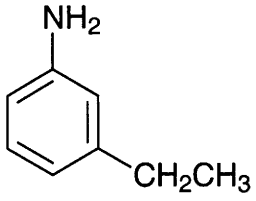
Other effects

Other adverse effects (human)
Absorption into the body leads to the formation of methaemoglobin, which in sufficient concentrations could lead to cyanosis (7).

References

1. Leegwater, D. C. *Aquat. Toxicol.* 1989, **15**(2), 109-196.
2. Nendza, M. et al *Chemosphere* 1988, **17**(8), 1585-1602.
3. Kuehn, R. et al *Water Res.* 1989, **23**(4), 495-499.
4. Meissner, B. *Wasserwirtsch.-Wassertech., WWT* 1954, **4**, 166.
5. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
6. *Toxicol. Appl. Pharmacol.* 1972, **22**, 153.
7. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1576, Sigma-Aldrich, Milwaukee, WI, USA.
8. Yoshimi, N. et al *Mutat. Res.* 1988, **206**(2), 183-191

E93 3-ethylaniline



$C_8H_{11}N$ **Mol. Wt.** 121.18 **CAS Registry No.** 587-02-0

Synonyms 3-ethylbenzenamine; 3-ethylphenylamine; *m*-ethylaniline

EINECS No. 209-594-8 **RTECS No.** BX 9770000

Uses Chemical intermediate.

Physical properties

M. Pt. –8°C **B. Pt.** 212°C **Flash point** 85°C **Specific gravity** 0.975 at 20°C
Partition coefficient log P_{ow} 2.07 (1)
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2810

Ecotoxicity

Fish toxicity
LC_{50} (14 days) guppy 43 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Tetrahymena pyriformis* 77 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, quail 315, 750 mg kg^{-1}, respectively (3).
LD_{50} oral starling >1000 mg kg^{-1} (3).

Irritancy
Irritating to the skin, eyes, mucous membranes and upper respiratory tract (species unspecified) (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538, G46, C3076, D3052 with and without metabolic activation negative (5).
Escherichia coli WP2, WP2 *uvr*A- with and without metabolic activation negative (5).
In vitro primary rat hepatocytes, unscheduled DNA synthesis negative (5).

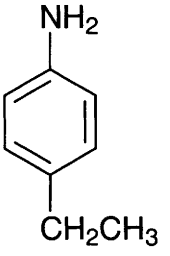
Other effects

Other adverse effects (human)
Absorption into the body leads to the formation of methaemoglobin which in sufficient concentration could lead to cyanosis (4).

References

1. Leegwater, D. C. *Aquat. Toxicol.* 1989, **15**(2), 157-168.
2. Schultz, T. W. et al *Bull. Environ. Contam. Toxicol.* 1989, **43**(4), 564-569.
3. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
4. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1575, Sigma-Aldrich, Milwaukee, WI, USA.
5. Thompson, C. Z. et al *Environ. Mutagen.* 1983, **5**(6), 803-811

E94 4-ethylaniline



$C_8H_{11}N$ **Mol. Wt.** 121.18 **CAS Registry No.** 589-16-2

Synonyms 4-aminoethylbenzene; 4-ethylbenzenamine; 4-ethylphenylamine; *p*-ethylaminobenzene; *p*-ethylaniline

EINECS No. 209-637-0 **RTECS No.** BX 9900000

Uses Chemical intermediate in the manufacture of pharmaceuticals, dyestuffs and pesticides.

Physical properties

M. Pt. -5°C **B. Pt.** 216°C **Flash point** 85°C **Specific gravity** 0.975 at 20°C
Partition coefficient log P_{ow} 1.96
Solubility Water: slightly soluble. Organic solvents: carbon tetrachloride, ethanol, toluene

Occupational exposure

UN No. 2810

Ecotoxicity

Fish toxicity
LC_{50} (14 days) guppy 29 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 0.211 ppm, Microtox test (2).
EC_{50} (48 hr) *Tetrahymena pyriformis* 110 mg l^{-1} (3).
EC_{50} (48 hr) *Daphnia magna* 2 mg l^{-1}, (24 hr) *Daphnia magna* 19 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, coturnix, starling 75, 420, 750 mg kg^{-1}, respectively (5).
LD_{50} intraperitoneal mouse 133 mg kg^{-1} (6).
LD_{50} intravenous mouse 56 mg kg^{-1} (7).

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538, G46, C3076, D3052 with and without metabolic activation negative (9).
Escherichia coli WP2, WP2 *uvr*A- with and without metabolic activation negative (9).
In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (9).

Other effects

Other adverse effects (human)

Absorption into the body leads to the formation of methaemoglobin which in sufficient concentrations causes cyanosis (8).

Any other adverse effects

In vitro Balb/3T3 cells, aniline derivatives showed significant liver metabolism-mediated changes in cytotoxicity when co-cultivated with primary rat liver cells. No direct interaction of nucleosides observed following *in vitro* reaction with aniline derivatives (10).

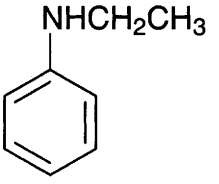
Other comments

In vitro skin absorption to a series of 4-alkylanilines is described (11).

References

1. Leegwater, D. C. *Aquat. Toxicol.* 1989, **15**(2), 157-168.
2. Kaiser, K. L. E. *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Schultz, T. W. et al *Bull. Environ. Contam. Toxicol.* 1989, **43**(4), 564-569.
4. Kuehn, R. et al *Water Res.* 1989, **23**(4), 495-499.
5. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355.
6. *J. Med. Chem.* 1974, **17**, 900.
7. *Report* NX02908, US Army Armament Research and Development Command, Chemical Systems Laboratory, Aberdeen Proving Ground, MD 21010, USA.
8. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1576, Sigma-Aldrich, Milwaukee, WI, USA.
9. Thompson, C. Z. et al *Environ. Mutagen.* 1983, **5**(6), 803-811.
10. Harada, A. *Kanazawa Daigaku Juzen Igakkai Zasshi* 1990, **99**(1), 233-247 (Japan.) (*Chem. Abstr.* **114**, 37308e).
11. Guzman, A. et al *Gene. Ind. Farm.* 1988, **7**(10), 275-280

E95 *N*-ethylaniline



$C_8H_{11}N$ **Mol. Wt.** 121.18 **CAS Registry No.** 103-69-5

Synonyms anilinoethane; *N*-ethylaminobenzene; ethylaniline; *N*-ethylbenzenamine; ethylphenylamine; *N*-ethyl-*N*-phenylamine

EINECS No. 203-135-5 **RTECS No.** BX 9780000

Uses Organic synthesis. Solvent.

Physical properties

M. Pt. –63°C **B. Pt.** 205°C **Flash point** 85°C (open cup) **Specific gravity** 0.963 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.16 **Volatility** v.p. 1 mmHg at 38.5°C ; v.den. 4.18
Solubility Water: insoluble. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2272 **HAZCHEM Code** 3X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R23/24/25, R33)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) red killifish 31 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (24 hr) *Tetrahymena pyriformis* 160 mg l^{-1} (1).
EC_{50} (30 min) *Photobacterium phosphoreum* 10.3 ppm, Microtox test (2).

Environmental fate

Carbonaceous inhibition
EC_{50} (4 hr) activated sludge respiration inhibition test, 100 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 290-500 mg kg^{-1} (3,4).
LC_{50} (4 hr) inhalation rat >1130 mg m^{-3} (5).
LD_{50} dermal rat 4700 mg kg^{-1} (6).
LD_{50} intraperitoneal rat 180 mg kg^{-1} (6).
Oral rat, mouse, single doses of 150-250 mg kg^{-1} caused normochromic anaemia and a 60% increase in methaemoglobin in rats (7).

Metabolism and toxicokinetics

May be absorbed by inhalation, ingestion or through the skin (8).
In rabbit metabolised to aniline, *N*-ethyl-4-aminophenol and phenylhydroxylamine (9).

Irritancy

Vapour in mist is irritating to the eyes, mucous membranes and upper respiratory tract (10).
Dermal rabbit (24 hr) 2 mg caused severe irritation (11).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (12).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).

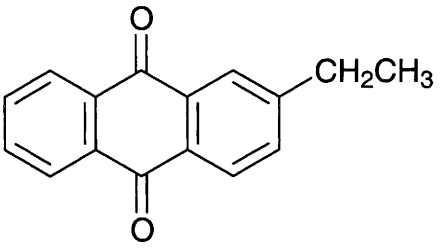
Other comments

Occurs in cigarette smoke. Reported to leach from rubbers incorporating *N,N'*-dithiodimorpholine vulcanisation accelerators (7).
Physical properties, use, occurrence, mammalian toxicity and metabolism reviewed (7,14).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (15).
Autoignition temperature 479°C.

References

1. Yoshioka, Y. et al *Ecotoxicol. Environ. Saf.* 1986, **12**, 206-212.
2. Kaiser, K. L. E. *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Marhold, J. V., Personal Communication to RTECS, Cincinatti, OH, USA, 29 March 1977.
4. Yalkut, S. I. *Gig. Primen. Toksikol. Pestits. Klin. Otravlenii* 1971, **9**, 360-362.
5. US EPA, Office of Pesticides and Toxic Substances, 8EHQ-0282-0429.
6. *Arch. Gewerbepathol. Gewerbehyg.* 1957, **15**, 447.
7. Snyder, R. (Ed.) *Ethel Browning's Toxicity and Metabolism of Industrial Solvents* 2nd ed., 1990, **2**, 197-201.
8. *Fire Protection Guide on Hazardous Materials* 7th ed. 1978, 49-150, National Fire Protection Association, Boston, MA, USA.
9. Goodwin, B. L. *Handbook of Intermediary Metabolism of Aromatic Compounds* 1976, E-8, Wiley, New York, NY, USA.
10. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1575, Sigma-Aldrich, Milwaukee, WI, USA.
11. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, 773, Avicenum, Prague, Czechoslovakia.
12. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
13. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
14. *Chemical Safety Data Sheets* 1991, **4a**, 243-245, The Royal Society of Chemistry, London, UK.
15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E96 2-ethylanthraquinone



$C_{16}H_{12}O_2$ **Mol. Wt.** 236.27 **CAS Registry No.** 84-51-5

Synonyms 2-ethyl-9,10-anthracenedione; β-ethylanthraquinone

EINECS No. 201-535-4 **RTECS No.** CB 0525000

Uses Cross-linking catalyst. Photoinitiator. Fuel oil additive.

Physical properties

M. Pt. 108-111°C **Partition coefficient** log P_{ow} 4.370 (1)

Ecotoxicity

Fish toxicity

Not toxic to brown trout, bluegill sunfish, yellow perch or goldfish exposed to 5 ppm for 24 hr. Test conditions: pH 7, dissolved oxygen content 7.5 ppm, total hardness (soap method) 300 ppm, methyl orange alkalinity 310 ppm, free carbon dioxide 5 ppm and temperature 12.8°C (2).

Bioaccumulation

2-Ethylanthraquinone was administered to carp via diet to detect bioaccumulation potential. The study found diet, fish size, feeding time intervals and temperature has a profound effect on bioaccumulation (3).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (4).

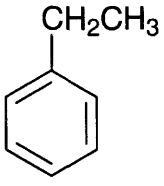
Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (5).

References

1. de Bruijn, J. et al *Environ. Toxicol. Chem.* 1989, **8**(6), 499-512.
2. Wood, E. M. *The Toxicity of 2300 Chemicals to Fish* 1987, EPA 560/6-87-002, PB-87-200-275, Washington, DC, USA.
3. Kajiwara, Y. *Seitai Kagaku* 1981, **4**(3), 3-13 (Japan.) (*Chem. Abstr.* **96**, 15775n).
4. *NTIS Report* AD 277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
5. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EC Directive 91/32/EEC* 1991, HMSO, London, UK

E97 ethylbenzene



C_8H_{10} **Mol. Wt.** 106.17 **CAS Registry No.** 100-41-4

Synonyms phenylethane; NCI-C56393

EINECS No. 202-849-4 **RTECS No.** DA 0700000

Uses Intermediate in organic synthesis. Manufacture of rubber products. Solvent for resins. Fuel additive.

Physical properties

M. Pt. -95°C **B. Pt.** 136°C **Flash point** 18°C (closed cup) **Specific gravity** 0.867 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.15 **Volatility** v.p. 10 mmHg at 26°C ; v.den. 3.66
Solubility Water: 152 mg l^{-1} at 20°C. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 100 ppm (440 mg m^{-3})
FR-VME 100 ppm (435 mg m^{-3})
JP-OEL 100 ppm (430 mg m^{-3})
SE-LEVL 50 ppm (200 mg m^{-3}) **SE-STEL** 100 pm (450 mg m^{-3})
UK-LTEL 100 ppm (441 mg m^{-3}) **UK-STEL** 125 ppm (552 mg m^{-3})
US-TWA 100 ppm (434 mg m^{-3}) **US-STEL** 125 ppm (543 mg m^{-3})

UN No. 1175 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid
Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful by inhalation (R11, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Avoid contact with skin and eyes – Do not empty into drains (S2, S16, S24/25, S29)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, goldfish, guppy, fathead minnow 12-96 mg l^{-1} (1,2).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 9.68 ppm Microtox test (3).
EC_{50} (48 hr) *Daphnia magna* 2.1 mg l^{-1} (4).
LC_{50} (96 hr) bahia shrimp 88 mg l^{-1} (5).
LC_{50} (24 hr) grass shrimp 10-14 mg l^{-1} (6).

Bioaccumulation
Bioaccumulation factor for goldfish 15.5 (7).
Bioaccumulation factor in Manila clams 4.7. Levels accumulated in tissues related to the concentration of the hydrocarbon fractions in the water. Rapid depuration on transfer to clean water, although a tendency towards protracted retention of a certain portion of the accumulated aromatics was observed (8).

Environmental fate

Nitrification inhibition
EC_{50} (25 day) *Nitrosomonas* sp. 96 mg l^{-1} (1).

Carbonaceous inhibition
EC_{50} (5 day) aerobic heterotrophic bacteria isolated from activated sludge 130 mg l^{-1} (1).

Anaerobic effects
EC_{50} (50 day) methanogenic bacterial culture 160 mg l^{-1} (1).

Degradation studies
ThOD 3.17 mg l^{-1} O_2; BOD_{35} mg l^{-1} O_2 at 25°C 1.73 mg l^{-1} O_2 (9).
Metabolised by *Pseudomonas putida* to (+)-*cis*-3-ethyl-3,5-cyclohexadiene-1,2-diol (10).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 5.5 hr in summer and 24 hr in winter. Degradation is more rapid under photochemical smog conditions. Photoxidation products include ethylphenol, benzaldehyde, acetophenone, and 3- and 4-ethylnitrobenzene (11-13).
Evaporation from model river water, $t_{1/2}$ (est.) ≈3.1 hr (14).
Adsorption by activated carbon, 0.018 g g^{-1} carbon (15).

Adsorption and retention
K_{oc} for silt loam soil 164 (16).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 5460 mg kg^{-1} (17).
LC_{Lo} (4 hr) inhalation rat 4000 ppm (18).
LD_{50} dermal rabbit 17800 mg kg^{-1} (19).
LD_{50} intraperitoneal mouse 2270 mg kg^{-1} (20).

Teratogenicity and reproductive effects
Inhalation rat, 600, 1200 or 2400 mg m^{-3} for 24 hr day^{-1} on days 7-15 of gestation. The highest dose retarded skeletal development and foetal weight gain, and increased the incidence of extra ribs (21).

Metabolism and toxicokinetics
In humans, 64% metabolised to mandelic acid and 25% to phenylglyoxylic acid which are excreted in the urine. Other metabolites include phenylacetic acid, phenylethanol and benzoic acid (22,23).

Irritancy
Dermal rabbit (24 hr) 15 mg caused mild irritation (18).
Severe eye irritant causing lachrymation and conjunctivitis, but no corneal damage (17).

Sensitisation
Reported to cause dermatitis (24).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (25).
In vitro human lymphocytes, sister chromatid exchanges weakly positive (26).
In vitro Chinese hamster ovary cells, chromosomal aberrations negative, sister chromatid exchanges positive (27).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (28).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (29).

Other comments

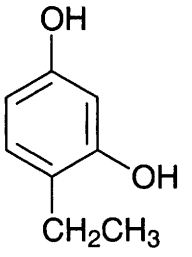
Occurs in motor vehicle exhaust and cigarette smoke. Residues have been isolated from waters, sediments, aquatic species and crops (11,30).
Environmental health criteria reviewed (31).

Physical properties, toxicity and environmental fate reviewed (30,23,32).
Reviews on experimental toxicology and human health effects listed (33).

References

1. Blum, D. J. W. et al *Res. J. Water Pollut. Control Fed.* 1991, **63**(3), 198-207.
2. Pickering, Q. J. et al *J. Water Pollut. Control Fed.* 1966, **38**, 1419.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Vighi, M. et al *Chemosphere* 1987, **16**(5), 1043-1051.
5. *In Depth Studies on Health Environmental Impacts of Selected Water Pollutants* 1978, US EPA68-01-4646.
6. *Ambient Water Quality Criteria: Ethylbenzene* 1980, US EPA440/5-80-048.
7. Nunes, P. et al *Bull. Environ. Contam. Toxicol.* 1979, **21**, 719-724.
8. Ogata, M. et al *Bull. Environ. Contam. Toxicol.* 1984, **33**, 561-567.
9. Claude, E. Z. et al *Z. Allg. Mikrobiol.* 1966, **6**(3), 143-162.
10. Gibson, D. T. et al *Biochemistry* 1973, **12**(8), 1520.
11. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, 628-630, Van Nostrand Reinhold, New York, NY, USA.
12. Ravisharkara, A. R. et al *Int. J. Chem. Kinet.* 1978, **10**, 783-804.
13. Singh, H. B. et al *Atmos. Environ.* 1981, **15**, 601-612.
14. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw Hill, New York, NY, USA.
15. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.
16. Chiou, C. T. et al *Environ. Sci. Technol.* 1983, **17**, 227-231.
17. Wolf, M. A. *Arch. Ind. Health* 1956, **14**, 387.
18. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
19. *Food Cosmet. Toxicol.* 1975, **13**, 803.
20. *Arch. Toxicol.* 1985, **58**, 106.
21. Tatrai, E. et al *Egeszsegtudomany* 1982, **26**(3), 297-303.
22. Thienes, C. et al *Clinical Toxicology* 5th ed., 1972, 162, Lea & Feliger, Philadelphia, PA, USA.
23. *Chemical Safety Data Sheets* 1989, **1**, 140-143, The Royal Society of Chemistry, London, UK.
24. Dutkiewicz, T. *Br. J. Ind. Med.* 1967, **24**, 330.
25. Milvey, P. et al *Mutat. Res.* 1976, **40**(1), 15-18.
26. Norpa, H. et al *Mutat. Res.* 1983, **116**(314), 379-387.
27. Rosenkranz, H. S. et al *Mutagenesis* 1990, **5**(6), 559-571.
28. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
29. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EC Directive 79/831/EEC; 7th Amendment EC Directive 91/32/EEC* 1991, HMSO, London, UK.
30. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1989, **1**, 325-334, Lewis Publishers, Chelsea, MI, USA.
31. *Environmental Health Criteria No. 186: Ethylbenzene* 1996, WHO/IPCS, Geneva, Switzerland.
32. Snyder, R. (Ed.) *Ethel Brownings Toxicity and Metabolism of Industrial Solvents* 2nd ed., 1987, **1**, 85-95, Elsevier, Amsterdam, Netherlands.
33. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E98 4-ethyl-1,3-benzenediol



$C_8H_{10}O_2$ **Mol. Wt.** 138.17 **CAS Registry No.** 2896-60-8

Synonyms 4-ethylresorcinol; 6-ethylresorcinol; 2,4-dihydroxyethylbenzene; *p*-ethylbenzenediol

EINECS No. 220-777-1

Uses Skin depigmentation agent. Chemical synthesis.

Physical properties

M. Pt. 95-98°C **B. Pt.** 131°C at 15 mmHg **Partition coefficient** log P_{ow} 1.89 (1)
Solubility Water: slightly soluble. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects
A CASE study reported 4-ethyl-1,3-benzenediol positive (1).

Irritancy
Irritancy to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (2).

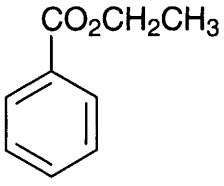
Other comments

Occurs in smoked food products (1).

References

1. Rosenkranz, H. S. et al *Mutat. Res.* 1990, **230**(1), 9-27.
2. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1655, Sigma-Aldrich, Milwaukee, WI, USA

E99 ethyl benzoate



$C_9H_{10}O_2$ **Mol. Wt.** 150.18 **CAS Registry No.** 93-89-0

Synonyms benzoic acid ethyl ester; benzoic ether; essence of Niobe; FEMA No. 2422

EINECS No. 202-284-3 **RTECS No.** DH 0200000

Uses Perfumery.

Physical properties

M. Pt. –34.6°C **B. Pt.** 213.4°C **Specific gravity** 1.050 at 25°C with respect to water at 4°C

Solubility Organic solvents: miscible with chloroform, diethyl ether, ethanol, light petroleum

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 6.7 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (24 hr) water flea 31.3 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit 2100, 2630 mg kg^{-1}, respectively (2).

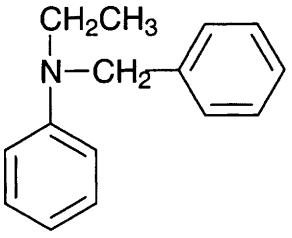
Irritancy

Dermal (24 hr) rabbit, 10 mg caused mild irritation (3).

References

1. Marchini, S. et al *Sci. Total Environ.* 1993, **Suppl.: Pt. 1**, 799-808.
2. Graham, B. E. et al *J. Pharmacol. Exp. Ther.* 1945, **84**, 358.
3. Smyth, H. F. et al *Archiv. Ind. Hyg. Occup. Med.* 1954, **10**, 61

E100 *N*-ethyl-*N*-benzylaniline



$C_{15}H_{17}N$ **Mol. Wt.** 211.31 **CAS Registry No.** 92-59-1

Synonyms *N*-ethyl-*N*-phenylbenzenemethanamine; ethylbenzylaniline

EINECS No. 202-169-8

Uses Bacteriocide and fungicide. Manufacture of dyestuffs.

Physical properties

M. Pt. 34°C **B. Pt.** 287°C at 710 mmHg **Specific gravity** 1.034 at 19°C with respect to water at 4°C
Solubility Water: <1 g l^{-1} at 22°C. Organic solvents: acetone, diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

UN No. 2274 **HAZCHEM Code** 3X **Conveyance classification** toxic substance

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E101 ethyl borate

$(CH_3CH_2)_3BO_3$

$C_6H_{15}BO_3$ **Mol. Wt.** 145.99 **CAS Registry No.** 150-46-9

Synonyms triethyl borate; boron ethoxide; boron triethoxide

EINECS No. 205-760-9 **RTECS No.** ED 5075000

Uses Polymerisation catalyst. Organic synthesis.

Physical properties

B. Pt. 120°C **Flash point** 8.3°C **Specific gravity** 0.864 at 20°C with respect to water at 4°C
Volatility v.den. 5.0
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1176 **HAZCHEM Code** 2[illegible]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 1800 mg kg^{-1} (1).

Irritancy
100 mg instilled into rabbit eye caused mild irritation (exposure not specified) (2).

References

1. *US Borax and Chemical Company Report*, US Borax and Chemical Company, New York, NY, USA.
2. Adams, R. M. *Boron, Metallo-Boron Compounds and Boranes* 1964, Wiley, New York, NY, USA

E102 ethyl bromoacetate

$$BrCH_2CO_2CH_2CH_3$$

$C_4H_7BrO_2$ **Mol. Wt.** 167.00 **CAS Registry No.** 105-36-2
Synonyms (ethoxycarbonyl)methyl bromide; ethyl 2-bromoacetate; ethyl bromoethanoate
EINECS No. 203-290-9 **RTECS No.** AF 6000000
Uses Alkylating agent. Has been used as a tear gas.

Physical properties

M. Pt. –13.8°C **B. Pt.** 159°C **Flash point** 47°C **Specific gravity** 1.514 at 13°C with respect to water at 4°C
Volatility v.p. 2.6 mmHg at 25°C ; v.den. 5.8
Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1603 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed (R26/27/28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7/9, S26, S45)

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Dermal ♀ mice (1 yr), 0.5 mg in 0.1 ml acetone, wkly injection induced papilloma in 8/30 animals and carcinoma in 1/30 animals. Subcutaneous mice (580 day), 0.1 mg in 0.05 ml tricaprylin induced sarcomas 9/50 animals. Intraperitoneal mice (450 day), 0.1 mg in 0.05 ml Nujol induced papillary tumours of lung in 9/30 animals (1).

Irritancy

Vapours are lachrymatory. Concentrations of 8 ppm for 1 min have been reported to cause severe eye and respiratory irritation (species unspecified) (2).

Sensitisation

Reported to cause skin sensitisation (species unspecified) (3).

Other comments

Physical properties, safety precautions and toxicity reviewed (3).
Reviews on toxicity listed (4).

References

1. van Duuren, B. L. et al *J. Natl. Cancer Inst.* 1974, **53**, 695.
2. Grant, W. M. *Toxicology of the Eye* 2nd ed. 1974, 473, Charles C. Thomas, Springfield, IL, USA.
3. *Chemical Safety Data Sheets* 1991, **4a**, 246-248, The Royal Society of Chemistry, London, UK.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E103 2-ethyl-1-butanol

$$CH_3CH_2CH(CH_2CH_3)CH_2OH$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 97-95-0

Synonyms 2-ethylbutan-1-ol; 2-ethylbutyl alcohol; 2-ethyl-*n*-butanol; 2-ethylbutanol; pseudohexyl alcohol

EINECS No. 202-621-4 **RTECS No.** EL 3850000

Uses Solvent. Intermediate in chemical synthesis.

Physical properties

M. Pt. –15 °C **B. Pt.** 146°C **Flash point** 58°C (open cup) **Specific gravity** 0.8326 at 20°C with respect to water at 4°C **Volatility** v.p. 0.9 mmHg at 20°C ; v.den. 3.4
Solubility Water: 4.3 g l^{-1} at 20°C. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2275 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Harmful in contact with skin and if swallowed (R21/22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Environmental fate

Abiotic removal

Adsorption by activated carbon 0.17 g g^{-1} carbon (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, rat 1200, 1850 mg kg^{-1}, respectively (2,3).

LD_{50} dermal rabbit 1260 mg kg^{-1} (2).

LD_{50} intraperitoneal rat, guinea pig 450-800 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Inhalation rat (8 hr) no fatalities occurred after exposure to saturated vapour (2).

Metabolism and toxicokinetics

Following oral administration to rabbits 40% excreted in urine as glucuronide. A small amount of methyl *N*-propylhexane was also excreted (4).

Irritancy

Dermal rabbit 415 mg caused mild irritation and 250 μg instilled into rabbit eye caused severe irritation (exposure unspecified) (2,5).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Physical properties, safety precautions and toxicity reviewed (7).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

References

1. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.
2. Smyth, H. F. et al *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
3. *J. Pharmacol. Exp. Ther.* 1944, **82**, 377.
4. Clayton, G. D. et al (Ed.) *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, 4611-4612, John Wiley and Sons, New York, NY, USA.
5. *Union Carbide Data Sheet* 1971, Union Carbide Corp., New York, NY, USA.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *Chemical Safety Data Sheets* 1992, **5**, 140-142, The Royal Society of Chemistry, London, UK.
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E104 2-ethylbutyraldehyde

$$CH_3CH_2CH(CH_2CH_3)CHO$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 97-96-1

Synonyms 2-ethylbutanal; 2-ethylbutyric aldehyde; α-ethylbutyraldehyde

EINECS No. 202-623-5 **RTECS No.** ES 2625000

Uses Intermediate in chemical synthesis.

Physical properties

M. Pt. –89°C **B. Pt.** 117°C **Flash point** 21°C **Specific gravity** 0.8110 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.12 (1) **Volatility** v.p. 13.7 mmHg 20°C ; v.den. 3.45
Solubility Water: slightly soluble. Organic solvents: carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

UN No. 1178 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy 78 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3980 mg kg^{-1} (2).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (2).

Irritancy
Dermal rabbit 500 mg caused mild irritation (exposure unspecified) (3).

References

1. Deneer, J. W. et al *Aquat. Toxicol.* 1988, **12**(2), 185-192.
2. *AMA Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119.
3. *Union Carbide Data Sheet* 1971, Union Carbide Corp., New York, NY, USA

E105 ethyl butyrate

$$CH_3CH_2CH_2CO_2CH_2CH_3$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 105-54-4
Synonyms ethyl butanoate; ethyl *n*-butyrate; butyric ether
EINECS No. 203-306-4 **RTECS No.** ET 1660000
Uses Manufacture of deodorants. Solvent.
Occurrence Aroma component of plants, wines and dairy products.

Physical properties

M. Pt. –93°C **B. Pt.** 120°C **Flash point** 19°C **Specific gravity** 0.879 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.73 (calc.) (1) **Volatility** v.p. 11.3 mmHg at 20°C ; v.den. 4.00
Solubility Water: 4.9 g l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol, propylene glycol, fixed oils

Occupational exposure

UN No. 1180 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) golden orfe 17 mg l^{-1} static bioassay (2).

Invertebrate toxicity

Toxicity threshold for *Microcystis aeruginosa* 700 mg l^{-1} and *Scenedesmus quadricauda* 47 mg l^{-1} (3,4).
Toxicity threshold for *Entosiphon sulcatum* 236 mg l^{-1} and *Uronema parduczi* 916 mg l^{-1} (4,5).

Bioaccumulation

Calculated bioconcentration factor 12 indicates that environmental accumulation is unlikely (6).

Environmental fate

Carbonaceous inhibition

Toxicity threshold for *Pseudomonas putida* 140 mg l^{-1} (4).

Abiotic removal

Volatilisation from model river water $t_{1/2}$ (est.) 5.3 hr (6).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ (calc.) 6 days (7).
Hydrolysis in water, $t_{1/2}$ (calc.) ~10 yr at pH 5, ~6 yr at pH 7, 229 days at pH 8 and 23 days at pH 9 (8).

Adsorption and retention

Calculated K_{oc} 41 indicates that ethyl butyrate will not adsorb strongly to soil and sediments (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, rat 5, 13 g kg^{-1}, respectively (9,10).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (9).

Legislation

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

References

1. *GEMS: Graphical Exposure Modeling System: Fate of Atmospheric Pollutants* 1986, US EPA Office of Toxic Substances, Washington, DC, USA.
2. Kamlet, M. J. et al *Environ. Sci. Technol.* 1987, **21**(2), 149-155.
3. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9).
4. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
5. Bringmann, G. et al Z. *Wasser/Abwasser Forsch.* 1980, (1), 26-31.
6. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
7. Mabey, W. et al *J. Phys. Chem. Ref. Data* 1978, **7**, 383-415.
8. Wallington, T. J. et al *J. Phys. Chem.* 1988, **92**, 5024-5028.
9. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1974, **12**, 703.
10. *Ind. Med. Surg.* 1972, **41**, 31.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E106 ethyl chloroacetate

$$ClCH_2CO_2CH_2CH_3$$

$C_4H_7ClO_2$ **Mol. Wt.** 122.55 **CAS Registry No.** 105-39-5

Synonyms ethyl α-chloroacetate; ethyl monochloroacetate; ethyl chloroethanoate; monochloroacetic acid, ethyl ester; chloracetic acid, ethyl ester

EINECS No. 203-294-0 **RTECS No.** AF 9110000

Uses Alkylating reagent in organic synthesis.

Physical properties

M. Pt. -26°C **B. Pt.** 144-146°C **Flash point** 54°C **Specific gravity** 1.1498 at 20°C with respect to water at 4°C
Volatility v.p. 10 mmHg at 37.5°C ; v.den. 4.3
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1181 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance
Supply classification toxic, dangerous for the environment
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Very toxic to aquatic organisms (R23/24/25, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and in a well ventilated place – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S7/9, S45, S61)

Mammalian & avian toxicity

Acute data
LD_{50} dermal rabbit 230 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 250 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Groups of 20 mice were given intraperitoneal injections of 0.25, 0.50 and 1.00 mg kg^{-1} ethyl chloroacetate 3 times wk^{-1} and sacrificed 24 wk after the first injection. An elevated lung tumour response was produced by only one of the statistical tests used (3).
Did not cause skin carcinomas in 50 mice treated with 2.0 mg in 0.1 ml acetone 3 times wk^{-1} for 580 days (4).
In a 580-day test, 50 mice were given weekly subcutaneous injections of 1.0 mg ethyl chloroacetate in 0.05 ml tricaprylin. Only one sarcoma was observed (4).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation negative (5).
Saccharomyces cerevisiae D7 and XV185-14C with and without metabolic activation negative (6).

References

1. Vernot, E. H. et al *Toxicol. Appl. Pharmacol.* 1977, **42**, 417.
2. *Jpn. J. Pharmacol.* 1954, **3**, 99.
3. Theiss, J. C. et al *Cancer Res.* 1979, **39**, 391.
4. Van Duuren, B. L. *J. Natl. Cancer Inst.* 1974, **53**, 695.
5. Sato, T. et al *Sci. Total Environ.* 1985, **46**, 229.
6. Nestmann, E. R. et al *Mutat. Res.* 1985, **155**, 53

E107 ethyl chloroformate

$ClCO_2CH_2CH_3$

$C_3H_5O_2Cl$ **Mol. Wt.** 108.52 **CAS Registry No.** 541-41-3

Synonyms carbonochloridic acid, ethyl ester; ethyl chlorocarbonate

EINECS No. 208-778-5 **RTECS No.** LQ 7000000

Uses Acetylating and alkylating agent.

Physical properties

M. Pt. –81°C **B. Pt.** 93°C **Flash point** 13°C (97% purity) **Specific gravity** 1.138 at 20°C with respect to water at 4°C **Volatility** v.p. 53 mmHg at 20°C ; v.den. 3.74

Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

UK-LTEL 1 ppm (4.5 mg m^{-3})

UN No. 1182 **HAZCHEM Code** 2WE

Supply classification highly flammable

Supply classification very toxic

Risk phrases Highly flammable – Harmful if swallowed – Very toxic by inhalation – Causes burns (R11, R22, R26, R34)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water – Take precautionary measures against static discharges – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S16, S26, S28, S33, S36/37/39, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 270 mg kg^{-1} (1).

LC_{50} (1 hr) inhalation rat 145 ppm (1).

LD_{50} dermal rabbit 7120 mg kg^{-1} (1).

LD_{Lo} intraperitoneal mouse 15 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Inhalation rat (30 day) exposed for 6 hr day^{-1} 5 day wk^{-1} (concentration unspecified) induced nasal cancer (3). Dermal mouse (22 month) showed marginal skin carcinogenicity as an initiator for phorbol myristate. Did not show skin carcinogenicity when tested alone (4).

Other comments

Physical properties, safety precautions and toxicity reviewed (5).

Reviews on toxicity listed (6).

Autoignition temperature 500°C.

References

1. *Toxicol. Appl. Pharmacol.* 1977, **42**, 417.
2. *Summary Talks of Biological Test* 1954, **6**, 220, Natl. Res. Council Chem-Biol. Coord. Centre, Washington, DC, USA.
3. Sellakumar, A. R. et al *J. Natl. Cancer Inst.* 1987, **79**(2), 285-289.

4. van Duuren, B. L. et al *J. Am. Coll. Toxicol.* 1987, **6**(4), 4790.
5. *Chemical Safety Data Sheets* 1991, **4a**, 252-259, The Royal Society of Chemistry, London, UK.
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E108 ethyl 2-chloropropionate

$$CH_3CHClCO_2CH_2CH_3$$

$C_5H_9ClO_2$ **Mol. Wt.** 136.58 **CAS Registry No.** 535-13-7

Synonyms (±)-ethyl 2-chloropropionate; ethyl α-chloropropionate

EINECS No. 208-610-0

Uses Alkylating agent.

Physical properties

B. Pt. 146-149°C **Flash point** 38°C **Specific gravity** 1.087 at 20°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2935 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

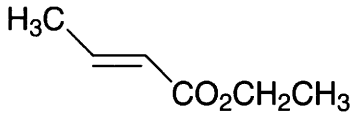
Other effects

Other adverse effects (human)
Harmful if swallowed or absorbed through the skin. Extremely destructive to mucous membranes and upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (1).

References

1. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1590, Sigma-Aldrich, Milwaukee, WI, USA

E109 (*E*)-ethyl crotonate



$C_6H_{10}O_2$ **Mol. Wt.** 114.14 **CAS Registry No.** 623-70-1

Synonyms ethyl crotonate; *E*-ethyl butenoate; *E*-crotonic acid, ethyl ester; α-crotonic acid, ethyl ester; ethyl *trans*-crotonate

EINECS No. 210-808-7 **RTECS No.** GQ 3500000

Occurrence Aroma component of plants.

Physical properties

M. Pt. 45°C **B. Pt.** 135-140°C **Flash point** 28°C (closed cup) (99% purity) **Specific gravity** 0.9175 at 20°C
Volatility v.den. 3.93
Solubility Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

UN No. 1862 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Mammalian & avian toxicity

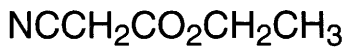
Acute data
LD_{50} oral rat 3000 mg kg^{-1} (1).
LD_{50} dermal guinea pig >5000 mg kg^{-1} (2).

Irritancy
Dermal rabbit (24 hr) 10 mg caused irritation (1).
5 mg instilled into rabbit eye caused severe irritation (duration unspecified) (3).

References

1. *J. Ind. Hyg. Toxicol.* 1944, **26**, 269.
2. *Food Cosmet. Toxicol.* 1981, **19**, 115.
3. *Am. J. Ophthalmol.* 1946, **29**, 1363

E110 ethyl cyanoacetate



$C_5H_7NO_2$ **Mol. Wt.** 113.12 **CAS Registry No.** 105-56-6

Synonyms ethyl cyanoethanoate; ethyl 2-cyanoacetate; malonic acid, ethyl ester nitrile

EINECS No. 203-309-0 **RTECS No.** AG 4110000

Uses Alkylating agent. Intermediate in the synthesis of vitamin A.

Physical properties

M. Pt. –22°C **B. Pt.** 208-210°C **Flash point** >110°C **Specific gravity** 1.063 at 25°C with respect to water at 25°C **Volatility** v.p. 1 mmHg at 67.8°C ; v.den. 3.9
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2666 **HAZCHEM Code** 3Z **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 400 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 500 mg kg^{-1} (2).
LD_{50} subcutaneous guinea pig 1115 mg kg^{-1} (3).

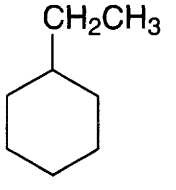
Other comments

Soluble in ammonium hydroxide.

References

1. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, 921, Prague, Czechoslovakia.
2. *NTIS AD277-689* Natl. Tech. Inf. Serv., Springfield, VA, USA.
3. *Med. Lav.* 1956, **47**, 192

E111 ethylcyclohexane



C_8H_{16} **Mol. Wt.** 112.22 **CAS Registry No.** 1678-91-7

Synonyms

EINECS No. 216-835-0

Uses Solvent.
Occurrence In fossil fuels.

Physical properties

M. Pt. –111°C **B. Pt.** 130-132°C **Flash point** 18°C **Specific gravity** 0.7880 at 20°C with respect to water at 4°C **Volatility** v.den. 3.9
Solubility Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol, lignoin

Occupational exposure

UN No. 1993

Ecotoxicity

Fish toxicity

Coho salmon, no chemically related mortalities up to 100 mg l^{-1} after 96 hr in artificial seawater at 8°C (1).

Environmental fate

Degradation studies

95% biodegradation when incubated with natural flora of groundwater after 192 hr at 13°C at an initial concentration of 0.06 µl l^{-1} in the presence of other components of high-octane gasoline (100 µl l^{-1}) (2).

Mammalian & avian toxicity

Acute data

Inhalation mouse, 15,000 mg m^{-3} caused loss of righting reflex; 35,000 mg m^{-3} was fatal (exposure unspecified) (3).

Metabolism and toxicokinetics

Urinary metabolites identified following gavage administration to rats included 4-ethylcyclohexanol, 2-hydroxy-4-ethylcyclohexanone and 2-hydroxy-4-ethylcyclohexanol (4).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991.

Other comments

Autoignition temperature 238°C.

References

1. Morrow, J. E. *Effects of Crude Oil and Some of its Components on Young Coho and Sockeye Salmon* 1974, EPA-660/3-73-018.
2. Jamison, V. W. et al *Proc. 3rd Int. Biodeg. Symp.* 1976, Applied Science Publishers.
3. Crisp, D. J. et al *Comp. Biochem. Physiol.* 1967, **22**, 629.
4. Serve, M. P. et al *Chemosphere* 1990, **20**(1-2), 43-49

E112 ethyldichloroarsine

$$CH_3CH_2AsCl_2$$

$C_2H_5AsCl_2$ **Mol. Wt.** 174.89 **CAS Registry No.** 598-14-1

Synonyms ethyl arsonous dichloride; dichloroethylarsine; arsenic dichloroethane; TL214

EINECS No. 209-919-3 **RTECS No.** CH 3500000

Uses Wood preservative.

Physical properties

M. Pt. –65°C **B. Pt.** 76°C **Flash point** –1°C **Specific gravity** 1.66 at 20°C with respect to water at 4°C

Volatility v.p. 2.29 mmHg at 21.5°C ; v.den. 6.03

Solubility Water: miscible. Organic solvents: benzene, ethanol

Occupational exposure

UK-LTEL MEL 0.1 mg m^{-3} (as As)

UN No. 1892 **HAZCHEM Code** 2XE **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LC_{50} (10 min) inhalation mouse 1555 mg m^{-3} (1).
LC_{Lo} (30 min) inhalation human 14 ppm (2).
LD_{Lo} dermal mouse 20 mg kg^{-1} (1).
LD_{Lo} subcutaneous cat 1 mg kg^{-1} (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic maximum admissible concentration 50 μg l^{-1}; chlorides guide level 25 mg l^{-1} (4).
Prescribed value for chlorides under UK Water Quality Regulation 400 mg l^{-1} (12 month average) (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
WHO guideline value for arsenic in drinking water 10 μg l^{-1} (7).

References

1. *NTIS Report* PB150-508, Natl. Tech. Inf. Ser., Springfield, VA, USA.
2. *NTIS Report* PB214-270, Natl. Tech. Inf. Ser., Springfield, VA, USA.
3. *Zeitschr. Gesamte Esp. Med.* 1921, **13**, 523.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1989 No 1147, The Water Supply (Water Quality) Regulation* 1989, HMSO, London, UK.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *Water Environ. Manage.* 1993, (1), 7

E113 ethylene

$$CH_2{=}CH_2$$

C_2H_4 **Mol. Wt.** 28.05 **CAS Registry No.** 74-85-1

Synonyms ethene; olefiant gas; elayl

EINECS No. 200-815-3 **RTECS No.** KU 5340000

Uses Oxyethylene welding and cutting of metals. Organic synthesis. Manufacture of plastics. Plant growth regulator. For accelerating ripening of fruits. Inhalation anaesthetic.
Occurrence Produced by all plant tissues and by soil microorganisms. Formed in photochemical smog and in gasoline and diesel exhausts. Residues have been isolated from natural waters (1,2).

Physical properties

M. Pt. −169°C **B. Pt.** −104°C **Specific gravity** 1.260 g l^{-1} at 0°C and 760 mmHg **Volatility** v.p. 38,000 mmHg at 8.9°C ; v.den. 0.978
Solubility Water: ~12% at 25°C. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1962 (compressed)

UN No. 1038 (refrigerated liquid) **HAZCHEM Code** 2PE (compressed) **HAZCHEM Code** 2WE (refrigerated liquid) **Conveyance classification** flammable gas
Supply classification extremely flammable
Risk phrases Extremely flammable (R12)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Ecotoxicity

Invertebrate toxicity
Toxicity threshold cell multiplication inhibition, *Pseudomonas putida* 6300 mg l^{-1}, *Scenedesmus quadricauda* 0.75 mg l^{-1}, *Entosiphon sulcatum* 300 mg l^{-1} (3).

Bioaccumulation
Reported to undergo no environmental accumulation (4).

Environmental fate

Nitrification inhibition
Inhibition of ammonia oxidation by *Nitrosomonas* 16% at 100 mg^{-1}; ≈50% at 12,200 mg l^{-1} (5,6).

Degradation studies
Utilised as sole carbon source by *Mycobacterium* E3, and *Xanthobacter* Py 2 (7).
ThOD 2.49 mg l^{-1} O_2; BOD^{20}_5 0.83 mg l^{-1} O_2 at 10 mg l^{-1} in unadapted sewage; BOD^{20}_{20} 1.0 at 10 mg l^{-1} in unadapted sewage (8).
COD 1.27 mg l^{-1} O_2 (9).

Abiotic removal
In photochemical smog $t_{1/2}$ (est.) 7.2 hr (10).
Adsorption onto activated carbon 0.015 g g^{-1} carbon (11).

Mammalian & avian toxicity

Acute data
LC_{50} (duration unspecified) inhalation mouse 95 pph (12).
Inhalation rat (4 hr) 10,000 ppm was acutely hepatotoxic to rats pretreated with 100 mg kg^{-1} day^{-1} with PCB Aroclor 1254 administered orally 100 for 3 days (13,14).

Carcinogenicity and chronic effects
No adequate data for evaluation of carcinogenicity to humans and to animals, IARC classification group 3 (15).

Metabolism and toxicokinetics
Metabolised to ethylene oxide following inhalation by mice (1).

Irritancy
Exposure to vapour at atmospheric and room temperature is reported not to cause irritation to the eyes and skin (16).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (17).
Induced gene expression in the tomato *Lycopersicon esculentum in vitro* (18)

Other effects

Other adverse effects (human)

High atmospheric concentrations can cause asphyxia by lowering the oxygen concentration (19).
An increased rate of miscarriages and gynaecological diseases in pregnant polyethylene plant workers in the former USSR was attributed to exposure to high levels of ethylene (20).

Other comments

Physical properties, use, occurrence, analysis, mammalian toxicity and metabolism reviewed (2,16,21).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (22).
Autoignition temperature 425°C.

References

1. Toernquist, M. et al *J. Appl. Toxicol.* 1988, **8**(3), 159-170.
2. *IARC Monograph* 1979, **19**, 157-177.
3. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
4. *Government Canada; Technical Information for Problem Spills: Ethylene* 1981, 1.
5. Hockenbury, M. R. et al *J. Water Pollut. Control Fed.* May 1977.
6. Hooper, A. et al *J. Bacteriol.* 1973, **115**, 480.
7. Van Ginkel, C. G. et al *Biotechnol. Bioeng.* 1987, **30**(6), 799-804.
8. Young, R. J. H. et al *J. Water Pollut. Control Fed.* 1968, **40**, 8.
9. Ford, D. L. et al *J. Water Pollut. Control Fed.* 1971, **43**(8), 1716.
10. Verschueren, K. *Handbook of Environmental Data of Organic Chemicals* 2nd ed., 1983, 633, Van Nostrand Reinhold, New York, NY, USA.
11. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.
12. *Pesticide Index* 1976, **5**, 109, College Science Publications, PA, USA.
13. Connolly, R. B. et al *Environ. Health Perspect.* 1977, **21**, 131-135.
14. Connolly, R. B. et al *Toxicol. Appl. Pharmacol.* 1977, **41**, 146.
15. *IARC Monograph* 1987, **Suppl. 7**, 63.
16. *Toxicty Profile; Ethylene* 1989, British Industrial Biological Research Association, Carshalton, UK.
17. Shepson. P. B. et al *J. Environ. Sci. Health, Part A* 1985, **20**(5), 503-519.
18. Lincoln, J. E. et al *Mol. Gen. Genet.* 1988, **212**(1), 71-75.
19. Deichmann, W. B. et al *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
20. Yakubora, Z. N. et al *Kazan. Med. Zh.* 1976, **57**(4), 360-362.
21. *Chemical Safety Data Sheets* 1992, **5**, 143-147, The Royal Society of Chemistry, London, UK.
22. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E114 ethylenediamine

$$H_2NCH_2CH_2NH_2$$

$C_2H_8N_2$ **Mol. Wt.** 60.10 **CAS Registry No.** 107-15-3

Synonyms β-aminoethylamine; dimethylenediamine; 1,2-ethanediamine; 1,2-diaminoethane; Eda

EINECS No. 203-468-6 **RTECS No.** KH 8575000

Uses Solvent. Emulsifier. Rubber latex stabiliser. Antifreeze component.

Physical properties

M. Pt. 8.5°C **B. Pt.** 118°C **Flash point** 33°C **Specific gravity** 0.8995 at 20°C with respect to water at 4°C
Volatility v.p. 116 mmHg at 20°C ; v.den. 2.07

Solubility Water: ≥100 mg l^{-1} at 17°C. Organic solvents: carbon tetrachloride, diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

DE-MAK 10 ppm (25 mg m^{-3})
FR-VME 10 ppm (25 mg m^{-3}) **FR-VLE** 15 ppm (35 mg m^{-3})
JP-OEL 10 ppm (25 mg m^{-3})
SE-LEVL 10 ppm (25 mg m^{-3}) **SE-STEL** 15 ppm (35 mg m^{-3})
UK-LTEL 10 ppm (25 mg m^{-3})
US-TWA 10 ppm (25 mg m^{-3})

UN No. 1604 **HAZCHEM Code** 2W **Conveyance classification** corrosive substance, danger of fire (flammable liquid)
Supply classification corrosive
Risk phrases Flammable – Harmful in contact with skin and if swallowed – Causes burns – May cause sensitisation by inhalation and skin contact (R10, R21/22, R34, R42/43)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S26, S36/37/39, S45)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) rainbow trout 230 mg l^{-1} static bioassay (1).
LC_{50} (24 hr) creek chub 30-60 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 0.88 mg l^{-1} (3).
Toxicity threshold, cell multiplication inhibition test *Pseudomonas putida* 0.85 mg l^{-1}, *Scenedesmus quadricauda* 0.85 mg l^{-1}, *Entosiphon sulcatum* 1.8 mg l^{-1} (4).
Toxicity threshold, cell multiplication *Uronema parduczi* 52 mg l^{-1}, *Microcystis aeruginosa* 0.08 mg l^{-1} (5,6).

Environmental fate

Nitrification inhibition
Ammonia oxidation by *Nitrosomonas* 100 mg l^{-1} 73% inhibition; 10 mg l^{-1} 41% inhibition (7).

Degradation studies
ThOD 3.45 mg l^{-1} O_2 (3).
BOD_5 0.01 g g^{-1} O_2 (3).
BOD_5 COD 0.008 (3).
BOD_5 (acclimated) >1.00 mg l^{-1} O_2 (3).
Bench scale activated sludge, product as sole carbon source, 9.8 mg COD g^{-1} dry inoculum kg^{-1} 97.5% removal (8).
BOD river water (20°C) 1-10 days observed; concentration 50 mg l^{-1} 28-day acclimation 81% removed (9).

Abiotic removal
Concentration 0.021 g g^{-1}, 10.7% adsorption activated carbon (10).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 500 mg kg^{-1}.
LC_{50} (duration unspecified) inhalation mouse 300 mg m^{-3} (11).
LD_{50} dermal rabbit 730 mg kg^{-1} (12).

LD_{50} intraperitoneal rat 76 mg kg^{-1} (13).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (14).
LD_{50} subcutaneous rat 300 mg kg^{-1} (11).

Sub-acute and sub-chronic data
Hair loss, liver, kidney and lung damage occurred in rats after repeated inhalation exposure to 484 ppm, while no injury was noted at 125 ppm when continued for 37 hrly exposures (15).

Carcinogenicity and chronic effects
Studies of the induction of skin tumours in rats concluded that it does not produce skin cancers (16).

Teratogenicity and reproductive effects
No reproductive toxicity was observed in a two-generation study in Fischer 344 rats, although adverse effects to the liver and kidney were observed (17).

Irritancy
Dermal rabbit (24 hr) 10 mg caused severe irritation and 675 µg instilled into rabbit eye caused severe irritation (11).
Inhalation humans (duration unspecified) 200 ppm caused nasal irritation, while 400 ppm caused severe nasal irritation (18).

Sensitisation
May cause sensitisation in susceptible individuals, producing allergic contact dermatitis which may be reversible (19,20).
Asthmatic sensitisation has also been reported (21).
Significant cross-reactions to aliphatic polyamines were observed in patients allergic to topical ethylenediamine. Antihistamine, given topically or orally, failed to inhibit ethylenediamine-induced allergic dermatitis (22).

Genotoxicity

Did not have any mutagenic effects in the Chinese hamster ovary mutation assay, the sister chromatid exchange test with and without metabolic activation, or in unscheduled DNA synthesis assays (23).

Other effects

Other adverse effects (human)
Extremely destructive to tissues of mucous membranes, upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema. Repeated exposure can cause asthma and damage to kidneys and liver. May cause allergic respiratory and skin reactions (12).

Any other adverse effects
The acute neurotoxicity of a homologous series of diamines (ethylenediamine to 1,6-diaminohexane) was tested by injection into the lateral ventricle of conscious rats documented as changes in behaviour and EEG. Three distinct response patterns were seen ranging from prostration and EEG depression, to EEG seizures and convulsions to a mixture of the patterns. All compounds were acutely lethal after micromole doses (24).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (25).

Other comments

Threshold odour concentration 1 ppm (26).

References

1. Woodiwiss, F. S. et al *Water Pollut. Control* 1974, **73**, 396.
2. McKee, J. E. et al *Water Quality Criteria* 1963, The Resources Agency of California, CA, USA.

3. *Environmental Effect of Photoprocessing Chemicals* 1974, 10528, Harrison, New York, NY, USA.
4. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
5. Bringmann, G. et al *Z. Wasser Abwasser Forsch.* 1980, **1**, 26-31.
6. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(19).
7. Hockenbury, M. R. et al *J. Water Pollut. Control Fed.* May 1977.
8. Pitter, P. *Water Res.* 1976, **10**, 231-235.
9. Ludzak, F. J. et al *J. Water Pollut. Control Fed.* 1960, **32**(12), 1274.
10. Ginsti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.
11. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure* 1982, 66, CIP, Moscow, USSR.
12. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1604, Sigma-Aldrich, Milwaukee, WI, USA.
13. *Toxicol. Appl. Pharmacol.* 1972, **21**, 454.
14. *Chim. Ther.* 1969, **4**, 136.
15. Tsyrkunov, L. P. *Gig. Tr. Prof. Zabol.* 1987, (8), 45-46.
16. De Pass, L. R. et al *Fundam. Appl. Toxicol.* 1984, **4**(4), 641-645.
17. Yang, R. S. H. et al *Fundam. Appl. Toxicol.* 1984, **4**(4), 539-546.
18. Dernehl, C. V. *Ind. Med.* 1951, **20**, 541.
19. Epstein, E. et al *Arch. Dermatol.* 1968, **98**, 476.
20. Nielson, M. *Contact Dermatitis* 1987, **16**(5), 275-276.
21. Lam, S. et al *Am. Rev. Respir. Dis.* 1980, **121**(1), 151-155.
22. Balato, N. et al *Contact Dermatitis* 1986, **15**(5), 263-265.
23. Slesineki, R. S. *Mutat. Res.* 1983, **14**(3/4), 299-314.
24. Strain, G. M. et al *Res. Commun. Chem. Pathol. Pharmacol.* 1989, **64**(3), 489-592.
25. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
26. Hellman, T. M. et al *Chem. Eng. Prog.* 1973, **69**, 9

E115 ethylene dinitrate

$O_2NOCH_2CH_2ONO_2$

$C_2H_4N_2O_6$ **Mol. Wt.** 152.06 **CAS Registry No.** 628-96-6

Synonyms 1,2-ethanediol dinitrate; ethylene glycol dinitrate; EGDN; glycol dinitrate; nitroglycol

EINECS No. 211-063-0 **RTECS No.** KW 5600000

Uses Manufacture of explosives. Fuel additive.

Physical properties

M. Pt. –20°C **B. Pt.** (Explodes at 114°C) **Specific gravity** 1.4918 at 20°C with respect to water at 4°C
Volatility v.p. 0.05 mmHg at 20°C ; v.den. 5.25
Solubility Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol, toluene

Occupational exposure

DE-MAK 0.05 ppm (0.32 mg m^{-3})
FR-VME 0.17 ppm (1 mg m^{-3})
JP-OEL 0.05 ppm (0.31 mg m^{-3})
SE-LEVL 0.03 ppm (0.2 mg m^{-3}) **SE-STEL** 0.1 ppm (0.6 mg m^{-3})
UK-LTEL 0.2 ppm (1.3 mg m^{-3}) **UK-STEL** 0.2 ppm (1.3 mg m^{-3})
US-TWA 0.05 ppm (0.31 mg m^{-3})
Supply classification explosive, very toxic
Risk phrases Risk of explosion by shock, friction, fire or other sources of ignition – Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R2, R26/27/28, R33)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Take precautionary measures against static discharges – This material and its container must be disposed of in a safe way – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S33, S35, S36/37, S45)

Ecotoxicity

Fish toxicity

LD_{Lo} (3-4 day) perch 5 mg l^{-1} (1).

Environmental fate

Abiotic removal

Removed from wastewater by saponification with sodium hydroxide (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 616 mg kg^{-1} (3).

LD_{Lo} subcutaneous rabbit 50 mg kg^{-1}, cat 300 mg kg^{-1} (4).

Subcutaneous rat 65 mg kg^{-1} caused an initial fall in blood pressure, and a secondary decrease due to the release of the metabolites, ethylene glycol mononitrate and nitrite, into the blood (5).

Sub-acute and sub-chronic data

Rats and guinea pigs exposed to 80 ppm for 6 months suffered drowsiness and Heinz body formation in the red blood cells (6).

Other effects

Other adverse effects (human)

Headache and heart arrhythmia were related to exposure to explosives containing ethylene dinitrate (7).

Legislation

Limited under EC Directive in Drinking Water Quality 80/778/EEC. Nitrates: maximum admissible concentration 50 mg l^{-1}; guide level 25 mg l^{-1} (8).

WHO guide level for nitrates in drinking water 50 mg l^{-1} (9).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (10).

References

1. Meinck. F. et al *Les Eaux Residuaires Industrielle* 1970.
2. Koehler, H. *Int. Jahrestag. – Fraunhofer-Inst. Trieb- Explosivst.* 1987, 18th (Technol. Energ. Mater.) 76/1-76/8 (Ger.) (*Chem. Abstr.* **107**, 24194932).
3. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 48, Prague, Czechoslovakia.
4. *Naunyn-Schmiedebergs Arch. Exp. Pathol. Pharmakol.* 1940, **200**, 271.
5. Clerk, D. C. et al *Br. J. Ind. Med.* 1967, **24**(4), 320-325.
6. Clayton, G. D. et al (Ed.) *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, **2**, 4033, John Wiley & Sons, New York, NY, USA.
7. Bergert, K. D. et al Z. *Gesamte Inn. Med. Ihre Grenzgeb.* 1987, **42**(20), 581-583 (Ger.) (*Chem. Abstr.* **108**, 100432j).
8. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
9. *Water and Environment Management* 1993, (1), 7.
10. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E116 ethylene glycol

$$HOCH_2CH_2OH$$

$C_2H_6O_2$ **Mol. Wt.** 62.07 **CAS Registry No.** 107-21-1

Synonyms 1,2-ethanediol; 1,2-dihydroxyethane; 2-hydroxyethanol; glycol alcohol; ethane-1,2-diol; Glysantin; Ilexan E; Ureresolve; NPG; TMPD

EINECS No. 203-473-3 **RTECS No.** KW 2975000

Uses Solvent. Manufacture of cosmetics and pharmaceuticals. Antifreeze. Component of brake fluids. Manufacture of plastics, explosives, elastomers and synthetic waxes.

Physical properties

M. Pt. -13°C **B. Pt.** 196-198°C **Flash point** >110°C (open cup) **Specific gravity** 1.1135 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} -1.35 (1) **Volatility** v.p. 0.05 mmHg at 20°C ; v.den. 2.14
Solubility Water: miscible. Organic solvents: acetone, acetic acid, diethyl ether, ethanol, pyridine

Occupational exposure

DE-MAK 10 ppm (26 mg m^{-3})
FR-VLE 50 ppm (125 mg m^{-3})(vapour)
SE-LEVL 10 ppm (25 mg m^{-3}) **SE-STEL** 20 ppm (50 mg m^{-3})
UK-LTEL 10 mg m^{-3} (particulate); 60 mg m^{-3} (vapour) **UK-STEL** 125 mg m^{-3} (vapour)
US-STEL ceiling limit 100 mg m^{-3} (aerosols)
Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy 8850 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish, rainbow trout, goldfish 27,500-41,000 mg l^{-1} (2-4).

Invertebrate toxicity
LC_{50} (96 hr) crayfish 91,400 mg l^{-1} (2).
EC_{50} (30 min) *Photobacterium phosphoreum* 620 ppm Microtox test (5).
LC_{50} (48 hr) *Daphnia magna* 46,300 mg l^{-1} (6).
LC_{50} (48 hr) *Ceriodaphnia dubia* 25,800 mg l^{-1} at 20°C and 10,000 mg l^{-1} at 24°C (6).

Bioaccumulation
Bioconcentration factor in golden ide 10, and for *Chlorella fusca* 190 (7).

Environmental fate

Degradation studies
Biodegraded in aerobic systems using activated sludge and soil inocula. Degradation is almost complete under environmental conditions in <1-4 days (8).
Completely degraded at a concentration of 2500 mg l^{-1} within 12 days by methanogenic bacteria isolated from activated sludge (9).
ThOD 1.26 mg l^{-1} O_2; BOD^{20}_5 0.36 mg l^{-1} O_2 at 10 mg l^{-1}; BOD^{20}_{20} 0.91 mg l^{-1} O_2 at 10 mg l^{-1} (10,11).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ (est.) ≈24 hr (8,12).

Treatment of water with ozone yields glycoaldehyde, glyoxal, glyoxalic acid and formaldehyde (13).
Adsorption by activated carbon 0.0136 g g^{-1} carbon (14).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 4700, 7500 mg kg^{-1}, respectively (15,16).
LD_{50} subcutaneous rat 2800 mg kg^{-1} (17).
LD_{50} intraperitoneal rat, mouse 5010, 5610 mg kg^{-1}, respectively (18,19).
Death is usually due to kidney failure (20).
Gavage rat, dog single doses of 1000-2000 mg kg^{-1} induced an immediate but short-lived diuresis. Acidosis with no sedation was observed (21).

Sub-acute and sub-chronic data

Oral rat (16 wk) in ♂ rats 178 mg kg^{-1} day^{-1} caused the development of oxalate crystals in the urine and kidney damage (22).

Carcinogenicity and chronic effects

Subcutaneous mouse (110 wk) 3, 10 or 30 mg kg^{-1} wk^{-1} did not cause any local or systemic carcinogenicity (23).
Oral rats, mice (24 month) 40, 200 or 1000 mg kg^{-1} day^{-1}. An increased mortality rate was observed in the high-dose ♀ rats, all of which had died by 475 days. Histopathological change observed in this group included tubular cell hyperplasia, tubular dilation, peritubular nephritis, parathyroid hyperplasia and general soft tissue mineralisation. Increased blood urea and creatinine, reduced erythrocyte count, haematocrit and haemoglobin, increased neutrophil count and increased urine volume were also observed. Urinary calcium oxalate crystals and increased kidney weight were seen in all high-dose rats. Uric acid crystals were seen in the urine of high-dose rats after 18 months. Fatty changes in the liver were observed in the high- and intermediate-dose ♂ rats. No toxic effects were observed in mice at these dose levels. There was no evidence of treatment-related carcinogenicity in any group (24).

Teratogenicity and reproductive effects

Oral mouse, three-generation study, 40, 200 or 1000 mg kg^{-1} diet gave no evidence of reduced fertility or increased foetal toxicity (25).
Gavage rat 0, 250, 1250 or 2250 mg kg^{-1} day^{-1} on days 6-20 of gestation. No toxicity was observed at 250 mg kg^{-1}. At 1250 mg kg^{-1} and above, gestational period was lengthened and evidence of maternal renal toxicity was observed. At 2250 mg kg^{-1} reduced maternal body weight, kidney weight and postpartum uterine weights were observed. Reduced pup weight and viability and increased malformation incidence was observed in this group (26).

Metabolism and toxicokinetics

Following administration by gavage to rats and dogs, peak plasma levels were observed at 2 hr. $t_{1/2}$ for excretion was 1.7 hr in rats and 3.4 hr in dogs. Urinary excretion was the major route accounting for 20-30% of the dose (21). Metabolites include aldehydes, glycolate, oxalate and lactate (27).

Irritancy

Dermal rabbit (exposure unspecified) 555 mg caused mild irritation and 500 mg instilled into rabbit eye for 24 hr caused mild irritation (28,29)

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (30).
In vitro mouse lymphoma L5178Y tk^+/tk^- forward mutation assay with and without metabolic activation negative (31).

Other effects

Other adverse effects (human)

Fatal after 12 days in a woman who drank ~200 ml of an antifreeze formulation (Glysantin) as a substitute for ethanol (32).

Injection by humans at doses of ≈1000 mg kg^{-1} have resulted in central nervous system effects including lethargy, nausea and visual impairment. After ingesting doses of ≈3000 mg kg^{-1} subjects have exhibited ataxia, slurred speech and disorientation (33).
1000 and 2000 mg l^{-1} inhibited human erythrocytes but not leukocytes *in vitro* (34).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (35).

Other comments

Metabolites of ethylene glycol are reported to account for its toxicity (27).
Physical properties, metabolism, toxicity and safety precautions reviewed (36,37).
Environmental fate reviewed (8).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (38).
Autoignition temperature 413°C.

References

1. Konemann, W. H. *Toxicology* 1981, **19**, 209-221.
2. Khoury, G. A. et al *Trace Subst. Environ. Health* 1990, **23**, 371-378.
3. Jank, B. E. et al *Water Res.* 1984, **18**, 855-880.
4. Mayes, M. A. et al *Bull. Environ. Contam. Toxicol.* 1983 **31**, 139-147.
5. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
6. Cowgill, V. M. et al *Environ. Toxicol. Chem.* 1985, **4**, 415-422.
7. Freitag, D. et al *Chemosphere* 1985, **14**, 1589-1616.
8. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, **2**, 253-257, Lewis Publishers, Chelsea, MI, USA.
9. Dwyer, D. F. et al *Appl. Environ. Microbiol.* 1983, **46**(1), 185-190.
10. Ford, D. L. et al *J. Water Pollut. Control Fed.* 1971, **43**(8), 1716.
11. Young, R. H. J. *J. Water Pollut. Control Fed.* 1968, **40**, (8).
12. *Chemical Profile* 1984, Chemical Marketing Reporter 2/13.
13. Takahashi, N. et al *Ozone: Sci. Eng.* 1990, **12**(2), 115-131.
14. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.
15. *Gig. Tr. Prof. Zabol.* 1982, **26**(6), 28.
16. *J. Pharmacol. Exp. Ther.* 1939, **65**, 89.
17. *Raw Material Data Handbook* 1974, **1**, 49.
18. *Kriobiol. Kriomed.* 1981, **9**, 36.
19. *Fed. Proc.* 1947, **6**, 342.
20. *Toxicity Profile: Ethylene Glycol* 1988, British Industrial Biological Research Assoc., Carshalton, UK.
21. Hewlett, T. P. et al *Vet. Hum. Toxicol.* 1989, **31**(2), 116-120.
22. Gaunt, J. F. *British Industrial Biological Research Association* 1975, **14**, 109, Carlshalton, UK.
23. Dukelborg, H. *Zentralbl. Bakteriol., Mikrobiol. Hyg., Ser. B.* 1987, **183**(4), 358-365 (*Chem. Abstr.* **107**, 2423s).
24. De Pass, L. R. et al *Fundam. Appl. Toxicol.* 1986, **7**(4), 547-565.
25. De Pass, L. R. et al *Fundam. Appl. Toxicol.* 1986, **7**(4), 566-572.
26. *National Toxicology Program Report NTP- 88-079* 1988, Research Triangle Park, NC, USA.
27. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
28. *Union Carbide Data Sheet* 1965, Union Carbide Corp., New York, NY, USA.
29. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 37, Prague, Czechoslovakia.
30. Klopman, G. et al *Mutat. Res.* 1990, **228**, 1-50.
31. McGregor, D. B. et al *Environ. Mol. Mutgen.* 1991, **17**(3), 196-219.
32. Lux, E. A. Z. *Gesamte Inn. Med. Ihre Grenzeb.* 1990, **45**(20), 627-629, (*Chem. Abstr.* **114**, 57047x).
33. *US EPA Drinking Water Health Advisories: Reviews of Environment Contamination and Toxicology* 1988, Springer-Verlag, New York, NY, USA.
34. Green, R. J. et al *Biochem. Pharmacol.* 1986, **35**(20), 3457-3464.
35. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
36. Evirer, H. L. et al *Res. Commun. Subst. Abuse* 1988, **9**(2), 77-87.

37. *Chemical Safety Data Sheets* 1989, **1**, 147-150, The Royal Society of Chemistry, London, UK.
38. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E117 ethylene glycol acetate

$$HOCH_2CH_2OC(O)CH_3$$

$C_4H_8O_3$ **Mol. Wt.** 104.11 **CAS Registry No.** 542-59-6

Synonyms 1,2-ethanediol monoacetate; ethylene glycol monoacetate; glycol monoacetate; 2-hydroxyethyl acetate

EINECS No. 208-821-8 **RTECS No.** KW 7175000

Uses Binding agent. Plasticiser. Solvent.

Physical properties

B. Pt. 181°C **Flash point** 102°C (closed cup) **Specific gravity** 1.108 at 15°C **Volatility** v.den. 3.6
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
Toxicity threshold cell multiplication inhibition *Pseudomonas putida* 875 mg l^{-1} *Scenedesmus quadricauda* 9 mg l^{-1}, *Entosiphon sulcatum* 34 mg l^{-1} (1).

Environmental fate

Anaerobic effects
Suppressed *Desulfovibrio desulfuricans* and *Thiobacillus ferrooxidans* at 250 and 50 mg l^{-1}, respectively (2).

Mammalian & avian toxicity

Acute data
LD_{50} guinea pig, oral rat 3800, 8250 mg kg^{-1}, respectively (3).
LD_{50} intraperitoneal mouse 1310 mg kg^{-1} (4).

Irritancy
100 ml instilled into rabbit eye caused severe irritation (exposure unspecified) (5).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

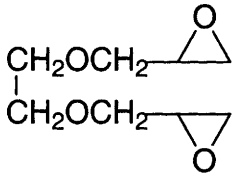
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

References

1. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
2. Khazipov, R. Kh. et al *Izv. Vyssh. Uchebn. Zaved., Neft Gaz* 1990, (1), 45-47 (Russ.) (*Chem. Abstr.* **115**, 68264n).
3. Smyth, H. F. et al *J. Ind. Hyg. Toxicol.* 1941, **23**, 259.

4. *J. Pharmacol. Exp. Ther.* 1947, **90**, 338.
5. *Am. J. Ophthalmol.* 1946, **29**, 1363.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E118 ethylene glycol diglycidyl ether



$C_8H_{14}O_4$ **Mol. Wt.** 174.20 **CAS Registry No.** 2224-15-9

Synonyms glycol diglycidyl ether; ethylene glycol bis(2,3-epoxypropyl) ether; 1,2-bis(2,3-epoxypropoxy)ethane; 1,2-bis(glycidyloxy)ethane; 1,2,9,10-diepoxy-4,7-dioxadecane; 2,2'-[1,2-ethanediylbis(oxymethylene)]bisoxirane; 1,2-ethanediol diglycidyl ether; diglycidyl ethylene glycol

EINECS No. 218-746-2 **RTECS No.** KH 5780000

Uses Cross-linking agent. Water-proofing agent.

Physical properties

B. Pt. 112°C at 4.5 mmHg **Flash point** >110°C **Specific gravity** 1.118 at 20°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 460 mg kg^{-1} (1).

Irritancy

Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (2).

Genotoxicity

Salmonella typhimurium TA100, TA1535, without metabolic activation positive (3).
Escherichia coli PQ37 with and without metabolic activation SOS-chromotest positive (3).
In vitro Chinese hamster V79 cells, sister chromatid exchanges positive (metabolic activation not specified) (4).

References

1. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, 775, Prague, Czechoslovakia.
2. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1610, Sigma-Aldrich, Milwaukee, WI, USA.
3. von der Hude, W. et al *Mutat. Res.* 1990, **231**(2), 205-218.
4. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70

E119 ethylene glycol dimethacrylate

$$CH_2=C(CH_3)C(O)OCH_2CH_2OC(O)C(CH_3)=CH_2$$

$C_{10}H_{14}O_4$ **Mol. Wt.** 198.22 **CAS Registry No.** 97-90-5

Synonyms 1,2-ethandiyl 2-methyl-2-propenoate; ethylene dimethacrylate; ethylene methacrylate; 1,2-ethanediol dimethacrylate; 1,2-bis(methacryloyloxy)ethane

EINECS No. 202-617-2 **RTECS No.** OZ 4400000

Uses Cross-linking agent. Vulcanising agent.

Physical properties

M. Pt. –40°C **B. Pt.** 98-100°C at 5 mmHg **Flash point** >110°C **Specific gravity** 1.05 at 20°C with respect to water at 20°C

Solubility Organic solvents: benzene, ethanol, lignoin

Occupational exposure

Supply classification irritant

Risk phrases Irritating to the respiratory system – May cause sensitisation by skin contact (R37, R43)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin – Wear suitable gloves (S2, S24, S37)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 2000, 3300 mg kg^{-1}, respectively (1).

LD_{50} intraperitoneal rat 2800 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation negative (3).

In vitro mouse lymphoma L5178Y tk^+/tk^- with metabolic activation positive, without metabolic activation negative (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

References

1. *Gig. Tr. Prof. Zabol.* 1980, **24**(4), 58.
2. *Arch. Mal. Prof. Med. Trav. Secur. Soc.* 1975, **36**, 58.
3. Cameron, T. P. et al *Environ. Mol. Mutagen.* 1991, **17** (4), 264-271.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E120 ethylene oxide

C_2H_4O **Mol. Wt.** 44.05 **CAS Registry No.** 75-21-8

Synonyms oxirane; epoxyethane; anprolene; 1,2-epoxyethane; ethene oxide; oxacyclopropane

EINECS No. 200-849-9 **RTECS No.** KX 2450000

Uses Production of ethylene glycol. Fumigant. Organic synthesis.

Physical properties

M. Pt. –111°C **B. Pt.** 11°C **Flash point** –20°C **Specific gravity** 0.891 at 4°C with respect to water at 4°C
Partition coefficient log P_{ow} –0.30 **Volatility** v.p. 1094 mmHg at 20°C ; v.den. 1.5
Solubility Water: soluble. Organic solvents: acetone, diethyl ether, ethanol, vegetable oils

Occupational exposure

FR-VME 1 ppm **FR-VLE** 5 ppm
JP-OEL 1 ppm (1.8 mg m^{-3})
SE-LEVL 1 ppm (2 mg m^{-3}) **SE-STEL** 5 ppm (9 mg m^{-3})
UK-LTEL MEL 5 ppm (9.2 mg m^{-3})
US-TWA 1 ppm (1.8 mg m^{-3})

UN No. 1040 **HAZCHEM Code** 2PE **Conveyance classification** toxic gas, danger of fire (flammable gas)
Supply classification extremely flammable, toxic
Risk phrases May cause cancer – May cause heritable genetic damage – Extremely flammable – Toxic by inhalation – Irritating to eyes, respiratory system and skin (R45, R46, R12, R23, R36/37/38)
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
LC_{50} (24 hr) goldfish 90 mg l^{-1} (1).

Environmental fate

Degradation studies
COD 1.74; BOD_5 0.06 (2).

Abiotic removal
Hydrolyses in fresh water to give ethylene glycol and in salt water to give ethylene glycol and ethylene chlorohydrin with $t_{1/2}$ of 12-14 days and 9-11 days, respectively (3).
Hydrolysis in an atmosphere of relative humidity >50% at room temperature, $t_{1/2}$ 16 days (4,5).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ ≈120 days (5,6).
Volatilisation from water, $t_{1/2}$ 1 hr with no wind and 0.8 hr with a 5 m sec^{-1} wind velocity, as determined in a laboratory experiment (7).

Adsorption and retention
K_{oc} (calc.) 16 for soil indicated that ethylene oxide will not adsorb strongly to soil and sediments (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig 270, 330 mg kg^{-1}, respectively (8).
LC_{50} (4 hr) inhalation rat, mouse, dog 960-2630 mg m^{-3} (9).
LD_{50} subcutaneous rat 187 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Inhalation rat 0, 500 or 1500 ppm (duration unspecified). The high dose reduced the levels of reduced glutathione and glutathione reductase in the cytosol of the liver by 10 and 60%, respectively. Levels in the liver mitochondria were only slightly affected (11).
Inhalation ♂ rat (13 wk) 500 ppm 6 hr day^{-1} 3 × wk^{-1} reduced the haemoglobin content, and a normocytic and normochromic anaemia was found. Alterations of hepatic porphyrin-haem metabolism was also identified (12).
Gavage rat, 15 repeat doses 100 mg kg^{-1} over 21 days caused marked loss of body weight, gastric irritation and slight liver damage. No injury resulted from 22 repeat doses of 30 mg kg^{-1} administered over 30 days (13).
Inhalation monkey (2 yr), 0, 50 or 100 ppm 7 hr day^{-1}, 5 days wk^{-1} for 24 months. Measurements of motor nerve conduction velocity and electroencephalograms showed no significant neurophysiological effects compared with controls. There were some cases of axonal dystrophy in the nucleus gracilis, but there was no dose-response relationship and the effect was not attributed to oxide exposure. Nerve conduction velocity and neuropathology were examined in the remaining animals after 7 yr. No treatment-related effects were detected (14).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence of carcinogenicity to animals, IARC classification group 2A (15).
Inhalation mouse (2 yr) 0, 50 or 100 ppm 6 hr day^{-1}, 5 day wk^{-1} for 102 wk. Clear evidence of carcinogenicity was indicated by a dose-related increased incidence of benign and/or malignant neoplasms of the lung and benign neoplasms of the Harderian gland in both sexes. In ♀ mice ethylene oxide caused additional malignant neoplasms of the uterus, mammary gland and haematopoietic system (16).
Inhalation rat (2 yr) 0, 50 or 100 ppm 7 hr day^{-1} 5 day wk^{-1} for 2 yr caused an increase in the incidence of mononuclear-cell leukaemia, peritoneal mesotheliomas and gliomas of the brain. Non-neoplastic proliferative lesions in the adrenal cortex were also observed in treated rats (17).
Gavage rat 7.5 or 30 mg kg^{-1} 2 × wk^{-1} for 107 wk caused a dose-related increase in squamous cell carcinomas, fibrosarcomas of the forestomach, and papillomas, hyperplasia or hyperkeratosis of the squamous epithelium of the forestomach. One fibrosarcoma was found in the glandular stomach in the high-dose group (18).
Dermal mouse 100 mg 3 × wk^{-1} for life did not induce skin tumours. The median survival time was 493 days (19).
Subcutaneous mouse 0.1, 0.3 or 1.0 mg $mouse^{-1}$ wk^{-1} for 95 wk induced a dose-related increase in local fibrosarcomas and pleomorphic sarcomas; haemangiosarcoma was also reported (20).

Teratogenicity and reproductive effects

Inhalation ♂ rat (13 wk) 500 ppm 3 × wk^{-1} caused significant testicular atrophy and reduction in DNA. However, plasma testosterone levels did not change significantly. In the testes the activity of glutathione reductase decreased by 45% and glutathione-*S*-transferase increased by 64%, indicating that the toxicity of ethylene oxide is related to its effects on glutathione metabolism (21). Inhalation rat 150 ppm for 7 hr day^{-1} 5 day wk^{-1} on days 7-16 of gestation, or days 1-16 of gestation, or for 3 wk prior to mating and then daily until day-16 of gestation resulted in an increased incidence of resorptions in the 3rd group. Foetal growth indices were reduced in all groups. An increased incidence of litters with foetuses with hydroureter occurred only when the mothers were exposed on days 7-15 of gestation. A moderate reduction in maternal body weight gain was reported for all groups (22).
Intravenous mouse, 0, 75 or 150 mg kg^{-1} day^{-1} on days 4-6, 6-8, 8-10 or 10-12 of gestation resulted in a significant increase in the incidence of craniofacial defects and fusions of vertebrae in the high-dose groups exposed on days 6-8 and 10-12. The high-dose level resulted in maternal mortality after treatment in the day 4-6, 8-10 and 10-12 groups (23).

Metabolism and toxicokinetics

Following inhalation exposure to 200 ppm or intravenous administration of 20 or 60 mg kg^{-1}, urinary metabolites identified in mice were *N*-acetyl-*S*-(2-hydroxyethyl)-L-cysteine, *S*-(2-hydroxethyl)-L-cysteine, ethylene glycol and

S-carboxymethyl-L-cysteine (8.3, 5.8, 3.3 and 1.9% of the dose, respectively), in 24 hr. In rats only *N*-acetyl-*S*-(2-hydroxyethyl)-L-cysteine (31%) and ethylene glycol (6%) were apparent. Rabbits excreted only ethylene glycol (2%) (24).

Irritancy

Dose-related eye irritation was observed in rabbits exposed to concentrations >1800 mg m^{-3} (duration unspecified) (25).

18 mg instilled into rabbit eye for 6 hr caused moderate irritation (26).

Sensitisation

Skin burns and dermatitis have been reported in a number of medical personnel after contact with materials sterilised with ethylene oxide (27).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (28).

Drosophila melanogaster, somatic and sex-linked recessive lethal mutations and heritable translocations positive (29,30).

In vitro Chinese hamster ovary cells, gene mutation with and without metabolic activation positive (31).

In vitro cyanomolgus monkey lymphocytes, sister chromatid exchanges positive (32).

In vitro mouse bone marrow cells and primary spermatocytes, chromosomal aberrations positive (33).

In vitro binding to human, rat and mouse DNA, major reaction product was N^7-(2-hydroxyethyl)guanine. The major reaction products with haemoglobin were 2-hydroxyethylations of cysteine, *N*-terminal valine, the two imidazole nitrogens in histidine, and carboxylic groups (34).

In vivo ♂ mouse, dominant lethal mutations and heritable translocations positive (35).

In vivo human lymphocytes, a significant increase in sister chromatid exchanges was reported among exposed workers (36).

75 workers exposed to 2 to 5 ppm (time-weighted average) in an 8 hr day for 3 months showed a significant increase in chromosomal aberrations. Micronuclei in binucleated lymphocytes were also observed (37).

Other effects

Other adverse effects (human)

In three cohort studies in Sweden a total of eight cases of leukaemia were observed, compared with 0.83 expected. Stomach cancer occurred in excess (6/89 workers) in one plant only (38).

Five cases of peripheral neuropathy, one case of encephalopathy and three cases of cataract development were reported after exposure to ethylene oxide sterilisers (39-41).

In a study of hospital sterilising staff, a statistically signicant excess of spontaneous abortions was reported among women exposed during pregnancy (42).

Mortality study of ethylene oxide workers working between 1940 and 1988. Average duration of exposure was >5 yr. The data did not support associations with all cancer types combined, (leukaemic, non-Hodgkin's lymphoma, brain, pancreatic or stomach cancers), in contrast to previous animal and occupational exposure studies that found an association between exposure and cancer incidence (43).

Other comments

Product of combustion of hydrocarbon fuels. Residues have been isolated from crops which have been fumigated (27).

Physical properties, use, occurrence, carcinogenicity, mammalian toxicity, mutagenicity and teratogenicity reviewed (27,44-46).

Environmental fate reviewed (4).

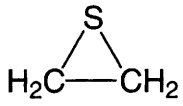
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (47).

Autoignition temperature 429°C.

References

1. Lipnick, R. L. et al *Xenobiotica* 1987, **17**(8), 1011-1025.
2. *Shell Industrie Chemicalien Gids* 1975, Shell Nederland Chemie, 's-Gravenhage, Netherlands.
3. Conway, R. A. et al *Environ. Sci. Technol.* 1983, **17**, 107-112.
4. *Report to the Air Resources Board on Ethylene Oxide* 1987, State of California, CA, USA.
5. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1989, **1**, 335-341.
6. Atkinson, R. *Chem. Rev.* 1985, **85**, 69-201.
7. Conway, R. A. et al *Environ. Sci. Technol* 1983, **17**, 107-112.
8. Smyth, H. F. et al *J. Ind. Hyg. Toxicol.* 1941, **23**, 259-268.
9. Jacobson, K. H. et al *Arch. Ind. Health* 1956, **13**, 237-244.
10. *Gig. Sanit.* 1983, **48**(1), 23.
11. Katoh, T. et al *Toxicol. Lett.* 1990, **54**(2-3), 235-239.
12. Fujishio, K. et al *Toxicology* 1990, **61**(1), 1-11.
13. Hollingsworth, R. L. et al *Arch. Ind. Health* 1956, **13**, 217-227.
14. Setzer, J. V. et al *Toxicol. Ind. Health* 1996, **12**(5), 667-682.
15. *IARC Monograph* 1987, **Suppl. 7**, 205-207.
16. *National Toxicology Program Research and Testing Division* 1987, Report No. TR-326, NIEHS, Research Traingle Park, NC, USA.
17. Lynch, D. W. et al *Toxicol. Appl. Pharmacol.* 1984, **76** 69-84.
18. Durkelberg, H. *Br. J. Cancer* 1982, **46**, 924-933.
19. van Duuren, B. L. et al *J. Natl. Cancer Inst.* 1965, **35**, 707-717.
20. Durkelberg, H. *Zentralbl. Bakteriol., Mikrobiol. Hyg., Abt. 1, Orig. B* 1981, **174**, 383-404.
21. Mori, K. et al *J. UOEH* 1988, **10**(4), 427-431, (Japan.) (*Chem Abstr.* **110**, 226741u).
22. Hackett, P. L. et al *Teratogenic Study of Ethylene and Proplyene Oxide and n-Butyl Acetate* 1982, National Institute for Occupational Safety and Health, Cincinnati, OH, USA.
23. La Borde, J. B. et al *Toxicol. Appl. Pharmacol.* 1980, **56**, 16-22.
24. Tardif, R. et al *Fundam. Appl. Toxicol.* 1987, **9**(3), 448-453.
25. McDonald, T. D. et al *Bull. Parenter. Drug Assoc.* 1973, **27**, 153-164.
26. *Bull. Parenter. Drug Assoc.* 1977, **31**, 25.
27. *IARC Monograph* 1985, **36**, 189-226.
28. Klopman, G. et al *Mutat. Res.* 1990, **228**, 1-50.
29. Watson, W. A. F. *Mutat. Res.* 1966, **33**, 455-457.
30. Fahmy, O. G. et al *Cancer Res.* 1970, **30**, 195-205.
31. Tan, E.-L. et al *Environ. Mol. Mutagen.* 1981, **3**, 683-686.
32. Kelsey, K. T. et al *Cancer Res.* 1989, **49**(7), 1727-1731.
33. Ribeiro, L. R. et al *Arch. Toxicol.* 1987, **59**(5), 332-335.
34. Segerbacek, D. *Carcinogenesis (London)* 1990, **11**(2), 307-312.
35. Generoso, W. M. et al *Environ. Mol. Mutagen.* 1990, **16**(2), 126-131.
36. Stolley, P. D. et al *Mutat. Res.* 1984, **129**, 89-102.
37. Ribeiro, L. R. et al *Mutat. Res.* 1994, **313**(1), 81-87.
38. Hoegstedt, C. et al *J. Am. Med. Assoc.* 1986, **255**, 1575-1578.
39. Gross, J. A. et al *Neurology* 1979, **29**, 978-983.
40. Kuzuhora, S. et al *Neurology* 1983, **33**, 377-380.
41. Jay, W. M. et al *Am. J. Ophthalmol.* 1982, **93**, 727-732.
42. Hemminki, K. et al *Br. Med. J.* 1983, **286**, 1976-1977.
43. Tetra, M. J. et al *J. Ind. Med.* 1993, **50**(8), 704-709.
44. *Dangerous Properties Industrial Materials Report* 1989, **9**(4), 64-76.
45. *ICPS Environmental Health Criteria 55* 1985, WHO, Geneva, Switzerland.
46. *Chemical Safety Data Sheets* 1991, **4a**, 260-264, The Royal Society of Chemistry, London, UK.
47. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E121 ethylene sulfide



C_2H_4S **Mol. Wt.** 60.12 **CAS Registry No.** 420-12-2

Synonyms 2,3-dihydrothiirene; ethylene episulfide; thiacyclopropane; thiirane

EINECS No. 206-993-9 **RTECS No.** KX 3500000

Physical properties

B. Pt. 55-56°C (decomp.) **Flash point** 10°C **Specific gravity** 1.0046 at 20°C with respect to water at 4°C
Volatility v.p. 375 mmHg at 25°C
Solubility Water: immiscible with water. Organic solvents: miscible with acetone, chloroform, ethanol, diethyl ether

Occupational exposure

UN No. 1992

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 178 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 42 mg kg^{-1} (1).
LD_{50} subcutaneous rat 90 mg kg^{-1} (2).
LC_{50} inhalation rat (1/2, 1, 6 hr) 4000, 2800, 690 ppm, respectively (3).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (4).
Subcutaneous rat (50 wk intermittent administration) 400 mg kg^{-1} equivocal tumorigenic agent (2).

Irritancy
20 mg instilled into rabbit eye caused irritation (5).
Irritating to surface tissues and mucous membranes in rats (6).

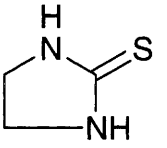
Other effects

Any other adverse effects
Ingestion of high doses caused depression of the central nervous system and unconsciousness in rats (1).
Inhalation in animals caused congestion, oedema and haemorrhage in the lungs (7).

References

1. Brown, J. R. et al *Am. Ind. Hyg. Assoc. J.* 1964, **25**, 560.
2. Druckey, H. et al Z. *Krebsforsch.* 1970, **74**, 241-270.
3. MacFarland, H. N. et al *Bull. Environ. Contam. Toxicol.* 1971, **6**, 509-512.
4. *IARC Monograph* 1987, **Suppl. 7**, 63.
5. *Am. J. Ophthalmol.* 1946, **29**, 1363.
6. Eisengart, R. S. *Farmakol. Toksikol.* 1967, **30**, 608-609.
7. Kurlyandksy, B. A. et al *Gig. Tr. Prof. Zabol.* 1966, **10**, 44-49

E122 ethylenethiourea



$C_3H_6N_2S$ **Mol. Wt.** 102.16 **CAS Registry No.** 96-45-7

Synonyms 2-imidazolidinethione; *N,N'*-ethylenethiourea; 4,5-dihydroimidazole-2(3*H*)-thione; ETU; Akroform ETU-22 PM; Perkacit ETU; Rhenogram SF ETU-50

EINECS No. 202-506-9 **RTECS No.** NI 9625000

Uses Cross-linking catalyst in rubber industry.

Physical properties

M. Pt. 197-200°C **Flash point** 252°C **Partition coefficient** log P_{ow} –0.66 (1)
Solubility Water: 2 g l^{-1} at 30°C. Organic solvents: acetic acid, ethanol, ethylene glycol, ligroin, methanol, naphtha, pyridine

Occupational exposure

Supply classification toxic
Risk phrases May cause harm to the unborn child – Harmful if swallowed (R61, R22)
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
LC_{50} (24 hr) creek chub ~7000 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (15 min) *Photobacterium phosphoreum* 2080-2450 ppm Microtox test (3).

Bioaccumulation
Calculated bioconcentration factor 2.3 indicated that environmental accumulation is unlikely (4).

Environmental fate

Degradation studies
Degradation in soil by oxidation and microbial action, $t_{1/2}$ <1 wk. Degradation products are ethyleneurea and carbon dioxide (5-7).

Abiotic removal
Undergoes photooxidation in water yielding glycine sulfate and ethyleneurea (5).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ (estimated) 205 hr (8).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 1830, 3000 mg kg^{-1}, respectively (9,10).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (11).

Sub-acute and sub-chronic data

Oral rat (8 month) 1, 5, 50 or 500 mg l^{-1} in drinking water. Rats receiving the highest dose exhibited alteration in hepatic cell morphology after 4-month exposure. These alterations indicated a dramatic increase in the amount of smooth endoplasmic reticulum with a concomitant reduction in rough endoplasmic reticulum, and a relocation of microbodies and mitochondria to the periphery of the smooth endoplasmic reticulum. No tumours were detected (12).

Oral rat (28 day) 0-300 mg l^{-1} in drinking water caused an alteration in thyroid function characterised by a dose-dependent inhibition of T_3 and T_4 secretion and a consequent 10-fold increase in thyrotropin secretion. Ultrastructural changes induced included an increase in the number of myelin bodies, dilation of the rough endoplasmic reticulum and increased vacuolisation in the epithelial cells of thyroid follicles (13).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (14).

National Toxicology Program tested rats and mice via feed. Clear evidence of carcinogenicity was demonstrated (increased incidence of chemically-related neoplasms, malignant, benign or combined) in ♂ and ♀ rats and mice (15).

Gavage mouse (83 wk) 215 mg kg^{-1} day^{-1} for 3 wk followed by administration in the diet at a concentration of 646 ppm. An increased incidence of hepatomas and lymphomas were reported in both sexes (16).

Oral rat (2 yr) 175 or 350 mg kg^{-1} diet for 18 month induced dose-related increase in the incidence of hyperplastic goitre and thyroid carcinomas. Solid-cell adenomas of the thyroid and hyperplastic liver nodules were also induced in treated animals (17).

Teratogenicity and reproductive effects

Gavage rat 0, 15, 25 or 35 mg kg^{-1} day^{-1} on days 6-20 of gestation. Teratogenic effects were identified, but no maternal or foetal toxicity was observed (18).

Whole rat embryos cultured from days 11-13 of gestation were exposed to ethylenethiourea concentrations up to 300 μg l^{-1}. Malformations were found in cultured embryos in the head, tail and limbs at concentrations of 30 μg and above. Protein content of the cultured embryos decreased in a dose-dependent manner (19).

Metabolism and toxicokinetics

Metabolised in rat and mouse liver where ethylenethiourea is a substrate for flavin-dependent monooxygenase, which is a microsomal NADPH requiring enzyme, and for the cytochrome P_{450} enzyme system (20).

Unchanged ethylenethiourea has been detected in cow's milk following oral administration (21).

Irritancy

500 mg instilled into rabbit eye for 24 hr caused irritation (22).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (23).

Aspergillus nidulans induction of mitotic segregation positive, forward mutation and induction of mitotic cross-over negative (24).

Drosophila melanogaster sex-linked recessive lethal assay negative (25).

In vitro mouse lymphoma L5178 tk^+/tk^- forward mutation assay positive (26).

In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations negative (27).

In vivo mouse, micronucleus test negative (28).

Other effects

Other adverse effects (human)

In a case control study, 1929 workers were identified as having worked with ethylenethiourea. No case of thyroid cancer was reported in this group (29).

Other comments

Metabolite of ethylene bisdithiocarbamate fungicides (30,31).
Exists in equilibrium with 2-mercaptoimidazoline (32).
Physical properties, use, occurrence, carcinogenicity, and toxicology reviewed (21,32).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (33).

References

1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, 655, Van Nostrand Reinhold, New York, NY, USA.
2. McKee, J. E. et al *Water Quality Criteria* 1963, Resources Agency of California; State Water Quality Control Board.
3. Kaiser, K. L. E. et al *Water Pollut. Res J. Can.* 1991, **26**(3), 361-431.
4. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods, Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
5. Blazquez, C. H. *J. Agric Food Chem.* 1973, **21**, 330.
6. Rhodes, R. C. *J. Agric. Food Chem.* 1977, **25**, 528.
7. Kaufman, D. D. et al *Abstr. Am. Chem. Soc. 165th Natl. Meet., Dallas* 1973.
8. *GEMS: Graphical Exposure Modelling System: Fate of Atmosphere Pollutants* 1986, USEPA Office of Toxic Substances, Washington, DC, USA.
9. Graham, S. L. et al *Bull. Environ. Contam. Toxicol.* 1972, **7**, 19.
10. *Teratology* 1980, **21**, 71.
11. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
12. Moller, P. C. et al *J. Environ. Pathol., Toxicol. Oncol.* 1986, **6**(5-6), 127-142.
13. Kurttio, P. et al *Arch. Toxicol., Suppl.* 1986, **9**, 339-344.
14. *IARC Monograph* 1987, **Suppl. 7**, 207-208.
15. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-883, NIEHS, Research Triangle Park, NC, USA.
16. Innes, J. R. M. et al *J. Natl. Cancer. Inst.* 1969, **42**, 1101-1114.
17. Ulland, B. M. et al *J. Natl. Cancer. Inst.* 1972, **49**, 583-584.
18. Saillenfait, A. M. et al *Fundam. Appl. Toxicol.* 1991, **17**(2), 399-408.
19. Tsuchiya, T. et al *Teratology* 1991, **43**(4), 319-324.
20. Hui, Q. Y. et al *Toxicol. Lett.* 1988, **41**(3), 231-237.
21. *Dangerous Prop. Ind. Mat. Rep.* 1987, **7**(3), 106-111.
22. Marhold, J. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 167, Prague, Czechoslovakia.
23. Klopman, G. et al *Mutat. Res.* 1990, **228**, 1-50.
24. Crebelli, R. et al *Mutat. Res.* 1986, **172**(2), 139-149.
25. Valencia, R. et al *Mutat. Res.* 1981, **1**, 651-659.
26. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **12**(1), 85-154.
27. Natarajan, A. T. et al *Prog. Mutat. Res.* 1981, **1**, 551-559.
28. Tsuchimoto, T. et al *Prog. Mutat. Res.* 1981, **1**, 705-711.
29. Smith, D. *J. Soc. Occup. Med.* 1976, **26**, 92-94.
30. Nebbia, C. et al *Am. J. Vet. Res.* 1991, **52**(10), 1717-1722.
31. Searle, A. J. F. et al *Xenobiotica* 1987, **17**(6), 733-740.
32. *IARC Monograph* 1974, **7**, 45-52.
33. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E123 ethyl formate

$HCO_2CH_2CH_3$

$C_3H_6O_2$ **Mol. Wt.** 74.08 **CAS Registry No.** 109-94-4

Synonyms ethyl methanoate

EINECS No. 203-721-0 **RTECS No.** LQ 8400000

Uses Acylation agent. Catalyst. Gelling agent. Solvent. Fungicide. Virucide. Food flavouring.
Occurrence Aroma component of plants and fish.

Physical properties

M. Pt. –80°C **B. Pt.** 53-54°C **Flash point** –20°C (closed cup) **Specific gravity** 0.9236 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.23 (1) **Volatility** v.p. 100 mmHg at 5.4°C ; v.den. 2.6
Solubility Water: 105 g l^{-1} at 20°C. Organic solvents: acetone, diethyl ether, ethanol, propylene glycol, mineral oils, fixed oils

Occupational exposure

DE-MAK 100 ppm (310 mg m^{-3})
FR-VME 100 ppm (300 mg m^{-3})
UK-LTEL 100 ppm (308 mg m^{-3}) **UK-STEL** 150 ppm (462 mg m^{-3})
US-TWA 100 ppm (303 mg m^{-3})

UN No. 1190 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Ecotoxicity

Bioaccumulation
Did not bioconcentrate in rainbow trout (2).

Environmental fate

Degradation studies
30% removal from wastewater by acclimed sewage seed at concentrations of 200-1000 mg l^{-1} (3).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere $t_{1/2}$ (estimated) ≈11 days (4).
Evaporation from model river water $t_{1/2}$ (estimated) 270 min (5).
Gradually decomposed in water yielding formic acid and ethanol (6).

Adsorption and retention
Calculated K_{oc} 32 indicated that ethyl formate will not adsorb to soil or sediments (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, rabbit, guinea pig 1110-2075 mg kg^{-1} (7,8).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (9).
LC_{50} dermal rabbit 20,000 mg kg^{-1} (10).
LD_{Lo} subcutaneous rabbit 1000 mg kg^{-1} (10).

Carcinogenicity and chronic effects
Dermal mouse 10 × 276 mg wk^{-1} for 133 days, and promoted with 18 wkly applications of croton oil, did not induce any cancers (11).

Irritancy
Dermal rabbit (duration unspecified) 460 mg caused mild irritation (12).
Inhalation mouse (20 min) 5000 or 10,000 ppm caused irritation to the eyes (13).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).

Other comments

Physical properties, health precautions and toxicity reviewed (15).
Reviews on toxicity listed (16).
Autoignition temperature 440°C.

References

1. Hansch, C. et al *J. Org. Chem.* 1968, **33**, 347.
2. McKim, J. et al *Absorption Dynamics of Organic Chemical Transport Across Trout Gills as Related to Octanol-Water Partition Coefficient* 1985, NTIS PB-198315.
3. Ludzack, F. J. et al *J. Water Pollut. Control. Fed.* 1960, **32**, 1173.
4. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
5. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
6. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
7. *Food Cosmet. Toxicol.* 1964, **2**, 327.
8. *Ind. Med. Surg.* 1972, **41**, 31.
9. Smyth, H. F. et al *Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
10. *Food Cosmet. Toxicol.* 1978, **16**, 637.
11. Searle, C. E. (Ed.) *Chemical Carcinogens. ACS Monograph 173* 1976, 172, American Chemical Society, Washington, DC, USA.
12. *Union Carbide Data Sheet* 1968, Union Carbide Corp., New York, USA.
13. Clayton, G. D. (Ed.) *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, **2**, 2267, John Wiley and Sons, New York, NY, USA.
14. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
15. *Chemical Safety Data Sheets* 1989, **1**, 166-168, The Royal Society of Chemistry, London, UK.
16. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E124 *N*-ethyl-*N*-formylhydrazine

$$NH_2N(CHO)CH_2CH_3$$

$C_3H_8N_2O$ **Mol. Wt.** 88.11 **CAS Registry No.** 74920-78-8

Synonyms 1-ethyl-1-formylhydrazine; EFH

RTECS No. LQ 8450000

Physical properties

B. Pt. 50-51°C at 0.06 mmHg **Specific gravity** 1.002 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Oral mice were administered 0.02% solution in drinking water continuously for life. The incidence of tumours in lungs, blood vessels, liver, gallbladder and preputial gland in ♀ mice were 98, 94, 0, 2 and 0%, respectively, and in ♂ mice 78, 64, 26, 8 and 10%, respectively. Lesions identified were adenomas and adenocarcinomas of the lungs, angiomas and angiosarcomas of blood vessels, benign hepatomas, liver cell carcinomas, adenomas and adenocarcinomas of the gallbladder and squamous cell papillomas and carcinomas of preputial glands (1).

Other comments

Genotoxicity and carcinogenicity reviewed (2).

References

1. Toth, B. et al *Carcinogenesis (N.Y.)* 1980, 1(1), 61-65.
2. Ashby, J. et al *Mutat. Res.* 1993, **286**(1), 3-74

E125 2-ethylhexanal

$$CH_3(CH_2)_3CH(CH_2CH_3)CHO$$

$C_8H_{16}O$ **Mol. Wt.** 128.21 **CAS Registry No.** 123-05-7

Synonyms butylethylacetaldehyde; ethylbutylacetaldehyde; α-ethylcaproaldehyde; β-propyl-α-ethylacrolein; 2-ethylhexaldehyde

EINECS No. 204-596-5 **RTECS No.** MN 7525000

Uses Organic synthesis. Flavouring and fragrance material. Leak detector. Insecticide.

Physical properties

M. Pt. 100°C **B. Pt.** 164°C **Flash point** 42°C **Specific gravity** 0.8540 at 20°C **Volatility** v.p. 1.8 mmHg at 20°C ; v.den. 4.42

Solubility Water: <1 g l^{-1} at 21°C. Organic solvents: acetone, diethyl ether, dimethyl sulfoxide, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 3550 mg kg^{-1} (1).
LC_{50} (4 hr) Inhalation rat 4000 ppm (2).
LD_{50} dermal rabbit 5040 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 500 mg kg^{-1} (3).

Irritancy

Dermal rabbit (24 hr) 10 mg caused severe irritation (2).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, with and without metabolic activation negative (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).
Autoignition temperature 197°C.

References

1. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure* 1982, 103, CIP, Moscow, USSR.
2. *AMA Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119.
3. *Hydrometallurgy* 1978, **3**, 210.
4. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E126 2-ethyl-1,3-hexanediol

$$CH_3CH_2CH_2CH(OH)CH(CH_2CH_3)CH_2OH$$

$C_8H_{18}O_2$ **Mol. Wt.** 146.23 **CAS Registry No.** 94-96-2

Synonyms ethohexadiol; ethylhexylene glycol; carbide 6-12; ENT 375; 2-ethyl-3-propyl-1,3-propanediol; 3-(hydroxymethyl)-*n*-heptan-4-ol; octylene glycol

EINECS No. 202-377-9 **RTECS No.** MO 2625000

Uses Solvent. Lubricant. Plasticiser. Insect repellent. Preparation of cosmetics.

Physical properties

M. Pt. –40°C **B. Pt.** 241-249°C **Flash point** 129°C **Specific gravity** 0.9325 at 20°C with respect to water at 4°C **Volatility** v.p. <0.01 mmHg at 20°C ; v.den. 5.03
Solubility Water: 6 g l^{-1} at 20°C. Organic solvents: castor oil, chloroform, ethanol, isopropanol, propylene glycol

Occupational exposure

Supply classification irritant
Risk phrases Irritating to the eyes (R36)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S26)

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >100 mg kg^{-1} (1).
LD_{50} oral rat, mouse, guinea pig, rabbit 1400-2600 mg kg^{-1} (2-4).
LD_{50} dermal rabbit 2000 mg kg^{-1} (5).

Carcinogenicity and chronic effects
Oral rat (2 yr) 2, 4 or 8% of diet caused reduction in body weight gain. All rats receiving the high dose died within 18 wk due to inanition (6).

Teratogenicity and reproductive effects
Oral rat, lowest toxic dose 20,000 mg kg^{-1} day^{-1} days 6-15 of gestation, teratogenic effects (7).

Metabolism and toxicokinetics
Following intravenous administration of ^{14}C-labelled substance to rats, elimination from plasma occurred in a biexponential manner over a 48-hr period. Radioactivity was detected in the urine, but unchanged 2-ethyl-1,3-hexanediol was not detected, indicating that complete metabolism had occurred (8).

Irritancy
Dermal rabbit 500 mg caused mild irritation and 5 mg instilled into rabbit eye caused severe irritation (9,10). Single sustained contact to humans of undiluted 2-ethyl-1,3-hexanediol (concentration unspecified) caused minor primary skin irritation in 13% of subjects, and slight to moderate cumulative skin irritation by recurrent sustained dermal contact in 93% of subjects (11).

Sensitisation
May be a weak skin sensitiser in humans (11).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (12).
In vitro Chinese hamster ovary cells with and without metabolic activation forward mutation assay negative, sister chromatid exchanges positive (12).
In vivo rat bone marrow cells, chromosomal aberrations and mouse peripheral blood micronucleus test negative (12).

Other effects

Other adverse effects (human)
Ingestion causes central nervous system depression (13).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (14).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No 472, 1991 (15).

Other comments

Reviews on experimental toxicology and human health effects listed (16).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *Spec. Publ. – Entomol. Soc. Am.* 1978, **78-1**, 52.
3. *Pesticide Chemicals Official Compendium* 1966, **508**, Assoc. of the American Pesticide Control Officials, Topeka, KS, USA.
4. *J. Pharmacol. Exp. Ther.* 1948, **93**, 26.
5. Draize, J. H. et al *J. Pharmacol. Exp. Ther.* 1944, **82**, 377.
6. Clayton, G. D. (Ed.) *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, **2**, 3888, John Wiley & Sons, New York, NY, USA.
7. *US EPA Report 8EHQ-1288-0778* 1988, Office of Pesticides and Toxic Substances, Washington, DC, USA.
8. Frantz, S. W. et al *Drug Metab. Dispos.* 1991, **19**(5), 881-888.
9. *Am. J. Ophthalmol.* 1946, **29**, 1363.
10. Deichman, W. B. *Toxicology of Drugs and Chemicals* 1969, 731, Academic Press, New York, NY, USA.
11. Ballantyne, B. et al *J. Toxicol., Cutaneous Ocul. Toxicol.* 1989, **8**(2), 173-178.
12. Slesinski, R. S. et al *Toxicology* 1988, **53**(2-3), 179-198.

13. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
14. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
15. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
16. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E127 2-ethylhexanoic acid

$$CH_3(CH_2)_3CH(CH_2CH_3)CO_2H$$

$C_8H_{16}O_2$ **Mol. Wt.** 144.21 **CAS Registry No.** 149-57-5

Synonyms butylethylacetic acid; α-ethylcaproic acid; 2-butylbutanoic acid

EINECS No. 205-743-6 **RTECS No.** MO 7700000

Uses Catalyst. Corrosion inhibitor. Surfactant. Drying agent for paints and varnishes, Plasticiser.
Occurrence Odour component of plants, meat and dairy products.

Physical properties

M. Pt. –83°C **B. Pt.** 227°C **Flash point** 118°C (open cup) **Specific gravity** 0.903 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.64 **Volatility** v.p. 0.03 mmHg at 20°C ; v.den. 5.0
Solubility Water: soluble. Organic solvents: acetone, carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

Supply classification harmful
Risk phrases Possible risk of harm to the unborn child (R63)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Environmental fate

Degradation studies
Removed from wastewater at a concentration of 2500 mg l^{-1} in an aerobic two-stage biological system (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3000 mg kg^{-1} (2).
LD_{50} dermal rabbit 1260 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral rat (3 wk) 2% in diet caused hepatomegaly: liver/body weight ratio increased 50%. Serum triglyceride was decreased while hepatic peroxisomes increased significantly (4).

Teratogenicity and reproductive effects
Gavage rat 900 or 1800 mg kg^{-1} on day-12 of gestation caused a dose-related increase in skeletal malformations (5).

Irritancy
Dermal rabbit 450 mg caused mild irritation and 4.5 mg instilled into a rabbit eye caused severe irritation (exposure not specified) (3,6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, with and without metabolic activation negative (7).
In vitro human lymphocytes sister chromatid exchanges positive (8).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).

References

1. Ng, W. J. et al *Biol. Wastes* 1989, **29**(4), 299-311.
2. *J. Ind. Hyg. Toxicol.* 1944, **26**, 269.
3. *Union Carbide Data Sheet* 4 Nov. 1971.
4. *Patty's Industrial Hygiene and Toxicology* 3rd ed. 1982, **2**, 4925, John Wiley & Sons, New York, NY, USA.
5. Ritter, E. J. et al *Teratology* 1987,**35**, 41-46.
6. *Am. J. Ophthalmol.* 1946, **29**, 1363.
7. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-150.
8. Sipi, P. et al *Mutat. Res.* 1992, **279**(2), 75-82.
9. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E128 2-ethylhexanol

$$CH_3(CH_2)_3CH(CH_2CH_3)CH_2OH$$

$C_8H_{18}O$ **Mol. Wt.** 130.23 **CAS Registry No.** 104-76-7

Synonyms 2-ethyl-1-hexanol; 2-ethylhexyl alcohol

EINECS No. 203-234-3 **RTECS No.** MP 0350000

Uses Polymerisation catalyst. Antifoaming agent. Organic synthesis. Solvent. Plasticiser.
Occurrence Aroma component of plants and meats.
Mammalian metabolite of di-2-ethylhexyl phthalate (1).

Physical properties

M. Pt. –76°C **B. Pt.** 183-186°C **Flash point** 77°C **Specific gravity** 0.8344 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 2.81 (calc.) (2) **Volatility** v.p. 0.2 mmHg at 20°C ; v.den. 4.5
Solubility Water: 1 g l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr – static) rainbow trout 32-37 mg l^{-1} (3).

Invertebrate toxicity
IC_{50} (24 hr) *Daphnia magna* 26 mg l^{-1} (4).

Environmental fate

Carbonaceous inhibition
Inhibition of activated sludge process utilising glucose as carbon source, no inhibition at 1 mg l^{-1}, 32% inhibition at 10 mg l^{-1}, 100% inhibition at 100 mg l^{-1} (5).

Degradation studies
Biodegradation at 0.1 mg l^{-1} after 24 hr, 0% in normal sewage, 100% in adapted sewage (5).

Abiotic removal
Adsorption by activated carbon 0.138 g g^{-1} carbon (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, mouse, rat 1180, 2500 mg kg^{-1}, respectively (7,8).
LD_{50} dermal rabbit 1970 mg kg^{-1} (9).
LD_{50} intraperitoneal rat, mouse 500, 760 mg kg^{-1}, respectively (8,10).
Inhalation rat (6 hr) no fatalities at 235 ppm (11).

Sub-acute and sub-chronic data
Inhalation rat (90 day) 15, 40 and 120 ppm 6 hr day^{-1}. No adverse effects were observed in any of the groups (12).

Teratogenicity and reproductive effects
Inhalation rat, 850 mg m^{-3} 7 hr day^{-1} on day 1-19 of gestation caused a slight reduction in maternal food intake and a slight increase in resorptions. No teratogenic effect was observed (13).
Gavage rat (day 6-15 gestation) 0, 1, 5 and 10 mmol kg^{-1}. Strong maternal and foetal toxicity observed at 10 mmol kg^{-1} and slight maternal and foetal toxicity at 5 mmol kg^{-1} (14).

Metabolism and toxicokinetics
Following oral administration to rabbits about 90% was eliminated in the urine as glucuronide. Small amounts were excreted in the faeces and exhaled as carbon dioxide (15,16).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation and 20 mg instilled into rabbit eye for 24 hr caused moderate irritation (17,18).

Genotoxicity

Salmonella typhimurium TA90, TA100, TA1535, TA1537, TA1538, with and without metabolic activation negative (19).
In vitro Chinese hamster ovary cells chromosomal aberrations and forward mutation assay, with and without metabolic activation negative (20).
In vivo mouse, dominant lethal assay, negative (21).

Other effects

Any other adverse effects
Perfusion of rat livers *in vitro* with 390 mg l^{-1} solution reduced oxygen uptake and ketone body formation by 50 and 80%, respectively, and caused cell damage as assessed by the appearance of lactate dehydrogenese (1).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 B (22).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties are listed (23).

References

1. Keller, B.J. et al *J. Pharmacol. Exp. Ther.* 1990, **252**(3), 1355-1360.
2. Vaishnav, D. D. et al *Chemosphere* 1987, **16**(4), 695-703.
3. Dave, G. et al *Hydrometallurgy* 1978, **3**, 201.
4. Devillers, J. et al *Chemosphere* 1987, **16**(6), 1149-1163.

5. Gaffney, P. E. *J. Water Pollut. Control Fed.* 1976, **48**(12), 2731-2737.
6. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.
7. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
8. *Z. Gesamte Hyg. Ihre Grenzgeb.* 1974, **20**, 275.
9. *Raw Materials Data Handbook* 1974, **1**, 61.
10. *Hydrometallurgy* 1970, **3**, 201.
11. *Patty's Industrial Hygiene and Toxicology* 3rd ed. 1982, **2C**, 4620-4624, John Wiley and Sons, New York, NY, USA.
12. Klimisch, H.-J. et al *Food Chem. Toxicol.* 1998, **36**(3), 165-168.
13. Nelson, B. K. et al *J. Am. Coll. Toxicol.* 1989, **8**(2), 405-410.
14. Hellwig, J. et al *Food Chem. Toxicol.* 1997, **35**(5), 489-500.
15. Kamil, I. A. et al *Biochem. J.* 1953, **53**, 137.
16. Albro, P. W. *Xenobiotica* 1975, **5**(10), 625-636.
17. *Food Cosmet. Toxicol.* 1979, **17**, 775.
18. Marhold, J.V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 36, Prague, Czechoslovakia.
19. Litton Bionetics Inc. *Mutagenicity Evaluation of 2-Ethylhexenal in the Ames Salmonella/ Microsome Plate Test* 1982, EPA 40-8226118.
20. Litton Bionetics Inc. *Evaluation 2-Ethylhexanal in the CHO/HGPRT Forward Mutation Assay* 1985, EPA 40-8526196.
21. SRI International *Dominant Lethal Study of Three Compounds, Final Report* 1981, EPA Document No. 878210249.
22. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
23. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E129 2-ethylhexenal

$$CH_3(CH_2)_2CH{=}C(CH_2CH_3)CHO$$

$C_8H_{14}O$ **Mol. Wt.** 126.20 **CAS Registry No.** 26266-68-2

EINECS No. 247-571-4 **RTECS No.** MP 6100000

Uses Insecticide. Leak detector.

Physical properties

B. Pt. 55°C at 13.5 mmHg **Flash point** 43.3°C

Solubility Water: < 1 g l^{-1} at 21°C. Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2000 mg kg^{-1} (1).

Irritancy

Strong skin, eye and mucous membrane irritant (2).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. *Gig. Tr. Prof. Zabol.* 1988, **32**(3), 48.
2. Keith, L. H. et al (Ed.) *Compendium of Safety Data Sheets for Research and Industrial Chemicals* 1987, **5**, 2554, VCH, New York, NY, USA.
3. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E130 2-ethyl-2-hexenal

$$CH_3(CH_2)_2CH{=}C(CH_3CH_2)CHO$$

$C_8H_{14}O$ **Mol. Wt.** 126.20 **CAS Registry No.** 645-62-5

Synonyms α-ethyl-β-*n*-propylacrolein; 2-ethyl-3-propylacrolein

EINECS No. 211-448-3 **RTECS No.** MP 6300000

Uses Acaricide, nematocide and bacteriocide. Organic synthesis. Leak detector.

Physical properties

B. Pt. 175°C **Flash point** 68°C (open cup) **Specific gravity** 0.848 at 20°C with respect to water at 4°C
Volatility v.p. 1.0 mmHg at 20°C ; v.den. 4.35
Solubility Water: 700 mg l^{-1}. Organic solvents: acetone, ethanol

Ecotoxicity

Fish toxicity
Not toxic to brown trout, bluegill sunfish, yellow perch or goldfish at 5 ppm for 24 hr (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3000 mg kg^{-1} (2).

Sub-acute and sub-chronic data
Inhalation rat (8 hr) saturated vapour did not cause any fatalities (3).

Irritancy
Dermal rabbit (24 hr) 10 mg caused irritation (2).
500 mg instilled into rabbit eye caused severe irritation (exposure not specified) (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, with and without metabolic activation negative (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Autoignition temperature 200°C.

References

1. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002; PB 87-200-275, Washington DC, USA.
2. *J. Ind. Hyg. Toxicol.* 1944, **26**, 269.
3. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, 2651, John Wiley and Sons, New York, NY, USA.
4. *Am. J. Ophthalmol.* 1946, **29**, 1363.
5. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E131 2-ethylhexyl acrylate

$$CH_2=CHCO_2CH_2CH(CH_2CH_3)(CH_2)_3CH_3$$

$C_{11}H_{20}O_2$ **Mol. Wt.** 184.28 **CAS Registry No.** 103-11-7

Synonyms 2-ethylhexyl 2-propenoate; (±)-2-ethylhexyl acrylate; *sec*-octyl acrylate

EINECS No. 203-080-7 **RTECS No.** AT 0855000

Uses Manufacture of polymers.

Physical properties

M. Pt. -90°C **B. Pt.** 215-219°C **Flash point** 82°C (open cup) **Specific gravity** 0.8869 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 3.67 (1) **Volatility** v.p. 1 mmHg at 50°C ; v.den. 6.35
Solubility Organic solvents: acetone, dimethyl sulfoxide

Occupational exposure

Supply classification irritant
Risk phrases Irritating to respiratory system and skin – May cause sensitisation by skin contact (R37/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – Wear suitable gloves (S2, S24, S37)

Environmental fate

Degradation studies
Detected at concentration ranges of 0.6-11 ppb in the effluent from the last stage of an on-site waste treatment facility receiving its wastewater from a large petrochemical plant. The influent untreated wastewater contained 0.55-5.6 ppm (2)

Abiotic removal
Estimated $t_{1/2}$ for volatilisation from model river water ≈7 hr and from model pond water 65 hr (3,4).
$t_{1/2}$ for reaction with photochemically produced hydroxyl radicals and ozone in the atmosphere 10.3 hr (5).

Adsorption and retention
Calculated K_{oc} of 363 indicates that 2-ethylhexyl acrylate is unlikely to adsorb to soil and sediments (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 4400, 5660 mg kg^{-1} (6,7).
LD_{50} dermal rabbit 8480 mg kg^{-1} (8).
LD_{50} intraperitoneal mouse, rat 1330, 1670 mg kg^{-1} (9,10).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (11).

Dermal mouse (78 wk) 20 mg per animal 3 × wk^{-1}. 6/40 mice developed skin tumours, including 2 malignancies (12).

Metabolism and toxicokinetics

Rats were administered 10 mg kg^{-1} of ^{14}C-labelled substance by intravenous or intraperitoneal injection. Elimination of radioactivity from the blood was bi-exponential for both routes. $t_{1/2}$ for the 1st phase was 30-60 min in 4-month-old rats and 115-130 min in 7-month-old rats, and for the 2nd phase 5-6 hr and 14 hr, respectively. >50% of the administered dose was exhaled as CO_2. Exhalation of unchanged 2-ethylhexyl acrylate accounted for only 0.05% of the intravenous dose, or 0.3% of the intraperitoneal dose. Radioactivity excreted in the urine within the first 24 hr accounted for 7% of the intraperitoneal dose or 14% of the intravenous dose, and only 2% was excreted as thioethers (13).

Following intravenous administration to rats of 10 or 50 mg kg^{-1}, 2.2% was excreted in the bile, most of it (83%) during the first 3 hr. Highest radioactivity in the rats killed after 24 hr was found in the liver, less in the kidneys and least in the brain (14).

Irritancy

Dermal rabbit (24 hr) 20 mg caused moderate irritation and 5 mg instilled into rabbit eye for 24 hr caused severe irritation (15).

Sensitisation

Did not cause sensitisation in patch tests on 24 patients (16).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (17).

In vitro Chinese hamster ovary cells, induction of mutations in HGPRT locus negative (18).

In vitro mouse lymphoma L5178Y tk^+/tk^- mutagenicity assay negative (18).

Other comments

Exists in vapour phase in the atmosphere. Susceptible to photooxidation via vapour phase reaction with photochemically produced hydroxyl radicals and ozone.

Physical properties, toxicity and safety precautions reviewed (19).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (20).

Autoignition temperature 252°C.

References

1. Reinert, K. H. *Regul. Toxicol. Pharmacol.* 1987, **7**(4), 384-389.
2. Berglund, R. L. et al *Chem. Eng. Prog.* 1987, **83**, 46-54.
3. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
4. *USEPA-EXAMS II Computer Simulation* 1987, USEPA.
5. Atkinson R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
6. *Union Carbide Data Sheet* 15 Sept 1964.
7. *Gig. Tr. Prof. Zabol.* 1982, **26**(9), 52.
8. *AMA Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119.
9. *J. Dent. Res.* 1972, **51**, 526.
10. *Arch. Mal. Prof. Med. Trav. Secur. Soc.* 1975, **36**, 58.
11. *IARC* 1994, **60**, 475.
12. De Pass, L. R. et. al *J. Toxicol. Environ. Health* 1985, **16**(1), 55-60.
13. Gut, I. et al *Arch. Toxicol.* 1988, **62**(5), 346-350.
14. Ciknt, M. et al *J. Hyg., Epidemiol., Microbiol., Immunol.* 1986, **30**(4), 365-370.
15. Marhold, J. V. *Prehled Prumyslove Toxikologie; Organic Latky* 1986, 372, Avicerum, Prague, Czechoslovakia.
16. Karerva, L. et al *Contact Dermatitis* 1988, **18**(1), 10-15.

17. Zeiger, E. et al *Environ. Mutagen.* 1985, **7**(2), 213-232.
18. Moore, M. M. et al *Mutagenesis* 1991, **6**(1), 77-85.
19. *Chemical Safety Data Sheets* 1990, **3**, 100-102, The Royal Society of Chemistry, Cambridge, UK.
20. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E132 2-ethylhexylamine

$$CH_3(CH_2)_3CH(CH_2CH_3)CH_2NH_2$$

$C_8H_{19}N$ **Mol. Wt.** 129.25 **CAS Registry No.** 104-75-6

Synonyms 1-amino-2-ethylhexane; (±)-2-ethylhexylamine

EINECS No. 203-233-8 **RTECS No.** MQ 5250000

Uses Organic synthesis.

Physical properties

M. Pt. –76°C **B. Pt.** 169°C **Flash point** 52°C (open cup) (98% purity) **Specific gravity** 0.7894 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 2.82 **Volatility** v.p. 1.2 mmHg at 20°C ; v.den. 4.45 **Solubility** Organic solvents: acetone, dimethyl sulfoxide, ethanol

Occupational exposure

UN No. 2276 **HAZCHEM Code** 3W **Conveyance classification** flammable liquid, corrosive

Ecotoxicity

Invertebrate toxicity

Toxicity threshold, cell multiplication inhibition *Pseudomonas putida* 82 mg l^{-1}, *Scenedesmus quadricauda* 0.36 mg l^{-1}, *Entosiphon sulcatum* 12 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 450 mg kg^{-1} (2).
LC_{Lo} (4 hr) inhalation rat 250 ppm (3).
LD_{50} dermal rabbit 600 mg kg^{-1} (2).
LD_{Lo} intraperitoneal mouse 4 mg kg^{-1} (4).

Irritancy

Dermal rabbit (24 hr) 500 mg caused severe irritation and 50 µg instilled into rabbit eye for 24 hr caused severe irritation (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, with and without metabolic activation negative (6).

References

1. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
2. *Union Carbide Data Sheet* 20 Feb. 1963.
3. *Arch. Environ. Health* 1960, **1**, 343.

4. *Summary Tables of Biological Tests* 1950, **2**, 189, National Research Council Chemical-Biological Coordination Centre, Washington, DC, USA.
5. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 62, Prague, Czechoslovakia.
6. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl.12), 1-158

E133 2-ethylhexyl chloroformate

$$ClCO_2CH_2CH(CH_2CH_3)(CH_2)_3CH_3$$

$C_9H_{17}ClO_2$ **Mol. Wt.** 192.69 **CAS Registry No.** 24468-13-1

Synonyms 2-ethylhexyl carbonochloridic acid; (±)-2-ethylhexyl chloroformate

EINECS No. 246-278-9

Uses Organic synthesis.

Physical properties

B. Pt. 106-107°C at 30 mmHg **Flash point** 81°C **Specific gravity** 0.981 at 20°C
Volatility v.p. 1 mmHg at 45°C

Occupational exposure

UK-LTEL 1 ppm (8 mg m^{-3})

UN No. 2748 **HAZCHEM Code** 3W **Conveyance classification** toxic substance, corrosive

Other effects

Other adverse effects (human)
Extremely destructive to mucous membranes, upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (1).

References

1. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed. 1988, **1**, 1621, Sigma-Aldrich, Milwaukee, WI, USA

E134 2-ethylhexyl mercaptoacetate

$$HSCH_2CO_2CH_2CH(CH_2CH_3)(CH_2)_3CH_3$$

$C_{10}H_{20}O_2S$ **Mol. Wt.** 204.33 **CAS Registry No.** 7659-86-1

Synonyms 2-ethylhexyl sulfonylacetate; thioglycolic acid 2-ethylhexyl ester

EINECS No. 231-626-4 **RTECS No.** AI 7255000

Physical properties

B. Pt. 133.5°C **Specific gravity** 0.97 at 20°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, guinea pig, mouse 303, 534, 955, 1430 mg kg^{-1}, respectively (1).

LD_{50} intraperitoneal rat, mouse 265, 865 mg kg^{-1} respectively (1).

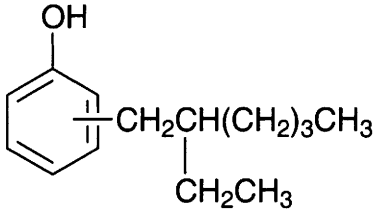
Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (2).

References

1. *Z. Gesamte Hyg. Ihre Grenzgeb.* 1974, **20**, 575.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E135 (2-ethylhexyl)phenol



$C_{14}H_{22}O$ **Mol. Wt.** 206.33 **CAS Registry No.** 1331-54-0

Synonyms 2-ethylhexylphenol

RTECS No. SL 4375000

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2460 mg kg^{-1} (1).

LD_{50} dermal rabbit 2520 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 10 mg caused severe irritation and 50 µg (exposure unspecified) caused severe irritation (1).

References

1. *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61

E136 ethyl hydrogen adipate

$$CO_2H(CH_2)_4CO_2CH_2CH_3$$

$C_8H_{14}O_4$ **Mol. Wt.** 174.20 **CAS Registry No.** 626-86-8

Synonyms monoethyl adipate; ethyl adipate; ethyl hydrogen hexanedioate; monoethyl hexanedioate; adipic acid monoethyl ester

EINECS No. 210-966-7 **RTECS No.** AV 2030000

Uses Preparation of skin-lightening cosmetics.

Physical properties

M. Pt. 28-29°C **B. Pt.** 180°C at 18 mmHg **Flash point** >110°C **Specific gravity** 0.9796 at 20°C with respect to water at 4°C

Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

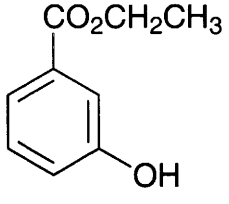
Acute data

LD_{50} oral rat 4100 mg kg^{-1} (1).

References

1. *Gig. Tr. Prof. Zabol.* 1977, **21**(10), 39

E137 ethyl 3-hydroxybenzoate



$C_9H_{10}O_3$ **Mol. Wt.** 166.18 **CAS Registry No.** 7781-98-8

Synonyms ethyl *m*-hydroxybenzoate; 3-(ethoxycarbonyl)phenol

EINECS No. 231-951-1

Uses Organic synthesis.

Physical properties

M. Pt. 72-74°C **B. Pt.** 187-188°C at 31 mmHg

Solubility Water: slightly soluble. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Irritancy

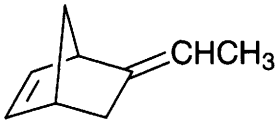
Causes irritation to the skin, eyes, mucous membranes and upper respiratory tract (species unspecified) (1).

o- and *p*-hydroxybenzoic acid esters (parabens) widely used as preservatives in cosmetic products have been shown to cause irritation to human skin (2).

References

1. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1623, Sigma-Aldrich, Milwaukee, WI, USA.
2. Sone, T. et al *Nippon Koshohin Kagakkaishi* 1990, **14**(1), 8-16 (Japan.) (*Chem. Abstr.* **113**, 197637u)

E138 5-ethylidene-2-norbornene



C_9H_{12} **Mol. Wt.** 120.19 **CAS Registry No.** 16219-75-3

Synonyms 5-ethylidenebicyclo[2.2.1]hept-2-ene; ethylidenenorbornene; ENB

EINECS No. 240-347-7 **RTECS No.** RB 9450000

Uses Heat stabiliser for rubbers.

Physical properties

M. Pt. –80°C **B. Pt.** 146°C **Flash point** 38°C (open cup) **Specific gravity** 0.8958 at 20°C
Volatility v.p. 4.2 mmHg at 20°C ; v.den. 4.1
Solubility Water: <1 g l^{-1} at 18°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Occupational exposure

FR-VLE 5 ppm (25 mg m^{-3})
US-STEL ceiling limit 5 ppm (25 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2530, 5670 mg kg^{-1}, respectively (1,2).
LC_{50} (4 hr) inhalation mouse, rat, guinea pig, rabbit 730, 1250, 2900, 3100 ppm, respectively (1,3).
LD_{50} dermal rabbit 8190 mg kg^{-1} (1).
LD_{50} intravenous rabbit 0.09 (♂), 0.11 (♀) mg kg^{-1} (4).

Sub-acute and sub-chronic data

Inhalation rat and dog (89 day), 61 or 93 ppm 7 hr day^{-1} caused hepatic lesions and testicular atrophy in dogs. 61 ppm caused a decrease in weight gain in ♂ but not ♀ rats or in dogs (5).
Inhalation rat (9 day), 52, 148 or 359 ppm, 6 hr day^{-1}. No mortalities, periocular swelling and urogenital area wetness. Body weight gain decreased in the 359 ppm ♀s (6).

Irritancy

Dermal rabbit 445 mg caused mild irritation (duration unspecified) (7).
Human volunteers (30 min) noted eye and nose irritation after exposure to 11 ppm and transient eye irritation at 6 ppm (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, with and without metabolic activation negative (9).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties are listed (10).

References

1. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
2. *Gig. Tr. Prof. Zabol.* 1974, **18**(10), 52.
3. *Toxicol. Appl. Pharmacol.* 1971, **20**, 250.
4. Ballantyne, B. et al *J. Appl. Toxicol.* 1997, **17**(4), 211-221.
5. Kinhead, et al *Toxicol. Appl. Pharmacol.* 1971, **20**(2), 250.
6. Ballantyne, B. et al *J. Appl. Toxicol.* 1997, **17**(14), 197-210.
7. *Union Carbide Data Sheet* 28 Nov 1967.
8. *Documentation of Threshold Limit Values* 4th ed. 1980, 188, American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH, USA.
9. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl.9), 1-109.
10. *ECETOC Technical Report No. 71* 1996, European Chemical Industry Ecology and Toxicology Centre, B-1160 Brussels, Belgium

E139 ethyl isobutyrate

$$(CH_3)_2CHCO_2CH_2CH_3$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 97-62-1

Synonyms ethyl 2-methylpropanoate; ethyl isobutanoate; ethyl 2-methylpropionate; FEMA No. 2428

EINECS No. 202-595-4 **RTECS No.** NQ 4675000

Uses Acylating agent. Manufacture of flavouring compounds and essences.

Physical properties

M. Pt. –88°C **B. Pt.** 110-113°C **Flash point** 13°C **Specific gravity** 0.870 at 20°C with respect to water at 20°C
Volatility v.p. 40 mmHg at 34°C ; v.den. 4.01
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2385 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 800 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (1).

References

1. *Food Cosmet. Toxicol.* 1978, **16**, 741

E140 ethyl isocyanate

$$CH_3CH_2N{=}C{=}O$$

C_3H_5NO **Mol. Wt.** 71.08 **CAS Registry No.** 109-90-0

Synonyms isocyanatoethane

EINECS No. 203-717-9 **RTECS No.** NQ 8825000

Uses Carbamylating and acylating agent. Reagent used for protecting cysteine groups in protein synthesis.
Occurrence Aroma component of plants. Insect pheromone. Formed by bacterial spoilage of meats.

Physical properties

M. Pt. <–50°C **B. Pt.** 60°C **Flash point** –6°C **Specific gravity** 0.90 at 20°C with respect to water at 4°C
Volatility v.p. 13 mmHg at 22.8°C ; v.den. 2.45
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

SE-LEVL 0.005 ppm **SE-CEIL** 0.01 ppm
UK-LTEL MEL 0.02 mg m^{-3} (as NCO) **UK-STEL** MEL 0.07 mg m^{-3} (as NCO)

UN No. 2481 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 56 mg kg^{-1} (1).

Sensitisation
Has been reported to cause asthma and allergic reactions (2).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (3).

Other effects

Other adverse effects (human)
Extremely destructive to mucous membranes and upper respiratory tract. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (2).

Other comments

Inhibits the uptake of substrates in hepatomas under conditions which have a smaller or no effect on the liver in tumour-bearing rats.

References

1. *Report US Army Armament Research and Development Command* NX02910, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD21010, USA.
2. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1627, Sigma-Aldrich, Milwaukee, WI, USA.
3. Yamaguchi, T. *Agric. Biol. Chem.* 1980, **44**(12), 3017-3018

E141 ethyl lactate

$$CH_3CH(OH)CO_2CH_2CH_3$$

$C_5H_{10}O_3$ **Mol. Wt.** 118.13 **CAS Registry No.** 97-64-3

Synonyms Actylol; Acytol; ethyl α-hydroxypropionate; ethyl 2-hydroxypropanoate; ethyl 2-hydroxypropionate; Solactol; Purasolv

EINECS No. 202-598-0 **RTECS No.** OD 5075000

Uses Solvent. Food flavouring. In the treatment of acne vulgaris.
Occurrence Occurs in alcoholic drinks, crops and bread (1).

Physical properties

M. Pt. –25°C **B. Pt.** 154°C **Flash point** 46°C (closed cup) **Specific gravity** 1.042 at 14°C
Volatility v.p. 5 mmHg at 30°C ; v.den. 4.07
Solubility Water: miscible. Organic solvents: acetone, chloroform, diethyl ether, ethanol

Occupational exposure

SE-LEVL 5 ppm (25 mg m^{-3}) **SE-STEL** 10 ppm (50 mg m^{-3})

UN No. 1192 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification flammable
Risk phrases Flammable (R10)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 2500 mg kg^{-1} (2).
LD_{50} oral rat >5000 mg kg^{-1} (3).
LD_{50} dermal rabbit >5000 mg kg^{-1} (3).
LD_{50} subcutaneous mouse 2500 mg kg^{-1} (2).
LD_{50} intravenous mouse 600 mg kg^{-1} (2).

Metabolism and toxicokinetics
^{14}C-label accumulated in the sebaceous glands of rats following dermal application of ^{14}C-ethyl lactate (4).

Irritancy
No skin irritation or sensitisation was observed using 8% in petrolatum in 48-hr patch-test on humans (5).

Sensitisation
Allergic dermatitis has been reported in one individual using anti-acne soap containing 10% ethyl lactate (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
Approved for use in food by the US Food and Drug Administration (8).
It was considered unnecessary to establish an acceptable daily intake for ethyl lactate as the total daily intake in food did not, in the opinion of the FAO/WHO committee, represent a hazard to health (9).

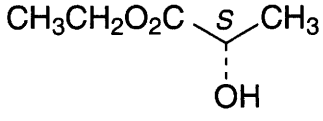
Other comments

Physical properties, occurrence, use, mammalian toxicity and metabolism reviewed (1).
Reviews on toxicity listed (10).
Autoignition temperature 400°C.

References

1. Snyder, R. (Ed.) *Ethel Browning's Toxicity and Metabolism of Industrial Solvents* 2nd ed. 1992, **3**, 347-350, Elsevier, New York, NY, USA.
2. *J. Pharmacol. Exp. Ther.* 1939, **65**, 89.
3. *Food Chem. Toxicol.* 1982, **20**, 677.
4. Prottey, C. et al *Br. J. Dermatol.* 1984, **110**, 475-485.
5. Opdyke, D. L. J. et al (Ed.) *Monographs on Fragrance Raw Materials* 1982 (Special Issue VI), 677, Pergamon Press, New York, NY, USA
6. Marot, L. et al *Contact Dermatitis* 1987, **17**, 45-46.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. Opdyke, D. J. L. et al *Food Chem. Toxicol.* 1982, **20**, 677-678.
9. *Evaluation of Certain Food Additives and Contaminants: 26th Report on the Joint FAO/WHO Expert Committee on Food Additives* 1982, WHO Tech. Rep. Series 683, Geneva, Switzerland.
10. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E142 (–)-ethyl lactate



$C_5H_{10}O_3$ **Mol. Wt.** 118.13 **CAS Registry No.** 687-47-8

Synonyms *S*-(–)-ethyl lactate; L-ethyl lactate; (*S*)-ethyl 2-hydroxypropanoate

EINECS No. 211-694-1 **RTECS No.** OD 5075000

Uses Solvent. Preparation of pharmaceuticals.

Physical properties

M. Pt. –26°C **B. Pt.** 154°C **Flash point** 48°C (closed cup) **Specific gravity** 1.042 at 20°C with respect to water at 4°C **Volatility** v.p. 5 mmHg at 30°C ; v.den. 4.1

Solubility Water: miscible. Organic solvents: acetone, ethanol

Occupational exposure

UN No. 1192 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Risk phrases Flammable (R10)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2500 mg kg^{-1} (1).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Autoignition temperature 400°C.

References

1. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1629, Sigma-Aldrich, Milwaukee, WI, USA.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E143 ethylmercury(II) chloride

$$CH_3CH_2HgCl$$

C_2H_5ClHg **Mol. Wt.** 265.10 **CAS Registry No.** 107-27-7

Synonyms Ceresan; chloroethylmercury; ethylmercuric chloride; EMC; Granosan

EINECS No. 203-478-0 **RTECS No.** OV 9800000

Uses Fungicide used as a seed dressing.

Physical properties

M. Pt. 192°C **Specific gravity** 3.24 **Volatility** v.p. 8×10^{-4} mmHg at 20°C

Solubility Water: 1.4 mg l^{-1}. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Hg) (total dust)

SE-LEVL 0.03 mg m^{-3} (as Hg)

UK-LTEL 0.01 mg m^{-3} (as Hg) **UK-STEL** 0.03 mg m^{-3} (as Hg)

US-TWA 0.01 mg m^{-3} (as Hg) **US-STEL** 0.03 mg m^{-3} (as Hg)

UN No. 2024 (liquid)

UN No. 2025 (solid) **Conveyance classification** toxic substance

Supply classification very toxic

Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R26/27/28, R33)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S13, S28, S36, S45)

Ecotoxicity

Fish toxicity

Guppy and *Ceratophyllum demersum* were exposed to radiolabelled compound. Uptake was positively related to the time of exposure over 200 hr and concentration up to 5×10^{-7} mol l^{-1}. Highest concentrations were accumulated in the internal organs, $t_{1/2}$ 20-23 days. Both species converted ethyl mercury chloride into inorganic mercury, 29 and 34% conversion, respectively, for the two species over 7 days (1).

Bioaccumulation

Taken up by plants from soil, thus accumulating in fodder and vegetable foodstuffs, presenting a potential hazard for organisms higher in the food chain (2).

Environmental fate

Degradation studies

Degraded by bacteria isolated from a river water in Tuscany, Italy, collecting cinnabar mine waters (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 40, 56 mg kg^{-1}, respectively (4,5).
LD_{50} dermal rat 200 mg kg^{-1} (6).
LD_{50} subcutaneous rat 66 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 16 mg kg^{-1} (8).

Teratogenicity and reproductive effects

Babies born to mothers with intra-uterine poisoning had puffy faces, indistinct features, dull eyes, scarlet dry lips, dry blue/grey skin, muscular hypotonia, tremors and convulsions. 50% of exposed babies died within 13 months, survivors were emaciated, had retarded physical and mental development and muscular atrophy (9).

Metabolism and toxicokinetics

Cattle were administered 0.2 mg kg^{-1} day^{-1} via feed for 8 days. Mercury concentration increased to a maximum of 0.314 mg kg^{-1} in faeces, 0.17 mg l^{-1} in blood and 0.012 mg l^{-1} in milk. Normal background levels in milk of 0.003 mg l^{-1} returned after ~3 months (10).
Principal entry routes are orally and by inhalation, however occupational exposure additionally allows uptake through the skin and mucous membranes (11).

Irritancy

Dermal rat, guinea pig 15 and 25 mg kg^{-1} (ethylmercury chloride), ulceration formed in 20 days accompanied by changes to biochemical state (12).

Genotoxicity

Drosophila melanogaster sex-linked recessive lethal mutation positive (13).
In vivo mouse bone marrow induction of chromosome aberrations positive (13).

Other effects

Other adverse effects (human)

Acute poisoning in humans by organomercury compounds is characterised by a metallic taste in the mouth, headache, nausea, salivation, vomiting, fainting, stomach pain, bloody diarrhoea, acute thirst, burning mouth, swelling and bleeding of gums. Initial symptoms are followed by unsteady gait, tremors, paralysis of extremities, loss of acute vision and hearing, pain in joints, obstructed swallowing, involuntary urination/defecation and blindness. Chronic poisoning results in disorders of the central nervous system and blood (2).

Any other adverse effects

Use in Europe led to the deaths of large number of granivorous birds together with birds of prey feeding on the corpses. Residues of mercury in birds' eggs have been associated with deaths of embryos in shell (14).
Sheep fed Granosan-treated grain had significant deposition of mercury in organ tissues (unspecified). Mercury was also detected in foetuses and new born lambs (15).
Evidence of neurotoxic effects in sub-acute Granosan poisoning (species unspecified) (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury maximum admissible concentration 1 μg l^{-1}, guide level for chlorides 25 mg l^{-1} (17).
Prescribed concentration for chlorides under UK Water Quality Regulation 400 mg l^{-1} (12-month average) (18).
Mercury and its compounds are included in Schedule 5 (Release into Water: Prescribed Substances) and organometallic compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (19).

Organomercuric compounds have been withdrawn for use in many Western countries and severely restricted in the former USSR. In the former USSR maximum admissible concentration for mercury in soil 2.1 mg kg^{-1} (irrespective of chemical form) (2).
WHO guideline value for drinking water 1 μg l^{-1} (20).

Other comments

The organomercury moiety is the active ingredient of the pesticide Granosan. Organomercury compounds enter the environment either during production or use, in the atmosphere as gaseous discharges, or as contaminants in water and soil. Transformation and transport is dependent on a combination of physical and chemical parameters, including volatility, solubility, soil adsorption and food chain accumulation.
A factor affecting the toxicity of organomercury compounds is the rate of uptake of the metal by cells. Mercury is bound to cell walls or cell membranes of microorganisms, apparently to a limited number of binding sites. Therefore effects are related to both cell density and concentration of mercury in the substrate. Effects are often irreversible (14).
Toxicity, human health effects and environmental fate have been extensively reviewed (2,21).

References

1. Fang, S. C. *Environ. Res.* 1974, **8**, 112-118.
2. Izmerov, N. F. *Scientific Reviews of Soviet Literature of Toxicity and Hazards of Chemicals: Organomercury Compounds* 1990, **117**, 1-73, CIP, Moscow, USSR.
3. Baldi, F. et al *Microbiol. Ecol.* 1989, **17**(3), 263-274.
4. *Gig. Tr. Prof. Zabol.* 1974, **9**, 25.
5. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure* 1982, 68, CIP, Moscow, USSR.
6. *Pharm. J.* 1960, **185**, 361.
7. *Jpn. J. Exp. Med.* 1969, **39**, 47.
8. *Organomet. Chem. Rev.* 1968, **3**, 137.
9. Goloma, E. A. *Gig. Sanit.* 1962, **9**, 101-103.
10. Zhulerko, V. N. et al *Veterinariya (Moscow)* 1988, (12) 56-58, (Russ.) (*Chem. Abstr* **110**, 109675q).
11. Bushtueva, K. A. et al *Metals: Hygienic Aspects of Assessment and Enhancement of the Environment* 1983, 109-118, Kasporov, A. A. (Ed.), Res. Inst. Ind. Hyg. Occup. Dis. USSR Acad. Med. Sci., Moscow, USSR.
12. Ramanauskaite, M. B. *Min. Health. Lith. SSR* 1973, 181-182, Iss. Epidem. Hyg., Vilnyus, USSR.
13. Lekevichus, R. et al *Mutat. Res.* 1978, **53**(2), 218-219.
14. *Environmental Health Criteria 86: Mercury Environmental Aspects* 1989, WHO, Geneva, Switzerland.
15. Bashmakova, E. V. *Toxicokinetics of Mercury in Sheep* 1980, 36, All Union Constituent Conference on Toxicology, Moscow, USSR.
16. Abramova, Zh. I. et al *Gig. Tr. Prof. Zabol.* 1972, **11**, 21-24.
17. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
18. *S.I. 1989 No. 1147, The Water Supply (Water Quality) Regulations* 1989, HMSO, London, UK.
19. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
20. *Water Environ. Manage.* 1993, (1), 7.
21. Richardson, M. L. *Environ. Manage. Health* 1993, **4**(3), 16-20

E144 ethylmercury(II) phosphate

$$CH_3CH_2HgOP(O)(OH)_2$$

$C_2H_7HgO_4P$ **Mol. Wt.** 326.64 **CAS Registry No.** 2235-25-8

Synonyms ethylmercuric phosphate; Granosan M; Lignasan; Ruberon granule; Soilsin

EINECS No. 218-790-2 **RTECS No.** OW 3750000

Uses Fungicide and timber preservative.

Physical properties

M. Pt. 178-179°C

Solubility Water: miscible

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Hg) (total dust)

JP-OEL 0.05 mg m^{-3} (as Hg)

SE-LEVL 0.03 mg m^{-3} (as Hg)

UK-LTEL 0.01 mg m^{-3} (as Hg) **UK-STEL** 0.03 mg m^{-3} (as Hg)

US-TWA 0.01 mg m^{-3} (as Hg) **US-STEL** 0.03 mg m^{-3} (as Hg)

UN No. 2024 (liquid)

UN No. 2025 (solid) **Conveyance classification** toxic substance

Supply classification very toxic

Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R26/27/28, R33)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S13, S28, S36, S45)

Ecotoxicity

Fish toxicity

Rainbow trout exposed to 125 μg l^{-1} for 1 hr. Raising the temperature from 13 to 15°C increased toxicity. Changes in water hardness from 23-120 mg $CaCO_3$ l^{-1} decreased toxicity. At saturation, no deaths occurred even at highest water hardness, however when dissolved oxygen levels were <6 mg l^{-1} (15°C) 72-76% of fish died; at 13°C 37% of trout died (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 48 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 76 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Inhalation mice 0.04 mg m^{-3} (as mercury) for 6 hr day^{-1} 6 day wk^{-1} caused 100% lethality by day-61. Symptoms of toxicity included unsettled posture, increased excitability, enhanced cutaneous sensitivity and weight loss (4).

Metabolism and toxicokinetics

Inhalation guinea pig 0.00095 mg m^{-3} reached maximum concentration in the blood within 13-19 days. Symptoms of poisoning included central nervous system effects. Elimination occurred predominantly via the kidneys (5,6).

Other effects

Other adverse effects (human)

Cases of acute poisoning in humans are characterised by a metallic taste in the mouth, headache, nausea, salivation, vomiting, fainting, stomach pain, bloody diarrhoea, acute thirst, burning mouth, swelling and bleeding of gums. These initial symptoms are followed by unsteady gait, tremors, paralysis, lost acute vision and hearing, joint pain, obstructed swallowing, involuntary urination and defecation and blindness (7).

In workers occupationally exposed, mercury content in urine was >0.01 mg l^{-1} in 37% of workers. Elimination of increased quantities of mercury was observed for ≤3 yr following poisoning in 50% of acute cases and 70% of chronic cases (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury maximum admissible concentration 1 μg l^{-1}; phosphate as P_2O_5, maximum admissible concentration 5000 μg l^{-1}, guide level 400 μg l^{-1} (9).

Mercury and its compounds are included in Schedule 5 (Release into Water: Prescribed Substances) and organometallic compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Maximum admissible concentration former USSR, in working zone atmosphere is 0.005 mg m^{-3}. Hazard class 1. The compound is additionally marked dangerous by absorption through the skin (11).

WHO guideline value for drinking water 1 μg l^{-1} (12).

Other comments

Organomercury compounds enter the environment either during production or use, in the atmosphere as gaseous discharges, or as contaminants in water and soil. Transformation and transport is dependent on a combination of physical and chemical parameters, including volatility, solubility, soil adsorption and food chain accumulation. Toxicity, human health effects and environmental fate have been extensively reviewed (11,13).

References

1. Amend, D. F. et al *Trans. Am. Fish. Soc.* 1969, **98**, 419-425.
2. *Jpn. J. Pharmacol.* 1963, **59**, 452.
3. *Proc. Congenital Anomalies Res. Assoc. Jpn.* 1967, **7**, 53.
4. Medved, L. I. *Vrach. Delo* 1949, **4**, 1-7.
5. Trakhtenberg, I. M. *Farmakol. Toksikol.* 1951, **1**, 48-51.
6. Trakhtenberg, I. M. *Abstr. Reps. XXIth Conf. Toxicological Chemistry* 1967, 48-49, Prague, Czechoslovakia.
7. Drogichina, E. M. et al *Intoxication with Mercury and its Organic Derivatives* 1966, 1- 102, Meditsina Publ., Moscow, USSR.
8. Giss, Yu. F. *Sc. Trans. Leningrad. Inst. Refr. Medicians* 1971, **98**, 127-133, Leningrad, USSR.
9. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. Izmerov, N. F. *Scientific Reviews of Soviet Literature of Toxicity and Hazards of Chemicals: Organomercury Compounds* 1990, **117**, 1-66, CIP, Moscow, USSR.
12. *Water Environ. Manage.* 1993, (1), 7.
13. Richardson, M. L. *Environ. Manage. Health* 1993, **4**(3), 16-20

E145 ethyl methacrylate

$$H_2C=C(CH_3)CO_2CH_2CH_3$$

$C_6H_{10}O_2$ **Mol. Wt.** 114.14 **CAS Registry No.** 97-63-2

Synonyms ethyl 2-methylpropenoate; ethyl α-methylacrylate; ethyl 2-methylacrylate

EINECS No. 202-597-5 **RTECS No.** OZ 4550000

Uses Manufacture of copolymers.

Physical properties

M. Pt. <–75°C **B. Pt.** 118-119°C **Flash point** 15°C (closed cup) (99% purity) **Specific gravity** 0.911 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 1.94 **Volatility** v.p. 15 mmHg at 20°C ; v.den. 3.94 **Solubility** Water: 5600 ppm at 20°C. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

SE-LEVL 50 ppm (250 mg m^{-3}) **SE-STEL** 75 ppm (350 mg m^{-3})

UN No. 2277 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Supply classification highly flammable, irritant

Risk phrases Highly flammable – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact (R11, R36/37/38, R43)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not empty into drains – Take precautionary measures against static discharges (S2, S9, S16, S29, S33)

Environmental fate

Abiotic removal

Volatilisation in model river water, $t_{1/2}$ (est.) 6 hr, and in model pond water ~3 days (1,2).

Readily undergoes polymerisation under environmental conditions (3).

Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ (est.) 8 hr (4).

Adsorption and retention

Estimated K_{oc} 38-271 indicates that adsorption to soil and sediments is unlikely (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 7840, 14,800 mg kg^{-1}, respectively (5,6).

LC_{50} (4 hr) inhalation rat 8300 ppm (7).

LD_{50} intraperitoneal rat, mouse 1220, 1370 mg kg^{-1}, respectively (8,9).

Teratogenicity and reproductive effects

Intraperitoneal rat, lowest toxic dose for teratogenic effects 735 mg kg^{-1} day^{-1} on days 5-15 of gestation (8).

Logistic regression and discriminant analysis was applied to animal toxicity studies to predict developmental toxicity to humans. When applied to ethyl methacrylate potential for human developmental toxicity was predicted to be negative (10).

Irritancy

May cause skin irritation (species unspecified) (11).

Concentrations of 4.5 ppm were detected in manicure salons. The only significant health effect noted was throat irritation (12).

Sensitisation

Caused moderate sensitisation in the guinea pig maximisation test and Freund's complete adjuvant test (13).

Human patch-testing for allergic contact dermatitis 2% in petrolatum vehicle positive (14).
No active sensitisation from patch-testing 543 patients with 1% ethyl methacrylate monomer (15).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (16).
In vitro mouse lymphoma L5178Y cells without metabolic activation chromosomal aberrations positive (17).
In vitro Chinese hamster ovary cells, chromosome aberrations negative, sister chromatid exchanges positive (18).

Other comments

The US Federal Toxic Substance Control Act requires manufacturers to undertake subchronic toxicity and/or metabolism studies (19).
Ecotoxicological properties of methacrylates discussed (20).
Physical properties, health hazards and toxicity reviewed (11,21).
Autoignition temperature 410.6°C.

References

1. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
2. *EXAMS II Computer Simulation* 1987, USEPA, Washington, DC, USA.
3. *Hawley's Condensed Chemical Dictionary* 11th ed. 1987, 496, Van Nostrand Reinhold, New York, NY, USA.
4. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
5. *J. Ind. Hyg. Toxicol.* 1941, **23**, 343.
6. *Toxicol. Lett.* 1982, **11**, 125.
7. *J. Toxicol. Environ. Health* 1985, **16**, 811.
8. *J. Dent. Res.* 1972, **51**, 1632.
9. *J. Pharm. Sci.* 1973, **62**, 778.
10. Jelousek, F. R. et al *Obstet. Gynecol.* 1989, **74**(4), 624-636.
11. *Chemical Safety Data Sheets* 1992, **5**, 127-129, The Royal Society of Chemistry, London, UK.
12. Hiipakka, D. et al *Am. Ind. Hyg. Assoc. J.* 1987, **48**(3), 230-237.
13. van der Walle, H. B. et al *Contact Dermatitis* 1982, **8**(3), 147-154.
14. Kanaerva, L. et al *Contact Dermatitis* 1988, **18**, 10-15.
15. Maibach, H. T. et al *Contact Dermatitis* 1978, **4**, 60.
16. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
17. Moore, M. M. et al *Environ. Mol. Mutagen.* 1988, **11**(1), 49-63.
18. *National Toxicology Program Fiscal Year 1987 Annual Plan* 1987, 87, NTP-87-001.
19. *Fed. Regist.* 1988, **53**(115), 22300-22325.
20. Reinert, K. H. *Regul. Toxicol. Pharmacol.* 1987, **7**(4A), 384-389.
21. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E146 ethyl methanesulfonate

$$CH_3SO_2OCH_2CH_3$$

$C_3H_8O_3S$ **Mol. Wt.** 124.16 **CAS Registry No.** 62-50-0

Synonyms half-Myleran; NSC26805; EMS

EINECS No. 200-536-7 **RTECS No.** PB 2100000

Uses Has been considered for use as a human ♂ contraceptive and for use as a ♂ chemosterilant for mammalian and insect pests. Intermediate in organic synthesis.

Physical properties

B. Pt. 213°C **Flash point** 100°C **Specific gravity** 1.1452 at 22°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.09 (1) **Volatility** v.p. 0.328 mmHg at 25°C
Solubility Organic solvents: acetone, dimethyl sulfoxide, ethanol

Ecotoxicity

Fish toxicity
Medaka embryos in early organogenesis (stage 20) exposed for 2 hr to 0.09-15 g l^{-1} suffered concentration-dependent decrease in viability and increase in malformations (2).

Bioaccumulation
Calculated bioconcentration factor <1 indicates that environmental accumulation is unlikely (1).

Environmental fate

Abiotic removal
Hydrolysis in water $t_{1/2}$ 96 hr at 20°C (3).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ (est.) 30 days (4).

Adsorption and retention
Estimated K_{oc} 27 indicates that adsorption by soil and sediments is unlikely (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 470 mg kg^{-1} (6).
LD_{50} intraperitoneal rat, mouse 350, 435 mg kg^{-1}, respectively (7,8).

Sub-acute and sub-chronic data
Intravenous Japanese quail 2, 20 or 200 mg kg induced haemolytic anaemia and lymphocytopenia within 24 hr (9).

Carcinogenicity and chronic effects
No adequate data on carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (10).
Subcutaneous mouse (40 wk) 200 μg day^{-1} in aqueous gelatin for the first 5 days of life. 31/31 surviving mice developed lung tumours compared with 4/48 controls. In another group administered 200 μg day^{-1} in arachis oil for the first 5 days of life, 5/39 survivors developed lung adenomas compared with 0/47 controls at 55-60 wk (11).
Intraperitoneal mouse, single dose of 175 mg kg^{-1} in saline solution. 18/31 treated mice developed lung tumours compared with 25/52 controls. The first tumours appeared at 350 and 367 days, respectively (12).
Intraperitoneal mouse single undiluted dose of 372 mg kg^{-1} produced lung adenomas in 20/22 mice surviving 20-210 days. Lung tumours occurred in 4/29 controls after 210 days (13).
Intraperitoneal rat (110 wk) single dose of 0, 100, 200 or 300 mg kg^{-1} in saline. 5/78 animals given 100 or 300 mg kg^{-1} developed malignant kidney tumours. In similar groups given an additional single intraperitoneal injection of 30 mg kg^{-1} dimethylnitrosamine 8 hr before, an additive effect in relation to the incidence of malignant kidney tumours was observed (14).

Teratogenicity and reproductive effects
Intraperitoneal ♂ rat single injection of 300 mg kg^{-1} caused complete sterility, 100 mg kg^{-1} impaired fertility for 3 wk (15).
Intraperitoneal ♂ mouse single injection of 200 mg kg^{-1} induced changes in sperm morphology (16).

Metabolism and toxicokinetics
$t_{1/2}$ in rat blood serum 6.5 hr (17).
Metabolism involves reaction with glutathione to give ethylmercapturic acid, and by hydrolysis to ethanol (18).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA157, TA1538 with and without metabolic activation positive (19).
Escherichia coli K12 AB1157, SOS-chromotest positive (20).
Saccharomyces cerevisiae 1000 μg ml^{-1} did not induce malsegregation but was a potent inducer of genetic events detected by an increase in the frequencies of cyhR cells (21).
Drosophila melanogaster sex-linked dominant lethal assay positive (22).
In vitro Chinese hamster lung cells, chromosomal aberrations negative, mutations assayed by frequency of thioguanine-resistant colonies positive (23).
In vitro human hair follicles, rat hepatocytes unscheduled DNA synthesis positive (24).
In vivo mouse induction of micronucleated polychromatic erythrocytes by gavage and intraperitoneal administration positive (6).
Intraperitoneal ♂ mouse 60, 150, 300 or 600 mg kg^{-1}. The treated ♂ mice were mated with untreated ♀ mice at 2 and 5 wk. Heritable behaviour mutations were demonstrated by a computer-monitored open-field behaviour test, a negative geotactic response, body weight and limb use (20).
In vivo rat, ethyl methanesulfonate caused ethylation in the 7-position of guanine in nucleic acid of several organs, and with the thiol position of cysteine (17,25).
Hibiscus sabdoriffa induction of chlorophyll mutations positive (26).

Other comments

Physical properties, use, carcinogenicity and mammalian toxicity reviewed (27-29).

References

1. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
2. Solomon, F. P. *Environ. Toxicol. Chem.* 1987, **6**(10), 747-753.
3. Ehrenberg, L. et al *Radiat. Bot.* 1975, **15**, 185-194.
4. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
5. Versar, *Physical-Chemical Properties and Categorization of RCRA Wastes According to Volatility* 1985, US EPA-450/3-85/007, 33.
6. Kondo, K. et al *Mutat. Res.* 1989, **223**(4), 373-375.
7. *Chem. Pharm. Bull.* 1960, **8**, 807.
8. *Chem.-Biol. Interact.* 1971, **3**, 117.
9. Clark, M. W. et al *Comp. Biochem. Physiol. C: Comp. Pharmacol. Toxicol.* 1988, **89C**(1), 15-30.
10. *IARC Monograph* 1987, **Suppl. 7**, 63.
11. Walters, M. A. et al *Br. J. Cancer* 1967, **21**, 367-372.
12. Clapp, N. K. *Int. J. Cancer* 1973, **12**, 728-733.
13. Frei, J. V. *Chem.-Biol. Interact.* 1971, **3**, 117-121.
14. Montesano, R. et al *Br. J. Cancer* 1974, **29**, 50-58.
15. Jackson, H. et al *J. Reprod. Fertil.* 1961, **2**, 447-465.
16. Jaszczaz, K. et al *Genet. Pol.* 1985, **26**(4), 499-504.
17. Roberts, J. J. et al *Biochem. Pharmacol.* 1958, **1**, 60-75.
18. Parke, D. V. *The Biochemistry of Foreign Compounds* 1968, 194, Pergamon Press, Oxford, UK.
19. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
20. Ficsor, G. et al *Teratog., Carcinog., Mutagen.* 1988, **8**(3), 153-160.
21. Albertini, S. *Mutat. Res.* 1991, **260**(2), 165-180.
22. Hashimoto, T. et al *J. Toxicol. Sci.* 1987, **12**(1), 33-45.
23. Heddle, J. A. et al *Mutagenesis* 1990, **5**(2), 179-184.
24. van Erp, Y. H. M. et al *Mutat. Res.* 1992, **271**(2), 201-208.
25. Swann, P. F. et al *Biochem. J.* 1971, **125**, 841-847.
26. Singh, V. L. et al *Indian J. Phys. Natl. Sci., Sect. A* 1989, **8**, 31-34.
27. *IARC Monograph* 1974, **7**, 245-208.
28. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(2), 67-74.
29. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E147 ethyl methyl ether

$H_3COCH_2CH_3$

C_3H_8O **Mol. Wt.** 60.10 **CAS Registry No.** 540-67-0

Synonyms methoxyethane; ethoxymethane

RTECS No. KO 0260000

Uses Solvent. Refrigerant. Formerly used as an anaesthetic.

Physical properties

B. Pt. 11°C **Flash point** –37°C (closed cup) **Specific gravity** 0.7252 at 0°C with respect to water at 0°C
Partition coefficient log P_{ow} 0.341 (calc.) (1) **Volatility** v.p. 760 mmHg at 7.5°C ; v.den. 2.1
Solubility Water: miscible. Organic solvents: acetone, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 1039 **HAZCHEM Code** 2PE **Conveyance classification** flammable gas
Supply classification extremely flammable
Risk phrases Extremely flammable (R12)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor 1.1 indicates that the potential for environmental accumulation is very low (2).

Environmental fate

Abiotic removal
Volatilisation from model river water, $t_{1/2}$ (est.) 270 min, and from model pond water 49 hr (3,4).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ (est.) 54 hr (5).

Adsorption and retention
Estimated K_{oc} 37 indicates that adsorption to soil and sediments is unlikely (2).

Mammalian & avian toxicity

Acute data
LC_{50} (15 min) inhalation mice 1082 mg m^{-3} (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

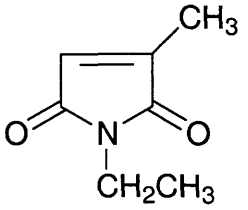
Reviews on experimental toxicology and human health effects listed (8).

References

1. *GEMS: Graphical Exposure Modeling System* 1986, CLOGP3.
2. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
3. *Exams II Computer Simulation* 1987, USEPA, Washington, DC, USA.

4. Daubert, T. E. et al *Data Compilation Tables of Pure Compounds* 1989, American Institute of Chemical Engineers.
5. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
6. Marsh, D. F. *Anesthesiology* 1950, **11**, 455.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E148 *N*-ethyl-2-methylmaleimide



$C_7H_9NO_2$ **Mol. Wt.** 139.15 **CAS Registry No.** 31217-72-8

Synonyms 1-ethyl-3-methylpyrrole-2,5-dione; 1-ethyl-3-methyl-1*H*-pyrrole-2,5-dione

RTECS No. ON 5500000

Physical properties

B. Pt. 206-208°C **Specific gravity** 1.0899 at 20°C

Mammalian & avian toxicity

Acute data

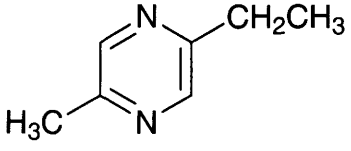
LD_{Lo} intraperitoneal rat 37 mg kg^{-1} (1).

LD_{Lo} intracerebral rat 8 mg kg^{-1} (1).

References

1. *J. Lab. Clin. Med.* 1972, **15**, 534

E149 2-ethyl-5-methylpyrazine



$C_7H_{10}N_2$ **Mol. Wt.** 122.17 **CAS Registry No.** 13360-64-0

Synonyms 5-methyl-2-ethylpyrazine

EINECS No. 236-416-6 **RTECS No.** UQ 3335500

Occurrence Aroma component of plants, meats and fish.

Physical properties

B. Pt. 168-170°C

Mammalian & avian toxicity

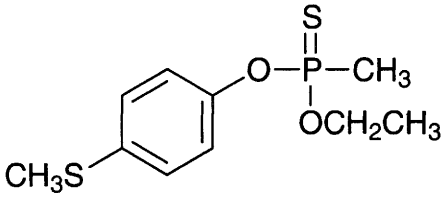
Acute data

LD_{50} oral rat 900 mg kg^{-1} (1).

References

1. *Drug Chem. Toxicol. (1977)* 1980, **3**, 249

E150 *O*-ethyl *O*-[4-(methylthio)phenyl] methylphosphonothioate



$C_{10}H_{15}O_2PS_2$ **Mol. Wt.** 262.33 **CAS Registry No.** 2703-13-1

Synonyms phosphonothioic acid, methyl-, *O*-ethyl *O*-[*p*-(methylthio)phenyl] ester; BAY 29952; ENT 25612

RTECS No. TB 1160000

Physical properties

B. Pt. 102°C at 0.01 mmHg **Specific gravity** 1.193

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 1 mg kg^{-1} (1).

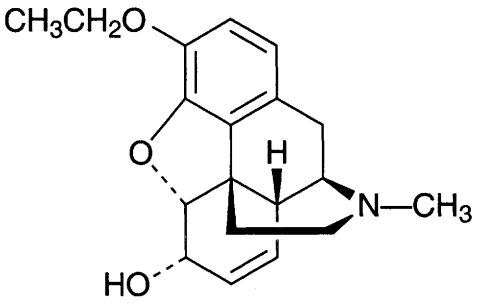
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. *USDA Information Memorandum* 1966, **20**, 4, Agricultural Research Service, Beltsville, MD, USA.
2. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E151 ethylmorphine



$C_{19}H_{23}NO_3$ **Mol. Wt.** 313.40 **CAS Registry No.** 76-58-4

Synonyms 5α,6α-morphinan; 3-*O*-ethylmorphine; codethyline; (5α,6α)-7,8-didehydro-4,5-epoxy-3-ethoxy-17-methylmorphinan-6-ol; 7,8-didehydro-4,5α-epoxy-3-ethoxy-17-methylmorphinan-6α-ol

EINECS No. 200-970-7 **RTECS No.** QD 0850000

Uses Narcotic analgesic. Antitussive.

Physical properties

M. Pt. 199-201°C

Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 810 mg kg^{-1} (1).

LD_{50} intraperitoneal rat, mouse 110, 120 mg kg^{-1}, respectively (1,2).

LD_{50} subcutaneous mouse, rat 136, 200 mg kg^{-1}, respectively (1,3).

LD_{50} intravenous rat 62 mg kg^{-1} (1).

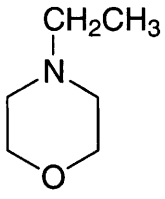
Sub-acute and sub-chronic data

Intraperitoneal ♂ rat, 60 mg kg^{-1} 2 × day^{-1} induced an increase in hepatic selenium glutathione peroxidase from the 2nd day, with a maximal increase of 2-fold after 4 days. Liver catalase was not induced by ethylmorphine. ♀ rats exhibited 2-3 fold higher hepatic selenium glutathione peroxidase activities (4).

References

1. *Jpn. J. Pharmacol.* 1973, **25**, 929.
2. *Ann. Pharm. Fr.* 1950, **8**, 261.
3. *Public Health Reports, Suppl.* 1938, **138**, 8.
4. Chaudiere, J. et al *Bioelectrochem. Bioenerg.* 1987, **18**(1-3), 247-256

E152 4-ethylmorpholine



$C_6H_{13}NO$ **Mol. Wt.** 115.18 **CAS Registry No.** 100-74-3

Synonyms *N*-ethylmorpholine; ethylmorpholine; NEM

EINECS No. 202-885-0 **RTECS No.** QE 4025000

Uses Fuel additive. Catalyst. Corrosion inhibitor. Electrolyte for lithium lattices. Chemical intermediate. Solvent.

Physical properties

M. Pt. –63°C **B. Pt.** 139°C **Flash point** 27°C (open cup) **Specific gravity** 0.916 at 20°C with respect to water at 20°C **Volatility** v.p. 6.1 mmHg at 20°C ; v.den. 4.0

Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

FR-VME 5 ppm (23 mg m^{-3})
SE-LEVL 5 ppm (25 mg m^{-3})
UK-LTEL 5 ppm (24 mg m^{-3})
US-TWA 5 ppm (24 mg m^{-3})

SE-STEL 10 ppm (50 mg m^{-3})
UK-STEL 20 ppm (96 mg m^{-3})

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 82 ppm Microtox test (1).

Environmental fate

Abiotic removal

Adsorption by activated carbon 0.107 g g^{-1} carbon (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1200, 1780 mg kg^{-1}, respectively (3,4).
LC_{50} (2 hr) inhalation mouse 18000 mg m^{-3} (4).
LD_{50} intravenous mouse 180 mg kg^{-1} (5).

Irritancy

Dermal rabbit, 453 mg caused mild irritation and 2 mg instilled into rabbit eye caused severe irritation (exposure not specified) (6,7).
Human volunteers noted eye, nose and throat irritation after exposure to 100 ppm for ~2.5 min (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation, weakly positive (9).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

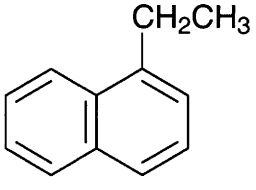
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (11).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 946-965.
3. *Documentation of Threshold Limit Values for Substances in Workroom Air, Suppl.* 1982, **4**, 190.
4. *Toxicol. New Ind. Chem. Sci.* 1979, **15**, 116.
5. *Report*, NX 04778, US Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD 21010, USA.
6. *Union Carbide Data Sheet* 3 Nov 1971.
7. *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
8. *Documentation of Threshold Limiting Values* 4th ed, 1980, 190, American Conference of Governmental Industrial Hygienists, Inc., Cincinnati, OH, USA.
9. Zeiger, E. et al *Environ. Mutagen.* 1987, **9** (Suppl. 9), 1-109.
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E153 1-ethylnaphthalene



$C_{12}H_{12}$ **Mol. Wt.** 156.23 **CAS Registry No.** 1127-76-0

EINECS No. 214-432-4 **RTECS No.** QJ 6950000

Physical properties

M. Pt. –15°C **B. Pt.** 259°C **Flash point** 111°C **Specific gravity** 1.008

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Dermal mouse (78 wk) 100 μg l^{-1} in acetone 3 × wk^{-1}, did not induce tumours (1).

Other effects

Other adverse effects (human)

One of a number of PAHs of compounds suggested to cause Kaskin-Beck disease (a condition leading to premature osteoarthritis, marked by shortness of the long bones with swelling of the joints, especially those of the phalanges) in a Chinese village (2).

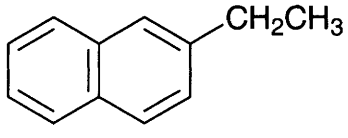
Other comments

Found in the neutral fraction of tobacco smoke, automobile exhaust gas, contaminant in tap water (3-6).
Naphthalenes are common products arising from the combustion of organic matter, such as cellulose. They also occur in high concentrations in mixtures of thermally produced PAHs.
Photodegradability in aquatic organisms discussed (7).
Likely to be leachate from XAD resins (6).

References

1. Schmeltz, I. et al *Carcinog. – Compr. Surv.* 1978, **3**, 47-60.
2. Li, Z. et al *Xi'an Yike Daxue Xuebao* 1988, **9**(1), 53-58 (Ch.) (*Chem. Abstr.* **114**, 170718e).
3. Schmeltz, I. et al *Anal. Chem.* 1976, **48**, 645.
4. Snook, M. E. et al *Beitr. Tabakforsch.* 1976, **8**, 250 (*Chem. Abstr.* **85**, 156723d).
5. Grimmer, G. et al *Erdoel Kohle, Erdgas, Petrochem.* 1977, **30**, 411.
6. Benoit, F. M. et al *Int. J. Environ. Anal. Chem.* 1979, **6**, 277 (*Chem. Abstr.* **92**, 10980h).
7. Fukuda, K. et al *Chemosphere* 1988, **17**(4), 651-658

E154 2-ethylnaphthalene



$C_{12}H_{12}$ **Mol. Wt.** 156.23 **CAS Registry No.** 939-27-5

EINECS No. 213-360-0 **RTECS No.** QJ 6960000

Physical properties

M. Pt. –70°C **B. Pt.** 251-252°C **Flash point** 104°C **Specific gravity** 0.992

Environmental fate

Degradation studies

One of a number of PAHs from tar spills which are degraded microbially. In water, at concentrations of 1.4 g l^{-1}, 91% was degraded after 35 days and ~98% within 60 days. In soil 76 g kg^{-1} (tar oil) degradation was 69% and 85% in 2 and 5 months, respectively (1).

Component in oil fractions, incubated with microbes adapted/unadapted to the compound. Adapted microbes degraded 2-ethylnaphthalene completely (after shorter lag times). At initial concentration of 170 µg l^{-1} complete degradation occurred between 12 to 21 days. Degradation occurred ~4 days earlier when soil was added (2).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Dermal mouse (78 wk) 100 µg l^{-1} in acetone 3 × wk^{-1}, did not induce tumours. In an assay as a cocarcinogen with benzo[*a*]pyrene, 2-ethylnaphthalene acted as an inhibitor of induced skin carcinogenesis (3).

Other effects

Other adverse effects (human)

Reported as one of a number of compounds suggested to cause Kaskin-Beck disease (a condition leading to premature osteoarthritis, marked by shortness of the long bones with swelling of the joints, especially those of the phalanges) in a Chinese village (4).

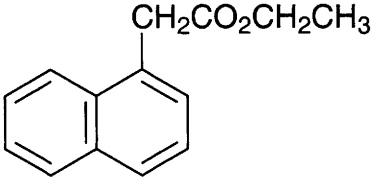
Other comments

Found in tobacco smoke, automobile exhaust gas, contaminant in tap water (5-8).
Photodegradability in aquatic system discussed (9).

References

1. Kahle, A. et al *GWF, Gas-Wasserfach: Wasser/Abwassser* 1990, **131**(4), 245-250 (Ger.) (*Chem. Abstr.* **113**, 197402p).
2. Aamand, J. et al *J. Contam. Hydrol.* 1989, **4**, 299-312.
3. Schmeltz, I. et al *Carcinog. – Compr. Surv.* 1978, **3**, 47 (*Chem. Abstr.* **89**, 85595h).
4. Li, Z. et al *Xi'an Yike Daxue Xuebao* 1988, **9**(1), 53-58 (Ch.) (*Chem. Abstr.* **114**, 170718e).
5. Schmeltz, I. et al *Anal. Chem.* 1976, **48**, 645.
6. Snook, M. E. et al *Beitr. Tabakforsch.* 1976, **8**, 250 (*Chem. Abstr.* **85**, 156723d).
7. Grimmer, G. et al *Erdoel Kohle, Erdgas, Petrochem.* 1977, **30**, 411.
8. Benoit, F. M. et al *Int. Environ. Anal. Chem.* 1979, **6**, 277 (*Chem. Abstr.* **92**, 10980h).
9. Fukuda, K. et al *Chemosphere* 1988, **17**(4), 651-658

E155 ethyl 1-naphthylacetate



$C_{14}H_{14}O_2$ **Mol. Wt.** 214.26 **CAS Registry No.** 2122-70-5

Synonyms ethyl 1-naphthaleneacetate

EINECS No. 218-332-1 **RTECS No.** QJ 0948000

Uses Herbicide and growth regulator.

Physical properties

B. Pt. 175°C **Specific gravity** 1.106 at 25°C with respect to water at 4°C
Solubility Organic solvents: acetone, acetic acid, benzene, chloroform, diethyl ether, kerosene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluefill sunfish 57, 82 mg l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3580 mg kg^{-1} (2,3).

LC_{50} inhalation rat >206.5 mg l^{-1} (1).
LD_{50} dermal rabbit >5000 mg kg^{-1} (3).

Sub-acute and sub-chronic data
LC_{50} (8 day) mallard duck, bobwhite quail >10 g kg^{-1} in feed (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *Pestic. Tox. Chem. News* 1980, **9**, 10.
3. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E156 ethyl nitrite

$$CH_3CH_2NO_2$$

$C_2H_5NO_2$ **Mol. Wt.** 75.07 **CAS Registry No.** 109-95-5

Synonyms nitrous acid, ethyl ester; spirit of ethyl nitrite; nitrous ether

EINECS No. 203-722-6 **RTECS No.** RA 0810000

Uses Diuretic and diaphoretic. Chemical intermediate. Flavour in foods and beverages.

Physical properties

M. Pt. –58°C **B. Pt.** 16-17°C at 725 mmHg **Flash point** 15°C **Specific gravity** 0.90 at 15°C with respect to water at 15°C **Volatility** v.den. 2.59
Solubility Water: miscible. Organic solvents: ethanol, heptane

Occupational exposure

UN No. 1194 **Conveyance classification** flammable liquid, toxic
Supply classification explosive, harmful
Risk phrases Risk of explosion by shock, friction, fire or other sources of ignition – Harmful by inhalation, in contact with skin and if swallowed (R2, R20/21/22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) inhalation rat 160 ppm. Toxic signs observed included cyanosis, prostration and convulsions. No effects on body weight gain during 14-day post-exposure. Pulmonary haemorrhage was found in rats which died during exposure period. Rapid recovery after cessation of exposure in survivors (1).

Sub-acute and sub-chronic data
Inhalation (15 min) cat, mouse, 15 ppm did not cause any observable effects (2).

Other effects

Other adverse effects (human)
Intoxication is characterised by headache, tachycardia and methaemoglobinaemia. A fatality has been reported after accidental inhalation exposure to spirits of ethyl nitrite (2).

Other comments

Contaminant in engine exhausts which use ethanol and methanol as fuels. The ethyl nitrite content in the exhaust from an ethanol fuelled engine operated on a dynamometer decreased from 550-750 ppm after 30 min to <353 ppm in 28 hr. In a vehicle operated at highway conditions, concentrations are 1-9 ppm (30 min) and 16.5-27 ppm (28 hr) (3).
Reviews on experimental toxicology and human health effects listed (4).
Spirits of ethyl nitrite contains ethyl nitrite in alcohol. Autoignition temperature 90°C.

References

1. Klonne, D. R. et al *Fundam. Appl. Toxicol.* 1987, **8**(1), 101-106.
2. Clayton, G. D. (Ed.) *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, **2**, 4203, John Wiley and Sons, New York, NY, USA.
3. Roby, R. J. et al *J. Air Pollut. Control Assoc.* 1981, **31**(9), 995-996.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E157 ethylnitrosocyanamide

$$CH_3CH_2N(NO)CN$$

$C_3H_5N_3O$ **Mol. Wt.** 99.09 **CAS Registry No.** 38434-77-4

Synonyms *N*-cyano-*N*-nitrosoethylamine; ENC; nitrosoethanecarbamonitrile

RTECS No. KH 7250000

Physical properties

Specific gravity 1.044 at 25°C
Solubility Water: 17 g l^{-1}

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal rat 15 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Reported to be carcinogenic in rats (details not given) (2).

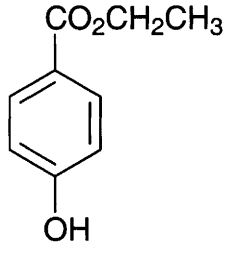
Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation negative (2).

References

1. *J. Org. Chem.* 1973, **38**, 1325.
2. Lee, K. et al *Mutat. Res.* 1977, **48**(2), 131-138.

E158 ethylparaben



$C_9H_{10}O_3$ **Mol. Wt.** 166.18 **CAS Registry No.** 120-47-8

Synonyms ethyl 4-hydroxybenzoate; ethyl *p*-hydroxybenzoate; 4-carbethoxyphenol; 4-(ethoxycarbonyl)phenol; *p*-hydroxybenzoic acid, ethyl ester; ethyl butex; ethyl paraben; Aseptin A; Easeptol; Sobrol A; Nipagin A; Paridol Ethyl

EINECS No. 204-399-4 **RTECS No.** DH 2190000

Uses Disinfectant, used as a preservative in medicines and cosmetics.

Physical properties

M. Pt. 116-118°C **B. Pt.** 297-298°C (decomp.)

Solubility Water: 0.07% at 20°C. Organic solvents: carbon disulfide, diethyl ether, ethanol, glycerol, propylene glycol, peanut oil

Environmental fate

Degradation studies

Completely degraded by *Pseudomonas cepacia* after 3 wk culturing. After 2 wk culturing metabolites identified included *p*-hydroxybenzoic acid and methyl *p*-hydroxybenzoic acid, showing the bacteria cleaved the C-O linkage in ester bonds and the C-C linkage in alkyl groups (1).

Adsorption and retention

K_{oc} for podzol, alfisol and sediment 209, 162 and 119, respectively (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 3000 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 520 mg kg^{-1} (4).

Teratogenicity and reproductive effects

Oral rat, lowest dose for teratogenic effects 45, 600 mg kg^{-1} day^{-1} on days 8-15 of gestation (5).

Metabolism and toxicokinetics

Major urinary metabolites in dogs, *p*-hydroxyhippuric acid and *p*-hydroxybenzoic acid (6).

Sensitisation

May cause contact dermatitis (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with and without metabolic activation negative (8).
In vitro Chinese hamster lung cells, chromosomal aberrations positive (8).

Other effects

Other adverse effects (human)
EC_{100} human spermatozoa, immobilisation 8000 mg l^{-1} (9).

Other comments

Reviews on toxicology and human health effects listed (10).

References

1. Suemitsu, R. et al *Bokin Bobai* 1990, **18**(2), 579-582 (*Chem. Abstr.* **115**, 88939q).
2. von Oepen, B. et al *Chemosphere* 1991, **22**(3-4), 285-304.
3. *Bromatol. Chem. Toksykol.* 1984, **14**, 301.
4. *Drug Standards* 1952, **20**, 89.
5. *Acta Obstet. Gynecol. Jpn. (Engl. Ed.)* 1975, **22**, 94.
6. Phillips, et al *Toxicol. Lett.* 1978, **40**(3), 237-242.
7. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
8. Ishidate, M. et al *Gann Monogr. Cancer Res.* 1981, **27**, 95-108.
9. Song, B. et al *Contraception* 1989, **39**(3), 331-335.
10. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E159 ethyl perchlorate

$$CH_3CH_2OClO_3$$

$C_2H_5ClO_4$ **Mol. Wt.** 128.51 **CAS Registry No.** 22750-93-2

RTECS No. SC 7970000

Physical properties

B. Pt. 74°C

Legislation

Oxidising agents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (1).
Use prohibited under the US Code of Federal Regulations (2).

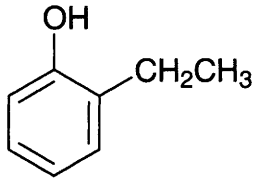
Other comments

Possibly the most explosive chemical known. Very sensitive to impact, friction and heat (3).

References

1. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
2. *Code of Federal Regulations* 1992, **49**, 172.101.
3. Lewis, R. J. *Dangerous Properties of Industrial Materials* 8th ed., 1992, **1**, 1649, Van Nostrand Reinhold, New York, NY, USA

E160 2-ethylphenol



$C_8H_{10}O$ **Mol. Wt.** 122.17 **CAS Registry No.** 90-00-6

Synonyms *o*-ethylphenol; phlorol; 1-ethyl-2-hydroxybenzene

EINECS No. 201-958-4 **RTECS No.** SL 4025000

Occurrence Pyrolysis product of fossil fuels (1).

Physical properties

M. Pt. –18°C **B. Pt.** 195-197°C **Flash point** 78°C **Specific gravity** 1.037 at 12°C

Partition coefficient log P_{ow} 2.47

Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol, glacial acetic acid

Occupational exposure

UN No. 3145

Environmental fate

Abiotic removal

Removal from water effected by moist air oxidation (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 600 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 172 mg kg^{-1} (4).

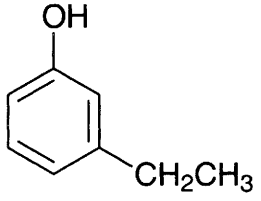
Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (5).

References

1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed. A 1983, 661, Van Nostrand Reinhold, New York, NY, USA.
2. Joglekar, H. S. et al *Water Res.* 1991, **25**(2), 135-145.
3. *Pharmazie* 1975, **30**, 147.
4. *J. Med. Chem.* 1975, **18**, 868.
5. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141

E161 3-ethylphenol



$C_8H_{10}O$ **Mol. Wt.** 122.17 **CAS Registry No.** 620-17-7

EINECS No. 210-627-3

Uses Organic synthesis.

Occurrence Present in coal tar and essential oil of plants. Detected in cigarette smoke condensate (1).

Physical properties

M. Pt. -4°C **B. Pt.** 108-110°C at 15 mmHg **Flash point** 94°C **Specific gravity** 1.0283 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.50

Solubility Water: slightly soluble. Organic solvents: cyclohexane, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

IC_{50} (48 hr) *Tetrahymena pyriformis* 72 mg l^{-1} (2).

Environmental fate

Carbonaceous inhibition

IC_{50} (5 day) aerobic heterotrophic bacteria isolated from activated sludge 140 mg l^{-1} (3).

Degradation studies

Degraded under anaerobic conditions with other constituents of coal conversion wastewater (4).

Mammalian & avian toxicity

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (5).

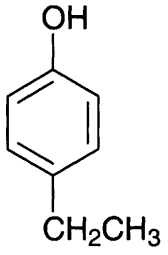
Genotoxicity

In vitro human lymphocytes, sister chromatid exchanges negative (1).

References

1. Jansson, T. et al *Mutat. Res.* 1988, **206**(1), 17-24.
2. Schultz, T. W. et al *Toxicol. Lett.* 1987, **37**(2), 121-130.
3. Blum, D. J. W. et al *Res. J. Water Pollut. Control Fed.* 1991, **63**(3), 198-207.
4. Blum, D. J. W. et al *J. Water Pollut. Control Fed.* 1986, **58**(2), 122-131.
5. Lenga, R. E. (Ed.) *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1645, Sigma-Aldrich, Milwaukee, WI, USA

E162 4-ethylphenol



$C_8H_{10}O$ **Mol. Wt.** 122.17 **CAS Registry No.** 123-07-9

Synonyms *p*-ethylphenol; 1-ethyl-4-hydroxybenzene; (*p*-hydroxyphenyl)ethane; (4-hydroxyphenyl)ethane

EINECS No. 204-598-6 **RTECS No.** SL 4040000

Uses Fuel additive. Flavour agent.

Occurrence Present in coal tar and essential oil of plants. Detected in cigarette smoke condensate (1).

Physical properties

M. Pt. 42-45°C **B. Pt.** 218-219°C **Flash point** 100°C **Specific gravity** 1.011 at 20°C

Partition coefficient log P_{ow} 2.50

Solubility Water: slightly soluble. Organic solvents: acetone, carbon disulfide, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 14 mg l^{-1} flow-through bioassay (2).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 0.051 ppm Microtox test (3).

IC_{50} (48 hr) *Tetrahymena pyriformis* 168 mg l^{-1} (4).

Environmental fate

Nitrification inhibition

IC_{50} (25 day) *Nitrosomonas* 14 mg l^{-1} (5).

Anaerobic effects

IC_{50} (50 day) methanogenic bacterial culture 240 mg l^{-1} (5).

Degradation studies

Effectively degraded in contaminated groundwater by treatment in upflow aerated column and rotating disk biological contactors. Volatilisation and adsorption processes were also reported to take part in the system (6).

Metabolised by *Pseudomonas putida* JD1 isolated from soil (7).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 138 mg kg^{-1} (8).

Metabolism and toxicokinetics

p-Ethylanisole is reported to be a metabolite in guinea pigs (9).

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (10).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (11).
In vitro human lymphocytes, sister chromatid exchanges negative (1).

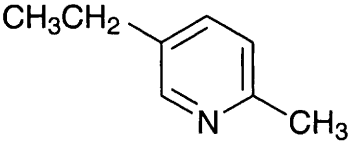
Other comments

Taste threshold concentration in water 0.01 mg l^{-1}, odour threshold concentration in water 0.6 mg l^{-1} (12).

References

1. Jansson, T. et al *Mutat. Res.* 1988, **206**(1), 17-24.
2. Schultz, T. W. et al *Ecotoxicol. Environ. Saf.* 1986, **12**(2), 146-153.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Schultz, T. W. et al *Toxicol. Lett.* 1987, **37**(2), 121-130.
5. Blum, D. J. W. et al *Res. J. Water Pollut. Control Fed.* 1991, **63**(3), 198-207.
6. Van der Hoek, J. P. et al *Environ. Technol. Lett.* 1989, **10**(2), 185-194.
7. Darby, J. M. et al *J. Gen. Microbiol.* 1987, **133**(8), 2137-2146.
8. *J. Med. Chem.* 1975, **18**, 868.
9. Axelrod, J. et al *Biochem. Biophys. Acta* 1968, **159**, 472.
10. Lenga, R. E. (Ed.) *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1646, Sigma-Aldrich, Milwaukee, WI, USA.
11. Epler, J. T. et al *Environ. Health Perspect.* 1979, **30**, 184.
12. Dietz, F. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1978, **119**(6)

E163 5-ethyl-2-picoline



$C_8H_{11}N$ **Mol. Wt.** 121.18 **CAS Registry No.** 104-90-5

Synonyms 2-methyl-5-ethylpyridine; pyridine, 5-ethyl-2-methyl-; aldehydecollidine; aldehydine; 5-ethyl-2-methylpyridine

EINECS No. 203-250-0 **RTECS No.** TJ 6825000

Occurrence Found at 24.4-73.5 μg g^{-1} in coke oven emissions; 3.12 mg g^{-1} in coal tar sample; and 0.37 g l^{-1} in raw wood preservative sludge sample (1).

Physical properties

B. Pt. 74-75°C at 20 mmHg **Specific gravity** 0.9184 at 23°C with respect to water at 4°C
Solubility Organic solvents: ethanol, diethyl ether, benzene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 81.2 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 282-368 mg kg^{-1} (3).
LC_{Lo} (4 hr) inhalation rat 1000 ppm (4).
LD_{50} dermal rabbit 1000 mg kg^{-1} (5).
LD_{50} subcutaneous mouse, rat 294, 826 mg kg^{-1}, respectively (3).

Irritancy

Dermal rabbit 10 mg (24 hr) caused severe irritation (4).
250 μg instilled into rabbit eye caused severe irritation (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

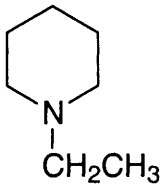
Other comments

All reasonable efforts have been made to find information on isomers of this compound, but no relevant data are available.

References

1. Lao, R. C. et al *J. Chromatogr.* 1975, **112**, 681-700.
2. Schultz, T. W. et al *Chemosphere* 1989, **18**(11-12), 2283-2291.
3. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
4. *AMA, Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119.
5. *Union Carbide Data Sheet* 6/29/66, Industrial Medicine and Toxicology Department, Union Carbide Corp., 270 Park Ave., New York, NY, USA.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E164 1-ethylpiperidine



$C_7H_{15}N$ **Mol. Wt.** 113.20 **CAS Registry No.** 766-09-6

Synonyms *N*-ethylpiperidine

EINECS No. 212-161-6 **RTECS No.** TN 0250000

Uses Catalyst. Solvent. Analytical reagent.
Occurrence Aroma component of shrimps.

Physical properties

B. Pt. 131°C **Flash point** 18°C **Specific gravity** 0.824 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.88

Occupational exposure

UN No. 2386 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, corrosive

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 56 mg kg^{-1} (1).

Irritancy

50 mg instilled into rabbit eye for 5 min caused irritation (2).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *Report* NX 00374, US Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA.
2. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1649, Sigma-Aldrich, Milwaukee, WI, USA.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E165 ethyl propionate

$$CH_3CH_2CO_2CH_2CH_3$$

$C_5H_{10}O_2$ **Mol. Wt.** 102.13 **CAS Registry No.** 105-37-3

Synonyms propionic ether; propanoic acid, ethyl ester

EINECS No. 203-291-4 **RTECS No.** UF 3675000

Physical properties

M. Pt. –73°C **B. Pt.** 99°C **Flash point** 12°C (closed cup) **Specific gravity** 0.891 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.32 **Volatility** v.p. 40 mmHg at 27.2°C ; v.den. 3.5
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1195 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Do not breathe vapour – Do not empty into drains – Take precautionary measures against static discharges (S2, S16, S23, S29, S33)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) rainbow trout 56 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia cucullata, Daphnia pulex, Daphnia magna* 45-170 mg l^{-1} (2).

NOEC *Selenastrum capricornutum* 140 mg l^{-1} (duration unspecified) (1).
EC_{50} (15 min) *Photobacterium phosphoreum* 811 ppm Microtox test (3).
Cell multiplication inhibition test *Pseudomonas putida, Scenedesmus quadricauda, Entosiphon sulcatum* 270, 14, 560 mg l^{-1}, respectively (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 3500 mg kg^{-1} (5).
LD_{50} intraperitoneal mouse 1300 mg kg^{-1} (5).
LD_{50} intraperitoneal rat 1200 mg kg^{-1} (6).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (6).

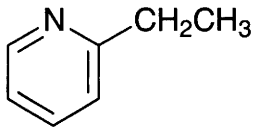
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

References

1. Sloof, W. et al *Aquat. Toxicol.* 1983, **4**, 113-128.
2. Canton, J. H. et al *Hydrobiologia* 1978, **59**(2), 135-140.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
5. Patty, F. A. (Ed.) *Industrial Hygiene and Toxicology* 2nd ed., 1963, **2**, Interscience Publishers, New York, NY, USA.
6. *Food Cosmet. Toxicol.* 1978, **16**, 749.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E166 2-ethylpyridine



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 100-71-0

EINECS No. 202-881-9

Uses Catalyst.
Occurrence Aroma component in cooked meat and coffee. Occurs in coal tar and shale oil.

Physical properties

B. Pt. 149°C **Flash point** 29°C **Specific gravity** 0.937 at 20°C **Partition coefficient** log P_{ow} 1.69
Solubility Organic solvents: diethyl ether, ethanol

Environmental fate

Nitrification inhibition
Threshold for inhibition of nitrification 10 mg l^{-1} (1).

Degradation studies
Degraded by *Arthrobacter pascens* (2).

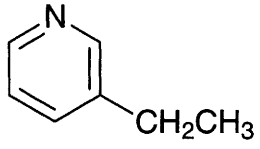
Mammalian & avian toxicity

Irritancy
Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (3).

References

1. Greenfield, J. H. et al *36th Ind. Waste Conf. Purdue Univ.* 1981, 772.
2. Pavlyuk, M. I. et al *Dokl. Akad. Nauk Ukr. SSR, Ser. B: Geol. Khim. Biol. Nauki* 1988, (9), 52-54 (Russ.) (*Chem. Abstr.* **111**, 28060d).
3. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1651, Sigma-Aldrich, Milwaukee, WI, USA

E167 3-ethylpyridine



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 536-78-7

Synonyms β-lutidine

EINECS No. 208-647-2

Uses Catalyst.

Physical properties

B. Pt. 166°C **Flash point** 48°C **Specific gravity** 0.954 at 20°C
Solubility Organic solvents: diethyl ether, ethanol

Other effects

Other adverse effects (human)
Extremely destructive to tissue of the mucous membranes and upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (1).

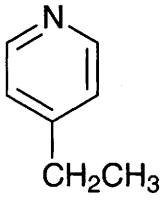
Other comments

Aroma component in cooked meat and fish. Occurs in tobacco, coal tar and shale oil.

References

1. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1652, Sigma-Aldrich, Milwaukee, WI, USA

E168 4-ethylpyridine



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 536-75-4

Synonyms γ-ethylpyridine

EINECS No. 208-646-7

Uses Catalyst.

Occurrence Aroma component in cooked fish and coffee. Occurs in shale oil.

Physical properties

B. Pt. 168°C **Flash point** 47°C **Specific gravity** 0.9404 at 22°C with respect to water at 4°C

Partition coefficient log P_{ow} 1.84 (1)

Solubility Water: soluble. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 5.5 ppm Microtox test (2).

Mammalian & avian toxicity

Acute data

LC_{50} oral redwing blackbird >100 mg kg^{-1} in diet (3).

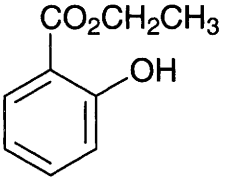
Irritancy

Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (4).

References

1. Schultz, T. W. et al *Ecotoxicol. Environ. Saf.* 1987, **13**(1), 76-83.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
4. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1652, Sigma-Aldrich, Milwaukee, WI, USA

E169 ethyl salicylate



$C_9H_{10}O_3$ **Mol. Wt.** 166.18 **CAS Registry No.** 118-61-6

Synonyms ethyl 2-hydroxybenzoate; FEMA No. 2458; salicylic ether; sal ethyl

EINECS No. 204-265-5 **RTECS No.** VO 3000000

Uses Fungicide. Acaricide. Insecticide. Chelating agent. Used in treatment of rheumatic and muscular pain in topical formulations. Manufacture of artificial perfumes.

Occurrence Flavour component of fruits. Has been used as a veterinary counter-irritant.

Physical properties

M. Pt. 1-3°C **B. Pt.** 233-234°C **Flash point** 107°C **Specific gravity** 1.131 at 20°C with respect to water at 4°C

Solubility Organic solvents: acetic acid, diethyl ether, ethanol, glycerin, fixed oils

Ecotoxicity

Fish toxicity

10 mg l^{-1} caused death of rainbow trout within 1 hr (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1320 mg kg^{-1} (2).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (2).

Legislation

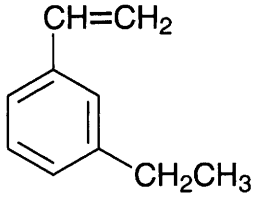
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

1. McPhee, C. et al *Lethal Effects of 2014 Chemicals to Fish* 1989 EPA 560/6-89-001; PB 89-156-715.
2. *Food Cosmet. Toxicol.* 1978, **16**, 637.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E170 3-ethylstyrene



$C_{10}H_{12}$ **Mol. Wt.** 132.21 **CAS Registry No.** 7525-62-4

Synonyms *m*-ethylstyrene

EINECS No. 231-386-0 **RTECS No.** WL 4725000

Uses Chemical intermediate.

Occurrence A component of some plant essential oils including *Eucalyptus tereticonus* (1).

Physical properties

M. Pt. 392°C **Specific gravity** 0.8945 at 20°C with respect to water at 4°C **Volatility** v.p. 100 mmHg

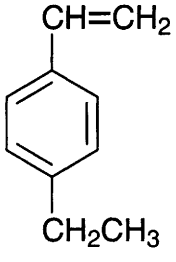
Other comments

Has been investigated as a possible cause of Kashin-Beck disease, which is endemic in some Chinese villages (2). Identified in groundwater in areas of China irrigated with sewage effluents (3).

References

1. Cheng, Z. et al *Fenxi Ceshi Tongbao* 1989, **8**, 51-58 (Ch.) (*Chem. Abstr.* **112**, 155254r).
2. Li, Z. et al *Xi'an Yike Daxue Xuebao* 1988, **9**(1), 538 (Ch.) (*Chem. Abstr.* **114**, 170718e).
3. Tu, J. et al *Huanjing Huaxue* 1986, **5**(5), 60-74 (Ch.) (*Chem. Abstr.* **106**, 22946x)

E171 4-ethylstyrene



$C_{10}H_{12}$ **Mol. Wt.** 132.21 **CAS Registry No.** 3454-07-7

Synonyms *p*-ethylstyrene

EINECS No. 222-381-4

Uses Chemical intermediate.

Physical properties

M. Pt. –49.7°C **B. Pt.** 68°C at 10 mmHg **Specific gravity** 0.892-0.907 at 20°C

Other comments

Has been investigated as a possible cause of Kashin-Beck disease, which is endemic in some Chinese villages (1).

References

1. Li, Z. et al *Xi'an Yike Daxue Xuebao* 1988, **9**(1), 538 (Ch.) (*Chem. Abstr.* **114**, 170718e)

E172 ethyl sulfide

$$CH_3CH_2SCH_2CH_3$$

$C_4H_{10}S$ **Mol. Wt.** 90.19 **CAS Registry No.** 352-93-2

Synonyms ethyl monosulfide; 1,1'-thiobisethane; ethylthioethane; diethyl sulfide; diethyl thioether; 3-thiapentane; thioethyl ether

EINECS No. 206-526-9 **RTECS No.** LC 7200000

Uses Solvent.

Occurrence Occurs in trace amounts in petroleum. Formed during the degradation of plant and animal tissues (1).

Physical properties

M. Pt. –102°C **B. Pt.** 92-93°C **Flash point** –10°C **Specific gravity** 0.837 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.95 **Volatility** v.p. 40 mmHg at 16.1°C ; v.den. 3.11
Solubility Water: 3.13 g l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies

Degraded by methanogenic bacteria in sediments, releasing ethane and hydrogen sulfide (2,3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5900 mg kg^{-1} (4).

LC_{50} (10 min) inhalation rat >1850 mg m^{-3} (4).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation, 20 mg instilled into rabbit eye for 24 hr caused moderate irritation (5).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

References

1. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, **2**, 2085, John Wiley and Sons, New York, NY, USA
2. Oremland, R. S. et al *Geochim. Cosmochim. Acta* 1988, **52**(7), 1895-1904.

3. Rajagopal, B. S. et al *Curr. Microbiol.* 1986, **14**(3), 137-144.
4. *Progress Rep.* 1942, NDCrc-132, National Defence Research Committee, Office of Scientific Research and Development, USA.
5. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E173 ethylsulfuric acid

$$CH_3CH_2OSO_3H$$

$C_2H_6O_4S$ **Mol. Wt.** 126.13 **CAS Registry No.** 540-82-9

Synonyms monoethylsulfuric acid; ethyl hydrogen sulfate; sulfethylic acid; sulfovinic acid

EINECS No. 208-758-6

Uses Catalyst.

Occurrence Occurs in wine.

Physical properties

B. Pt. 280°C (decomp.) **Specific gravity** 1.3657 at 20°C with respect to water at 4°C

Solubility Water: miscible. Organic solvents: diethyl ether

Occupational exposure

UN No. 2571 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Environmental fate

Degradation studies

Utilised as sole carbon source by *Xanthobacter* E5a isolated from sewage and M3c *Agrobacterium* isolated from canal water (1).

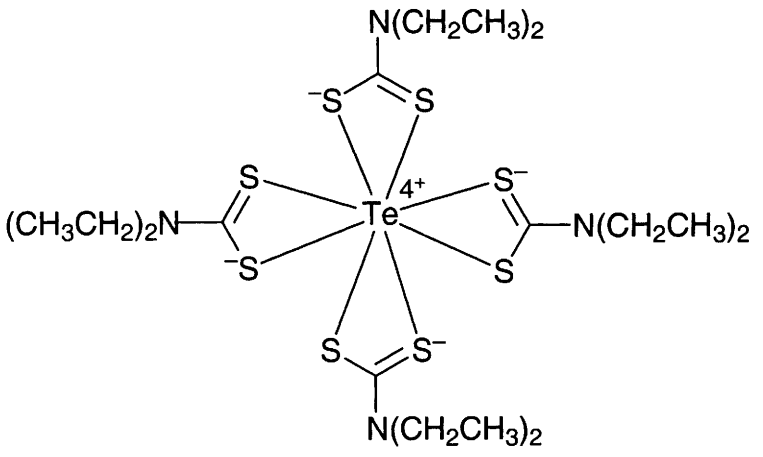
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sulfate guide level 25 mg l^{-1}, maximum admissible level 250 mg l^{-1} (2).

References

1. White, G. F. et al *FEMS Microbiol. Lett.* 1987, **40**(2-3), 173-177.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

E174 ethyl tellurac



$C_{20}H_{40}N_4S_8Te$ **Mol. Wt.** 720.69 **CAS Registry No.** 20941-65-5

Synonyms tetrakis(diethylcarbamodithioato-*S*,*S*')tellurium; tellurium diethyldithiocarbamate; tellurium tetrakis(diethyl dithiocarbamate); Akrochem TDEC; Perkacit TDEC; Rhenogran TDEC-75

EINECS No. 244-121-9 **RTECS No.** WY 2950000

Uses Antioxidant. Accelerator in rubber compounds.

Physical properties

M. Pt. 108-118°C **Specific gravity** 1.44 at 20°C

Solubility Water: <1 g l^{-1} at 23°C. Organic solvents: benzene, chloroform, carbon disulfide, dimethyl sulfoxide

Occupational exposure

SE-LEVL 0.1 mg m^{-3} (as Te)

UK-LTEL 0.1 mg m^{-3} (as Te)

US-TWA 0.1 mg m^{-3} (as Te)

UN No. 3284 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, inadequate evidence of carcinogenicity to animals, IARC classification group 3 (1).

National Toxicology Program tested rats and mice via feed. Equivocal results were reported for ♂ rats and mice and for ♀ mice. No evidence of carcinogenicity was observed in ♀ rats (2).

Oral mouse (78 wk) 46.4 mg kg^{-1} (7-day-old animals) by gavage and the same amount (not adjusted for increasing body weight) daily up to 4 wk of age. Subsequently the mice were given 145 mg kg^{-1} diet up to 78 wk of age. The dosage was the maximum tolerated for infant and young mice, but not necessarily for adult mice. Hepatomas occurred in 7/34 ♂ mice compared with 13/172 controls of both sexes. The incidence of lung tumours in both sexes was 7/36 compared with 12/172 in controls (3).

Subcutaneous (78 wk) single injection of 1000 mg kg^{-1} to 28-day-old mice did not cause an increase in tumour incidence compared with controls (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (5).

Legislation

Organometallic compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Reviews on experimental toxicology and human health effects listed (7).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 63.
2. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-152, NIEHS, Research Triangle Park, NC, USA.
3. Innes, J. R. M. et al *J. Natl. Cancer Inst.* 1969, **42**, 1101-1114.
4. *Evaluation of Carcinogenic, Teratogenic and Mutagenic Activities of Selected Pesticides and Industrial Chemicals* 1968, **1**, NTIS, US Department of Commerce, Washington, DC, USA.
5. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E175 ethyl thiocyanate

$$CH_3CH_2CNS$$

C_3H_5NS **Mol. Wt.** 87.15 **CAS Registry No.** 542-90-5

Synonyms ethyl sulfocyanate; ethyl rhodanate; thiocyanatoethane; thiocyanic acid, ethyl ester

EINECS No. 208-833-3 **RTECS No.** XK 9900000

Uses Polymerisation catalyst. Insecticide.

Physical properties

M. Pt. –85.5°C **B. Pt.** 145°C **Flash point** 42°C **Specific gravity** 1.012 at 20°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1992

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 200 mg kg^{-1} (1).
LD_{Lo} oral cat 10 mg kg^{-1} (1).
LD_{Lo} subcutaneous rabbit, rat, mouse, 15, 40, 70 mg kg^{-1}, respectively (1-3).
LD_{50} intraperitoneal mouse 10 mg kg^{-1} (3).
LD_{50} intravenous mouse 18 mg kg^{-1} (4).

Other effects

Other adverse effects (human)

May be fatal if absorbed through the skin, inhaled or swallowed. High concentrations are extremely destructive to tissues of the mucous membranes and upper respiratory tract, skin and eyes (5).

Legislation

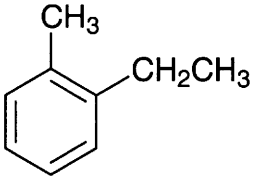
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

References

1. *J. Ind. Hyg. Toxicol.* 1936, **18**, 310.
2. *Naunyn-Schmiedebergls Arch. Exp. Pathol. Pharmakol.* 1930, **150**, 257.
3. *Jpn. J. Pharmacol.* 1954, **3**, 99.
4. *Report* NX 02865, US Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA.
5. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1656, Sigma-Aldrich, Milwaukee, WI, USA.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

E176 2-ethyltoluene



C_9H_{12} **Mol. Wt.** 120.19 **CAS Registry No.** 611-14-3

Synonyms 1-ethyl-2-methylbenzene; 1-methyl-2-ethylbenzene; *o*-ethyltoluene

EINECS No. 210-255-1 **RTECS No.** XT 2500000

Uses Organic synthesis. Solvent.

Occurrence Component of crude oil.

Physical properties

M. Pt. –17°C **B. Pt.** 164-165°C **Flash point** 39°C **Specific gravity** 0.884 at 16°C with respect to water at 4°C

Partition coefficient log P_{ow} 3.53 **Volatility** v.p. 45-780 mmHg at 80-166°C ; v.den. 4.2

Solubility Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol, petroleum ether

Environmental fate

Abiotic removal

Estimated t_{100} 27 hr under photochemical smog conditions in S.E. England (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 5000 mg kg^{-1} (2).

LC_{50} (4 hr) inhalation mouse 5400 mg m^{-3} (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (5).

Other comments

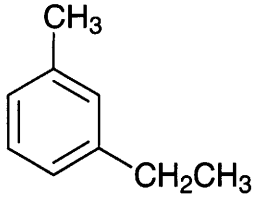
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

Autoignition temperature 440°C.

References

1. Brice, K. A. et al *Atmos. Environ.* 1978, **12**, 2045-2054.
2. Gerarde, H. *Toxicology and Biochemistry of Aromatic Hydrocarbons* 1960, 57, Elsevier, New York, NY, USA.
3. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, 69, CIP, Moscow, USSR.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E177 3-ethyltoluene



C_9H_{12} **Mol. Wt.** 120.19 **CAS Registry No.** 620-14-4

Synonyms 1-ethyl-3-methylbenzene; 1-methyl-3-ethylbenzene; *m*-ethyltoluene

EINECS No. 210-626-8

Uses Solvent.

Physical properties

M. Pt. –95.5°C **B. Pt.** 158-159°C **Flash point** 38°C **Specific gravity** 0.869 at 17°C with respect to water at 17°C **Volatility** v.p. 45-780 mmHg at 80-166°C ; v.den. 4.2

Solubility Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol, petroleum ether

Environmental fate

Degradation studies

Degraded in wastewater using a biocatalysed air-scrubber. Rate of removal was dependent on the oxygen supply (1).

Abiotic removal
Estimated t_{100} 1.9 hr under photochemical smog conditions in S.E. England (2).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

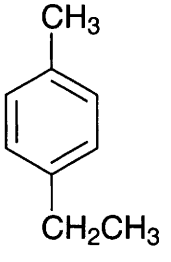
Other comments

Component of gasoline. Aroma component of cooked meat and fish.
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).
Autoignition temperature 480°C.

References

1. Feige, I. et al *DECHEMA Biotechnol. Conf.* 1989, **3**(Pt. B), 805-809.
2. Brice, K. A. et al *Atmos. Environ.* 1978, **12**, 2045-2054.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E178 4-ethyltoluene



C_9H_{12} **Mol. Wt.** 120.19 **CAS Registry No.** 622-96-8

Synonyms 1-ethyl-4-methylbenzene; 1-methyl-4-ethylbenzene; *p*-ethyltoluene

EINECS No. 210-761-2 **RTECS No.** XT 2550000

Uses Desorbant for ion-exchange resins. Solvent.
Occurrence Component of gasoline. Aroma component of cooked meats. Detected in motor vehicle exhaust fumes (1).

Physical properties

M. Pt. –62.4°C **B. Pt.** 162°C **Flash point** 36°C **Specific gravity** 0.8614 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.63 **Volatility** v.p. 45-780 mmHg at 80-166°C ; v.den. 4.2
Solubility Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol, petroleum ether

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 2.63 ppm Microtox test (2).

Environmental fate

Abiotic removal

Estimated t_{100} 2.9 hr under photochemical smog conditions in S.E. England (3).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 5000 mg kg^{-1} (4).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (6).

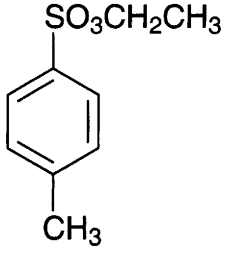
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).
Autoignition temperature 475°C.

References

1. Penny, R. et al *Atmos. Environ.* 1978, **8**, 57-62.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Brice, K. A. et al *Atmos. Environ.* 1978, **12**, 2045-2054.
4. Gerarde, H. *Toxicology and Biochemistry of Aromatic Hydrocarbons* 1960, 57, Elsevier, New York, NY, USA.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

E179 ethyl *p*-toluenesulfonate



$C_9H_{12}O_3S$ **Mol. Wt.** 200.26 **CAS Registry No.** 80-40-0

Synonyms ethyl 4-toluenesulfonate; ethyl *p*-tosylate; ethyl PTS; ethyl 4-methylbenzenesulfonate

EINECS No. 201-276-7 **RTECS No.** XT 6825000

Uses Polymerisation catalyst. Ethylating agent. Plasticiser.

Physical properties

M. Pt. 32-34°C **B. Pt.** 221.3°C **Flash point** 157°C **Specific gravity** 1.174 at 20°C **Volatility** v.den. 6.98
Solubility Organic solvents: diethyl ether, ethanol, ethyl acetate

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rat 500 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 1000 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Subcutaneous rat (600 days) 65 mg kg^{-1} wk^{-1} for 50 wk. 3/11 animals developed local sarcomas (3).

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (5).

Drosophila melanogaster sex-linked recessive lethal assay positive (6).

In vitro hamster embryo cell transformation assay positive (7).

Other effects

Any other adverse effects

In a report on the carcinogenic activity of single doses of 50 mg kg^{-1} of direct alkylating agents, ethyl 4-toluenesulfonate was reported to cause local tumours in 2/12 treated animals (8).

References

1. Z. *Krebsforsch.* 1970, **74**, 241.
2. *J. Natl. Cancer Inst.* 1979, **62**, 911.
3. Searle, C. E. (Ed.) *Chemical Carcinogens: ACS Monograph 173* 1976, 168, American Chemical Society, Washington, DC, USA.
4. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1660, Sigma-Aldrich, Milwaukee, WI, USA.
5. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
6. Zijlstra, J. A. et al *Mutat. Res.* 1988, **198**(1), 73-83.
7. Poiley, J. A. et al *Carcinogenesis (London)* 1980, **1**(4), 323-328.
8. Pressmann, R. et al *Food Cosmet. Toxicol.* 1968, **6**(5), 576-577

E180 ethyltrichlorosilane

$$CH_3CH_2SiCl_3$$

$C_2H_5Cl_3Si$ **Mol. Wt.** 163.51 **CAS Registry No.** 115-21-9

Synonyms ethylsilicon trichloride; trichloroethylsilicon; trichloroethylsilane; CE 6350

EINECS No. 204-072-6 **RTECS No.** VV 4200000

Physical properties

M. Pt. –105.6°C **B. Pt.** 99.5°C **Flash point** 14-22°C (open cup) **Specific gravity** 1.24 at 25°C with respect to water at 25°C

Occupational exposure

UN No. 1196 **HAZCHEM Code** 4WE **Conveyance classification** flammable liquid, corrosive

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1.33 g kg^{-1} (1).
LD_{Lo} intraperitoneal rat 30 mg kg^{-1} (2).
LC_{Lo} (4 hr) inhalation rat 500 ppm (3).
LC_{Lo} (2 hr) inhalation mouse 300 μg m^{-3} (4).

References

1. *J. Ind. Hyg. Toxicol.* 1949, **31**, 60.
2. *J. Ind. Hyg. Toxicol.* 1948, **30**, 332.
3. *J. Ind. Hyg. Toxicol.* 1949, **31**, 343.
4. *Toxicol. New Ind. Chem. Sci.* 1961, **3**, 23 (Russ.)

E181 ethyl vinyl ether

$$CH_2=CHOCH_2CH_3$$

C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 109-92-2

Synonyms vinyl ethyl ether; ethoxyethene; EVE; 3-oxa-1-pentene; Vinamar

EINECS No. 203-718-4 **RTECS No.** KO 0710000

Uses Organic synthesis, manufacture of polymers. Inhalation anaesthetic.

Physical properties

M. Pt. −115°C **B. Pt.** 35.6°C **Flash point** <-45°C (closed cup) **Specific gravity** 0.755 at 20°C
Partition coefficient log P_{ow} 1.04 **Volatility** v.p. 428 mmHg at 20°C ; v.den. 2.5

Occupational exposure

UN No. 1302 (inhibited) **HAZCHEM Code** 3YE (inhibited) **Conveyance classification** flammable liquid (inhibited)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6200 mg kg^{-1} (1).
LC_{50} (15 min) inhalation mouse 320,000 mg m^{-3} (2).
LD_{50} dermal rabbit >20,000 mg kg^{-1} (1).

Irritancy

Dermal rabbit 500 mg caused rapid irritation (exposure unspecified) (3).
Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (4).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation weakly positive (5).
In vitro Chinese hamster ovary cells with metabolic activation sister chromatid exchanges positive (6).

Other effects

Other adverse effects (human)

Reported to cause transitory corneal injury. Recovery was complete within 48 hr (7).

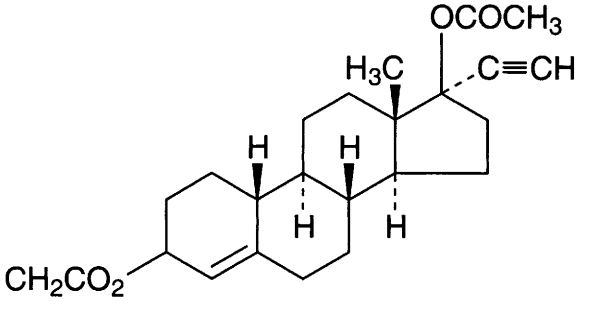
Other comments

Physical properties, uses, mammalian toxicity and safety precautions reviewed (8).
Autoignition temperature 202°C.

References

1. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
2. *Anesthesiology* 1980, **51**, 455.
3. *Union Carbide Data Sheet* 15 Nov 1971, Union Carbide Corp., New York, NY, USA.
4. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1** 1665, Sigma-Aldrich, Milwaukee, WI, USA.
5. Sone, T. et al *J. Pharmacobio-Dyn.* 1989, **12**(6), 345-351.
6. White, A. E. et al *Anesthesiology* 1979, **50**, 426-430.
7. Harrison, G. G. et al *Anesth. Analog. (Cleveland)* 1975, **55**(4), 529-533.
8. *Chemical Safety Data Sheets* 1992, **5**, 271-273, The Royal Society of Chemistry, London, UK

E182 ethynodiol diacetate



$C_{24}H_{32}O_4$ **Mol. Wt.** 384.52 **CAS Registry No.** 297-76-7

Synonyms 3β,17β-diacetoxy-17α-ethynyl-4-estrene; (3β,17α)-19-norpregn-4-en-20-yne-3,17-diol diacetate; aethynodiolum diaceticum; 3β,17β-diacetoxy-17α-ethynyl-4-oestrene; ethinodiol diacetate

EINECS No. 206-044-9 **RTECS No.** RC 8963000

Uses Used as a progestogen alone or in combination with oestrogen as an oral contraceptive. In treatment of progestione deficiency or related disorders.

Physical properties

M. Pt. 126-127°C
Solubility Organic solvents: acetone, diethyl ether

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (1).

Mice receiving the compound in diet for 80 wk did not develop an increased incidence of tumours, but castrated ♂ mice receiving 680 μg kg^{-1} showed an increased incidence of mammary tumours (2,3).
♂ rats receiving the compound in diet developed benign mammary tumours at doses which had no effect in ♀ rats (2).

Teratogenicity and reproductive effects
Oral or parenteral administration to mice 1 mg kg^{-1} on days 7, 8 and 9 of gestation resulted in anomalies of foetuses (4).
No such anomalies were seen in rats receiving 0.1-1.0 mg kg^{-1} subcutaneously 30 days before and 5 days after mating or in rabbits receiving doses 0.1-2 mg kg^{-1} orally or subcutaneously during pregnancy (5).
Inhibition or termination of pregnancy was seen in rats and rabbits in a dose-dependent manner (5).

Metabolism and toxicokinetics
The compound is well absorbed from the gastro-intestinal tract of humans and other mammals (6).
Rapidly metabolised to the active norethisterone (7).
In rats, deacetylation, ring A-saturation or 3-ketone formation occur, while dehydration of a 6-hydroxylated intermediate appears to result in formation of a metabolite with a 6(6)-double bond (8).
Enterohepatic circulation is a feature in the baboon, where the compound is excreted mainly in bile and urine.
3-Deacetylation occurs much faster than 17-deacetylation (9).

Genotoxicity

Rats treated orally for 5 days with 0.2 mg kg^{-1} showed no damage to bone marrow chromsomes on day 6 (10).
Drosophila melanogaster sex-linked recessive assay negative (11).

Other effects

Other adverse effects (human)
Foetal adrenal cytomegaly in humans has been reported (12).

Other comments

The progestational effects of orally administered ethynodiol diacetate have been reviewed (13,14).
No significant difference in the frequency of abnormal karyotypes or in sex ratios has been found in abortuses from women who had taken the compound in oral contraceptives, compared with other women (15).
Carcinogenicity reviewed (16).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 289, 292.
2. *Committee on Safety of Medicines* 1972, HMSO, London, UK.
3. Rudali, G. *J. Natl. Cancer. Inst.* 1972, **49**, 813-819.
4. Andrew, F. D. et al *Teratology* 1972, **5**, 249.
5. Saunders, F. J. et al *Toxicol. Appl. Pharmacol.* 1967, **11**, 229.
6. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
7. Tokuda, G. et al *Nippon Naibunpi Gakkai Zasshi* 1967, **43**, 905-914.
8. Freudenthal, R. I. *J. Pharmacol. Exp. Ther.* 1971, **177**, 468-473.
9. Ishihara, M. et al *Steroids* 1975, **25**, 829.
10. Edwards, C. W. et al *Toxicol. Appl. Pharmacol.* 1971, **19**, 421.
11. Paradi, E. *Mutat. Res.* 1981, **88**, 175.
12. Gau, G. S. et al *J. Clin. Pathol.* 1979, **32**, 305-306.
13. Neumann, F. *Handbuch der Experimentellen Pharmakologie* 1968, **22**, Springer, Berlin, Germany.
14. Tausk, M. et al *International Encyclopaedia of Pharmacology and Therapeutics*, **2** (Sec.48), Pergamon Press, Elmsford, New York, NY, USA.
15. Lauritsen, J. G. *Acta Obstet. Gynecol. Scand.* 1975, **54**, 261-264.
16. *IARC Monograph* 1979, **21**, 387-398

E183 etidronic acid

$$CH_3C(OH)(PO_3H_2)_2$$

$C_2H_8O_7P_2$ **Mol. Wt.** 206.03 **CAS Registry No.** 2809-21-4

Synonyms (1-hydroxyethylidene)-1,1-diphosphonic acid; Dequest 2010; EHDP; ethane-1-hydroxy-1,1-diphosphonic acid; (1-hydroxyethylidene)bis-[phosphonic acid]; (hydroxyethylidene)diphosphonic acid; hydroxyethanediphosphonic acid; xydiphone; Fostex P

EINECS No. 220-552-8 **RTECS No.** SZ 8562100

Uses Scale and corrosion inhibitor. Component of detergents. Sequestering and chelating agent.

Physical properties

Solubility Water: 60% at 20°C

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, channel catfish 366-695 mg l^{-1} (1).
LC_{50} (48 hr) carp 223 mg l^{-1} (1).
LC_{50} (96 hr) sheepshead minnow 1978 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 400 mg l^{-1} (1).
EC_{50} (96 hr) oyster shell deposition 81 mg l^{-1} (1).
Daphnia magna reproductivity seriously impaired at 25 mg l^{-1}, threshold effect at 6 mg l^{-1} (2).

Environmental fate

Degradation studies

No degradation observed in a semi-continuous activated sludge test (3,4).
Passed through a biological sewage treatment plant without mechanical pretreatment step and an activated sludge process with mechanical pretreatment. No irreparable damage to the plants, but only ~50% degradation and lower than expected removal. Concentration of 2 mg l^{-1} was considered a high loading (5).
Did not degrade in the modified OECD screening test, but showed good biodegradability in the modified SCAS test. Biodegradation does not occur readily either in sewage plant or in surface water. Phosphonates are not uniform in their behaviour and need to be evaluated individually (6).
Complete breakdown of phosphonates was achieved by bacteria, but not eukaryotes, via cleavage of the carbon-phosphorus bond (7).

Adsorption and retention

Adsorbs onto river solids and bottom mud (3,4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, mouse 1140, 1800 mg kg^{-1}, respectively (1,8).
LD_{50} intraperitoneal mouse, guinea pig 100-500 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Subcutaneous doses of 0.1 and 0.5 mg kg^{-1} day^{-1} in adult dogs produced reduction of bone mineralisation and reduction in resorption space, but no changes in osteoid seam widths in 1-2 yr. No treatment-related bone fractures were noted at lower dose, but the fracture incidence increased slightly at 0.5 mg kg^{-1} day^{-1} (9).

Teratogenicity and reproductive effects

100 mg kg^{-1} day^{-1} gave no increase of anomalies in first-generation rabbit foetuses (9).

Intraperitoneal mouse single injection 200 mg kg^{-1} on gestation days 7, 8, 9 and 10 caused adverse effects to foetal dental tissue. Effects varied depending on day of administration (10-12).

Intraperitoneal mouse single injection 200 mg kg^{-1} on gestation days 7-11 did not influence the number of implants and live foetuses, but foetal weight was lowered. Did not affect the dam, but crossed the placenta and directly affected the foetus (13).

Intraperitoneal mouse single injection 200 mg kg^{-1} on gestation days 7 to 11. By day-18, anomalies included internal haemorrhage around the cranial suture region, exencephalia and cleft lips (14).

Metabolism and toxicokinetics

Six-day faecal recovery accounted for 70-90% of the oral dose, hence it is transported across the intestine to only a small extent (15).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (16).

Other effects

Any other adverse effects

Enteral rat (3 wk) 0.25 mg kg^{-1} day^{-1} increased Ca, P and Mg levels in bones and hearts and decreased blood serum acid and alkaline phosphatase activities (17).

In vivo rat single subcutaneous, intraperitoneal 100 mg kg^{-1} or repeat subcutaneous injection 10 mg kg^{-1} day^{-1} for >6 days induced dysfunction of splenic B lymphocytes but not T lymphocytes (18).

Intravenous injection encapsulated within liposomes did not affect spleen macrophage subpopulations (19).

In rats a low dose caused suppression of bone resorption in the metaphysis with proliferation of osteoclasts with an increased number of nuclei. High doses led to enlargement of the hypertrophic zone of the epiphyseal plate and suppression of calcification of the cartilage matrix (20).

Sub-acute experiments (species unspecified) 40-400 mg kg^{-1} indicated increased peroxidase activity, decreased ceruloplasmin activity and phase changes of SH-groups content. Chronic exposure to 0.4-4.0 mg kg^{-1} produced significant changes in peroxidase and cholinesterase activity (21).

Doses of 5-20 mg kg^{-1} day^{-1} for 3-6 months (species unspecified) caused progressive changes in biochemical parameters and in the histological abnormalities of bone (22).

Other comments

Caused a high frequency of chromosome aberrations in root tips of barley and onion. Prior treatment of the plants with *N*-nitroso-*N*-dimethylurea reduced significantly the mutagenicity of pyrophosphate and phosphonates (23).

Has been used to treat Paget's disease (24).

In rats with coronary artery occlusion, 10, 15, 20 mg kg^{-1} pretreatment increased survival time and reduced the size of the infarction (25).

Oral rat, mouse (24 month) 9-14 mg kg^{-1} in drinking water reduced frequency of spontaneous tumours (26).

Environmental fate studied in aquatic model systems containing different adsorbents, sediments, clay minerals and sewage sludges (27).

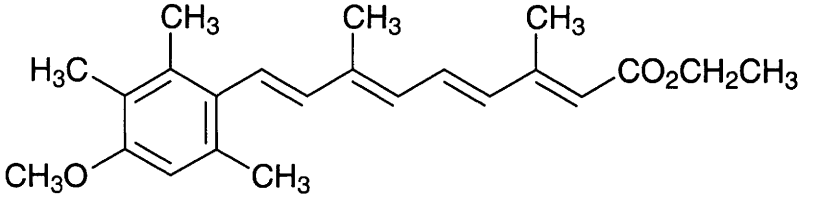
Therapeutically, normally only available as the sodium salts in solution; mono-, di-, tri-, and tetrasodium etidronate.

References

1. *Material Safety Data Sheet* 1985, Dow Chemicals.
2. Kastner, W. et al *Eau, Ind., Nuisances* 1983, **72**, 47.
3. Wehle, V. *VGB Kraftwerkstech.* 1976, **56**, 173.
4. Huber, L. D. *Tenside Deterg.* 1975, **12**, 316.
5. Metzner, G. *Muench. Beitr. Abwasser-, Fisch.- Flussbiol.* 1990, **44**, 323-336 (Ger.) (*Chem. Abstr.* **114**, 234402g).
6. Horstmann, B. *Vom Wasser* 1988, **70**, 163-178 (Ger.) (*Chem. Abstr.* **109**, 134410m).

7. Schowanek D. et al *Appl. Environ. Microbiol.* 1990, **56**(4), 898-903.
8. *Angewandte Chem.* 1975, **14**, 94.
9. Flora, L. et al *Metab. Bone Dis. Relat. Res.* 1981, **4-5**, 289.
10. Sakiyama Y. et al *Shika Igaku* 1987, **50**(4), 622-636 (Japan.) (*Chem. Abstr.* **108**, 31921d, 31922e).
11. Sakiyama, Y. et al *Shika Igaku* 1988, **51**(2), 354-361 (Japan.) (*Chem. Abstr.* **109**, 104761j).
12. Sakiyama, Y. et al *Shika Igaku* 1988, **51**(5), 997 (Japan.) (*Chem. Abstr.* **110**, 862x).
13. Sakiyama, Y. et al *J. Osaka Dent. Univ.* 1985, **19**(2), 87-90.
14. Sakiyama, Y. et al *J. Osaka Dent. Univ.* 1986, **20**(2), 91-100.
15. Taniggia, A. et al *Calif. Tissue Res.* 1977, **Suppl. 22**, 428.
16. Abelev, S. K. et al *Nov. Khelatiruyushchii Agent-Ksidifon Farmakol. Toksikol. Ter., Dokl. Vses. Rab. Soveshch. Primen. Kompleksonov Med.* 1990, 2nd ed., 74-78 (Russ.) (*Chem. Abstr.* **114**, 178350z).
17. Konoplya, E. F. et al *Vestsi Akad. Navuk BSSR, Ser. Biyal. Navuk* 1989, (3), 66-71 (Belorussian) (*Chem. Abstr.* **111**, 151046f).
18. Toda, Y. et al *Nippon Shishubyo Gakkai Kaishi* 1986, **28**(4), 1063-1069.
19. van Rooijen, et al *Calcif. Tissue Int.* 1989, **45**(3), 153-156.
20. Katoh, Y. et al *Bone* 1991, **12**(2), 59-65.
21. Dergachera, T. S. *Hyg. Sanit. (USSR)* 1981, **46**, 72.
22. Kanis, J. A. et al *Metab. Bone Dis. Relat. Res.* 1981, **3**, 219.
23. Gaivoroskaya, G. G. et al *Tsitol. Genet.* 1981, **15**, 41 (*Chem. Abstr.* **96**, 1392g).
24. Zeigler R. et al *DMW, Dtsch. Med. Wochenschr.* 1988, **113**(3), 102-105 (Ger.) (*Chem. Abstr.* **108**, 123833w).
25. Emguin, A. G. et al *Nov. Khelatiruyushchii Agent-Ksidifon Farmakol. Toksikol. Ter., Dokl. Vses. Rab. Soveshch. Primen. Kompleksonov Med.* 1990, 2nd ed., 42-44 (Russ.) (*Chem. Abstr.* **114**, 94921y).
26. Chalov I. B. et al *Nov. Khelatiruyushchii Agent-Ksidifon Farmakol. Toksikol. Ter., Dokl. Vses. Rab. Soveshch. Primen. Kompleksonov Med.* 1990, 2nd ed., 70-74 (Russ.) (*Chem. Abstr.* **114**, 94787j).
27. Fischer, K. *Chemosphere* 1991, **22**(1-2), 15-27

E184 etretinate



$C_{23}H_{30}O_3$ **Mol. Wt.** 354.49 **CAS Registry No.** 54350-48-0

Synonyms ethylall-*trans*-9-(4-methoxy-2,3,6-trimethyl phenyl)-3,7-dimethylnona-2,4,6,8-tetraenoate; Ro-10-9359; Tegison; Tigason

EINECS No. 259-119-3 **RTECS No.** RA 6620000

Uses Orally active antipsoriatic occasionally used in other skin disorders. The compound is reported to be of use in the treatment of some neoplastic disorders (1-3).

Physical properties

M. Pt. 104-105°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >4 g kg^{-1} (4).

LD_{50} oral mouse >2 g kg^{-1} (4).

LD_{50} intraperitoneal rat >2 g kg^{-1} (4).
LD_{50} intraperitoneal mouse 1.18 g kg^{-1} (4)

Sub-acute and sub-chronic data
Rats receiving 0.5 or 6 mg kg^{-1} day^{-1} for 12 wk, demonstrated inhibition of etretinate metabolism with an increase in plasma concentration. Both doses were hepatotoxic, but toxicity did not correlate with plasma or liver concentrations (5).

Teratogenicity and reproductive effects
Teratogenic effects in rat are reported to be dependent on day of administration. 10 or 25 mg kg^{-1} orally to rats on days 6 or 7 of pregnancy produced no effect, but on day-8 produced teratogenic effects. Doses ≤6 mg kg^{-1} had no effect (6).
Oral hamster 44 or 88 mg kg^{-1} on day-8 of pregnancy produced teratogenic effects (7).

Metabolism and toxicokinetics
Absorption varies between individuals and with diet. First-pass metabolism occurs to form the active metabolite acitrefin. Both compounds are extensively bound to plasma proteins and etretinate can accumulate in fat. $t_{1/2}$ ≈20 days, but detectable concentrations in plasma can persist for up to 3 yr (1).
Etretinate crosses the placenta and is excreted in breast milk (1).

Other effects

Other adverse effects (human)
Mucocutaneous dryness frequently occurs and raised serum lipids, musculoskeletal and liver symptoms may result from treatment (1,3).

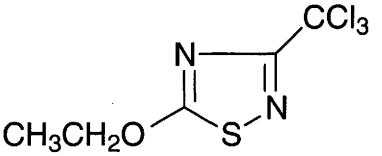
Other comments

Pregnancy and donation of blood should be avoided for at least 2 yr after cessation of treatment. Long-term treatment of children should be avoided (1).
Some beneficial results have been observed in the treatment of cutaneous lymphomas, actinic and Bowenoid keratoses and keratoacanthoma (1).
Compound has been shown to inhibit production of tumours in rat large intestine by 1,2-dimethylhydrazine (8).
The properties of the compound have been reviewed (3).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
2. Oreno, B. et al *Br. J. Dermatol.* 1991, **125**, 456-459.
3. Orfanos, C. E. et al *Drugs* 1987, **34**, 459-503.
4. Kamm, J. J. *J. Am. Acad. Dermatol.* 1982, **6**(4/2), 652-659.
5. AmoBernal, C. *Histol. Histopathol.* 1989, **4**(4), 435-441.
6. Agnish, N. D. et al *Teratology* 1990, **42**(1), 25-33.
7. *Fund. Appl. Toxicol.* 1984, **4**, 977.
8. Khadzholov, D. et al *Dokl. Bolg. Akad. Nauk* 1990, **43**(3), 79-80

E185 etridiazole



$C_5H_5Cl_3N_2OS$ **Mol. Wt.** 247.53 **CAS Registry No.** 2593-15-9

Synonyms 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole; ethyl 3-trichloromethyl-1,2,4-thiadiazol-5-yl ether; Echlomezol; Ethazole; AAterra; Dwell; Koban; Pansoil; Terrazole; Truban

EINECS No. 219-991-8 **RTECS No.** XI 3875000

Uses Foliar and soil fungicide for pre- and post-emergence use.

Physical properties

M. Pt. 20°C **B. Pt.** 95°C at 1 mmHg **Specific gravity** 1.503 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.37 **Volatility** v.p. 9.7×10^{-5} mmHg
Solubility Water: 117 mg l^{-1} at 25°C. Organic solvents: acetone, carbon tetrachloride, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) rainbow trout >4 mg l^{-1} (1).
LC_{50} (24 hr) bluegill sunfish >7.5 mg l^{-1} (1).

Environmental fate

Nitrification inhibition
The ability of the compound to inhibit nitrification has been reviewed (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral duck 1.64 mg kg^{-1} (1).
LD_{50} oral rat 1100 mg kg^{-1} (3).
LD_{50} oral rabbit 779 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Rats and dogs fed the compound for 90 days at a dose of 1.2 and 1.6 g kg^{-1} diet, respectively, showed no adverse effects (1).

Metabolism and toxicokinetics
In mammals, metabolites include the water-soluble substance 3-carboxy-5-ethoxy-1,2,4-thiadiazole (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
Log P_{ow} exceeds European Union limit of 3.0.
WHO Toxicity Class III (7).
EPA Toxicity Class III (formulation) (3).
ADI 0.025 mg kg^{-1} (3).

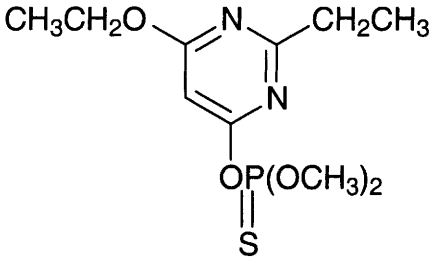
Other comments

Food contaminant. Environmental contaminant, including air.
The compound is not toxic to bees (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. McCarty, G. W. *Biol. Fertil. Soils* 1989, **8**(3), 204-211.
3. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
4. *Toxicol. Appl. Pharmacol.* 1980, **56**, 164.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

E186 etrimfos



$C_{10}H_{17}N_2O_4PS$ **Mol. Wt.** 292.30 **CAS Registry No.** 38260-54-7

Synonyms *O*-(6-ethoxy-2-ethyl pyrimidin-4-yl) *O,O*-dimethyl phosphorothioate; *O*-(6-ethoxy-2-ethyl-4-pyrimidinyl) *O,O*-dimethyl phosphorothioate; Ekamet; Satisfar; SAN 197; Grapil

EINECS No. 253-855-9 **RTECS No.** TF 8350000

Uses Non-systemic agricultural insecticide.

Physical properties

M. Pt. –3.35°C **Specific gravity** 1.195 at 20°C **Partition coefficient** log P_{ow} >3.3 **Volatility** v.p. 6.5×10^{-5} mmHg at 20°C

Solubility Water: 40 mg l^{-1} at 24°C. Organic solvents: miscible with acetone, diethyl ether, dimethylsulfoxide, ethanol

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed (R22)

Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity

LC_{50} (48, 96 hr) carp 13.6, 13.3 mg l^{-1}, respectively (1).

LC_{50} (96 hr) guppy 5.5 mg l^{-1} (2).
LC_{50} (96 hr) rainbow trout 24 μg l^{-1} (2).

Environmental fate

Degradation studies

In soil, $t_{1/2}$ has been reported to be 3-8 days (2).
Concentrations of 5, 10 and 15 ppm added to wheat grain remained effective for 7, 15 and 30 days, respectively (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂ rats 1.8 g kg^{-1} (1).
LD_{50} oral ♂ mice 437 mg kg^{-1} (1).
LD_{50} dermal rats >5 g kg^{-1} (4).
LD_{50} dermal ♂ rabbits >500 mg kg^{-1} (4).

Metabolism and toxicokinetics

After oral administration to mammals, the compound is rapidly metabolised and excreted in urine (2).
Metabolites include 6-ethoxy-2-ethylpyrimidin-4-ol, small amounts of 2-ethylpyrimidine-4,6-diol and other hydroxy derivatives (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
WHO Toxicity Class II (7).
EPA Toxicity Class III (formulation) (4).
ADI 0.003 mg kg^{-1} (4).

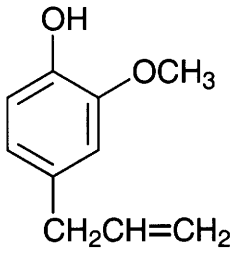
Other comments

Pollutant in water and soil, contaminant in food.
Toxic to bees by contact, or orally (2,8).
The effect of the compound ón beneficial organisms has been reviewed (9).

References

1. Knutti, H. J. *Proc. 8th Brit. Insect. Fungicide Conf.* 1975, **2**, 675.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Sahoo, B. K. et al *Environ. Ecol.* 1989, **7**(4), 826-828.
4. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
8. Sorthia, B. K. et al *J. Entomol. Res.* 1985, **9**(2), 195-197.
9. Hassan, S. A. et al *J. Appl. Entomol.* 1987, **103**(1), 92-107

E187 eugenol



$C_{10}H_{12}O_2$ **Mol. Wt.** 164.20 **CAS Registry No.** 97-53-0

Synonyms phenol, 2-methoxy-4-(2-propenyl)-; 4-allyl-2-methoxyphenol; caryophyllic acid; eugenic acid; 2-methoxy-1-hydroxy-4-allylbenzene; allyl guaiacol

EINECS No. 202-589-1 **RTECS No.** SJ 4375000

Uses Fragrance and flavouring agent. Analgesic in dental materials and non-prescription therapeutic products. Insect attractant. Chemical intermediate.

Occurrence In a variety of plant oils, particularly clove bud oil, clove leaf oil, cinnamon leaf oil, and oils of basil. Present in cigarette and wood smoke (1,2).

Physical properties

M. Pt. –9.2 to –9.1°C **B. Pt.** 254°C **Flash point** >110°C **Specific gravity** 1.0664 at 20°C with respect to water at 4°C **Volatility** v.p. 0.009 mmHg at ≈20°C

Solubility Organic solvents: glacial acetic acid; miscible with chloroform, diethyl ether

Ecotoxicity

Fish toxicity

LC_{50} (1-96 hr) fathead minnows 24 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig, mouse 2-3 g kg^{-1} (4).

LD_{50} intraperitoneal mouse 0.5 g kg^{-1} (5).

LD_{50} dermal rabbit 1.2 g kg^{-1} (6).

Acute mammalian toxicity is associated with drop in body temperature, muscle weakness, loss of righting reflex, cardiovascular and respiratory effects, and tissue irritation (7-11).

Sub-acute and sub-chronic data

Rats receiving ≤6000 ppm in diet for 13 wk showed no adverse effects. 12,000 ppm caused weight loss (12).

Oral rats (34 day) unspecified concentration caused damage to liver and gastro-intestinal tract, particularly the forestomach (13).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (14).

National Toxicology Program investigated eugenol in a 2-yr feeding study in rats and mice. Results with ♂ and ♀ rats were negative for carcinogenicity and equivocal for ♂ and ♀ mice (12).

♂ mice showed an increase in adenomas and carcinomas, but only at the lower of the two doses, while ♀ mice produced equivocal signs of hepatocellular neoplasms (12).

In a 1-yr feeding study in mice, no evidence of tumorigenicity was detected (15).

Rats receiving eugenol after a single dose of diethyl nitrosamine, for several wk in an assay based on the number and area of induced glutathione *S*-transferase placental positive foci in liver, showed a positive result at dietary dose of 10,000 ppm (16).
Dermal mice 10 mg, $3 \times wk^{-1}$ demonstrated a positive anti-tumorigenic action (17).
Rats receiving 10,000 ppm for 42 days showed a negative result in tumour initiation and promotion tests (18).

Metabolism and toxicokinetics
In mammals, the major organ responsible for metabolism is the liver, where microsomal mixed function oxidases effect some side-chain oxidation accompanied by some *O*-demethylation (19).
Formation of sulfate and glucuronide conjugates is the major route of metabolism, with the formation rate of the two conjugates altering with dose (20).
Reduction of the double bond is effected in rats and mice by gut microflora, but is more extensive in the rat. This does not appear to occur in humans (21).
Oral rats 203 mg kg^{-1} resulted in 50% of the dose being eliminated as conjugates in urine and 13% products (dihydrodiols) (22).
The pharmacokinetics of eugenol have been assessed in humans receiving oral doses of 50 mg. Rapidly absorbed and metabolised, almost completely excreted in the urine within 24 hr. Unmetabolised compound accounted for <0.1% of dose. Major metabolites were phenolic conjugates, 50% of the conjugated metabolites were eugenol-glucuronide and sulfate (23).

Irritancy
Eugenol can be an irritant to lungs (11).
In human patch-tests, eugenol was moderately irritating (24).
In irritation tests using guinea pigs, 10% caused irritant reactions (25).

Sensitisation
The frequency of allergic-type positive reactions in cosmetic dermatitis patients to 5% eugenol was 2.6% (25).
Studies have produced mixed results, but sensitisation has been reported in guinea pigs, mice and humans (24,26,27).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (28).
In vitro Chinese hamster ovary cells with metabolic activation chromosomal aberrations positive (28).
In vitro Chinese hamster ovary cells induced sister chromatid exchanges with and without metabolic activation at concentrations which caused severe cell cycle delay (29).
Unscheduled DNA synthesis in rat liver cells was negative. The compound was cytotoxic at higher doses (30,31).

Other comments

Detected in untreated effluent from a paper mill and municipal wastewater (32,33).
Sensitisation reviewed (34).

References

1. Hawthorne, S.B. *Environ. Sci. Technol.* 1988, **22**(10), 1191-1196.
2. Jansson, T. et al *Mutat. Res.* 1988, **206**, 17-24.
3. Mattson, V. R. et al EPA/600/3-76.097, 1976.
4. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1964, **2**(3), 327.
5. Caujolle, F. et al *Ann. Pharm. Fr.* 1960, **18**, 601-612.
6. Beroza, M. et al *Toxicol. Appl. Pharmacol.* 1975, **31**, 421-429.
7. Dallmeir, K. *Pharmacology* 1981, **22**(2), 113-127.
8. Lauber, F. U. et al *Gastroenterology* 1950, **15**(3), 481-486.
9. Sticht, F. D. *Dokl. Bolg. Akad. Nauk* 1971, **20**(12), 1341-1344.
10. Sober, H. A. *Proc. Soc. Exp. Biol. Med.* 1950, **73**(1), 148-151.
11. LaVoie, E. J. et al *Atherosclerosis* 1986, **59**(2), 78-81.

12. *National Toxicology Program Research and Testing Division* 1992, Report No. TR223, NIEHS, Research Triangle Park, NC, USA.
13. Hagan, E. C. et al *Toxicol. Appl. Pharmacol.* 1965, **7**, 18-24.
14. *IARC Monograph* 1987, **Suppl. 7**, 63.
15. Miller, E. C. *Cancer Res.* 1983, **43**(3), 1124-1134.
16. Ito, N. *Teratog., Carcinog., Mutagen.* 1992, **12**(2), 79-95.
17. Van Duuren, B. L. *J. Natl. Cancer Inst.* 1976, **56**(6), 1237-1242.
18. Ward, J. M. et al *Fundam. Appl. Toxicol.* 1989, **12**(1), 163-171.
19. *IARC Monograph* 1985, **36**, 75.
20. Sutton, J. D. *Biochem. Pharmacol.* 1985, **34**, 465-466.
21. Caldwell, J. *J. Nutr. Biochem.* 1990, **1**, 396-409.
22. Delaforge, M. *Xenobiotica* 1980, **10**, 737-744.
23. Fischer, I. U. *Xenobiotica* 1990, **20**, 209-222.
24. Motoyoshi, K. et al *Cosmet. Toiletries* 1979, **94**, 41-48.
25. Itoh, M. *J. Dermatol.* 1982, **9**(3), 223-233.
26. Fujii, T. et al *Yukagaku* 1972, **21**(12), 904-908.
27. Gerberick, G. F. et al *Fund. Appl. Toxicol.* 1992, **19**(3), 438-445.
28. Ishidate, M. et al *Food Chem. Toxicol.* 1984, **22**(8), 623-636.
29. Galloway, S. M. *Environ. Mol. Mutagen.* 1987, **10**(10), 1-175.
30. Allavena, A. et al *Teratog., Carcinog., Mutagen.* 1992, **12**(1), 31-41.
31. Howes, A. J. *Food Chem. Toxicol.* 1990, **28**(8), 537-542.
32. Turoski, V. E. et al *Tappi J.* 1983, **66**, 89-90.
33. Ellis, D. D. et al *Arch. Environ. Contam. Toxicol.* 1982, **11**, 373-382.
34. Rothenstein, A. S. et al *Food Chem. Toxicol.* 1983, **21**, 727-733

E188 Eulan WA new

CAS Registry No. 55069-01-7

Synonyms Major components are polychloro-2-[chloromethylsulfonamido]diphenyl ethers (PCSDs); minor components are polychloro-2-aminodiphenyls (PADs), such as 2',3,4,4',5-pentachloro-2-aminodiphenyl ether; 2',3,4,4',5,6-hexachloro-2-aminodiphenyl ether and their respective *N*-methylsulfone derivatives

Uses Used in mothproofing woollen textiles and carpeting to protect against moths and carpet weevils.

Ecotoxicity

Fish toxicity

Northern pike fed a diet of salmon fry exposed to high concentrations of PADs and PCSDs found in Eulan WA new concentrated the compounds in bile fat and spleen (1).

Goldfish liver metabolised PCSDs to PADs. Variation in metabolism between species is thought to occur (2).

LC_{50} (48 hr) rainbow trout 28 μg l^{-1} (technical active ingredient) at pH 8 and 18 μg l^{-1} (technical active ingredient) at pH 6. These concentrations correspond to ~0.14 and 0.09 ppm by volume of the formulated product (3).

LC_{50} (96 hr) rainbow trout 1.1-1.5 μg l^{-1} (active ingredient) at pH 7.4, total hardness 250 mg l^{-1} ($CaCO_3$) and temperature 15°C (4).

Bioaccumulation

The bioaccumulation in the muscle and viscera of rainbow trout at a range of concentrations in water was studied. Concentrations of 200 μg l^{-1} (formulated product) maximum tested in water gave bioconcentration factors of 36 in muscle, 106 in spleen, 413 in liver and 498 in kidney. The lowest concentration tested of 0.32 μg l^{-1} (formulated product) gave bioconcentration factors of 164 muscle, 123 spleen, 485 kidney and 602 liver (4).

Mammalian & avian toxicity

Metabolism and toxicokinetics

Mice fed a diet containing 2',3,4,4',5-pentachloro-2-aminodiphenyl ether 82.5 μg mouse^{-1} day^{-1} and 2',3,4,4',5,6-hexachloro-2-aminodiphenyl ether 190 μg mouse^{-1} day^{-1} and their respective *N*-chloromethyl sulfone derivatives (the active components of Eulan WA new) accumulated in the abdominal fat. Hydrolysis of the respective sulfones was calculated to be 7-44% or 10-25% in periods ranging up to 60 days (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).

Included in Schedule 6 (Released into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Environmental pollutant.

Active ingredients are the PCSDs (1,5,8).

References

1. Machon, A. et al *Environ. Pollut., Ser. A.* 1984, **33**(4), 295-302.
2. Machon, A. et al *Comp. Biochem. Physiol., C: Comp. Pharmacol. Toxicol.* 1986, **84C**(1), 113-117.
3. Abram, F. S. H. et al *The Effects of Hydrogen Ion Concentration on the Toxicity of Eulan WA New to Rainbow Trout, Report 156-M* 1982, WRC Environmental Protection, Stevenage, UK.
4. Abram, F. S. H. et al *The Toxicities of Mitin N and Eulan WA New to Rainbow Trout Report 156-M* 1981, WRC Environmental Protection, Stevenage, UK.
5. Westoeoe, G. et al *Bull. Environ. Contam. Toxicol.* 1985, **34**(1), 29-35.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S.I. 1991 No.472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. Grat, E. et al *Textilveredlung* 1989, **24**(11), 389-390 (Ger.) (*Chem. Abstr.* **113**, 116962w)

E189 europium

Eu

Eu **Mol. Wt.** 151.96 **CAS Registry No.** 7440-53-1

EINECS No. 231-161-7

Uses Salts are used in cathode ray tube coatings in colour television receivers. Organic derivatives are used as shift reagents in NMR. Capture of neutrons in atomic power stations.

Occurrence Abundance in Earth's crust 0.14-1.1 ppm. Occurs in monazite sand and gadolinite.

Physical properties

M. Pt. 826°C **Specific gravity** 5.244

Solubility liquid ammonia

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Oral Wistar rat (28 day) 0, 40, 200 or 1000 mg kg^{-1} day^{-1} by gavage. Hyperkeratosis of the forestomach and eosinocyte infiltration of the stomach mucosa were found in animals receiving 1000 mg kg^{-1} day^{-1}. This was attributed to an irritant effect. Europium levels increased dose dependently in the liver, kidneys, spleen and femurs. The no-observed-effect level was 200 mg kg^{-1} day^{-1} (1).

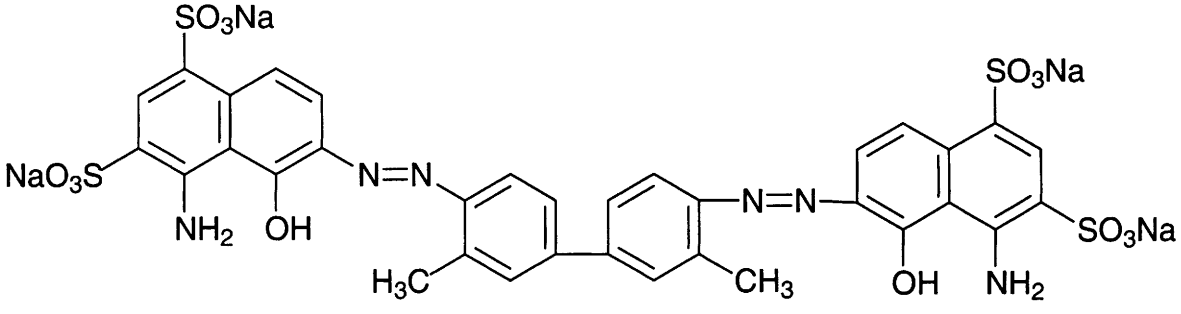
Metabolism and toxicokinetics

Following oral administration in humans, virtually no absorption of lanthanide salts into the blood system occurs (2). Following inhalation exposure to europium salts, 30% of the administered dose was detected in the liver and 40% in the skeleton. Elimination occurred via the kidneys and faeces in equal proportions (2).

References

1. Ogawa, Y. et al *J. Environ. Pathol. Toxicol. Oncol.* 1995, **14**(1), 1-9.
2. Goering, P. L. et al in *Metals and Their Compounds in the Environment – Occurrence, Analysis and Biological Relevance* 1991, 959-970, VCH, NY, USA

E190 Evans Blue



$C_{34}H_{24}N_6Na_4O_{14}S_4$ **Mol. Wt.** 960.82 **CAS Registry No.** 314-13-6

Synonyms C.I. Direct Blue 53; C.I. 23860; 6,6'-[(3,3'-dimethyl[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis(4-amino-5-hydroxy)-1,3-naphthalenedisulfonic acid, tetrasodium salt; 4,4'-bis[7-(1-amino-8-hydroxy-2,4-disulfo)-naphthylazo]-3,3'-bitolyl, tetrasodium salt; Azovan Blue; Geigy Blue 536

EINECS No. 206-242-5 **RTECS No.** QJ 6440000

Uses Dyestuff. Diagnostic aid in blood volume determination.

Physical properties

Solubility Water: soluble. Organic solvents: ethanol

Occupational exposure

UN No. 2811

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 200 mg kg^{-1} (1).

LD_{Lo} intravenous cat, rabbit, dog, rat 1, 1, 3, 5 g kg^{-1}, respectively (2).

Carcinogenicity and chronic effects

No adequate data on carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (3).

Intraperitoneal rat (340 day) 0.1 mg $animal^{-1}$ every 2 wk for 8 months. 10/40 animals developed histiocytic tumours of the liver and 1/40 showed a reticulum-cell sarcoma of the mesenteric lymph nodes. No tumours occurred in 20 controls (4).

Intraperitoneal rat (475 day) 0.2 mg $animal^{-1}$ every 2 wk for 8 months. No tumours developed in 15/40 animals which survived 351-475 days (5).

Teratogenicity and reproductive effects

Intraperitoneal rat, 70-200 mg kg^{-1} on day-8 of gestation caused dose-related increases in number of malformed foetuses and resorptions. The principal defect was ocular malformation (6).

Metabolism and toxicokinetics

A dose of 200 mg administered orally to dogs in which the intestinal flora had been eliminated was found to be substantially unabsorbed; 80-90% was recovered in the faeces, none being found in the tissues or plasma (7).

Following intravenous administration of 2-3 mg kg^{-1} in dogs, 36-47% of the dose was recovered from the liver, kidney, spleen and bile. No colour was excreted in the urine, although 3% was found in the faeces of dogs with ligated bile ducts. Only small amounts were found in the reticuloendothelial system. The remainder of the dyestuff was unaccounted for (7).

Evans Blue and ^{131}I-labelled human serum albumin were injected intravenously into hamsters. During the first 2 min the colour was removed from the circulation more rapidly than the albumin. Subsequently, blood clearance occurred at the same rate, probably through binding of the dye to albumin (8).

In vitro studies in human serum showed that low concentrations (5-25 mg 100 ml^{-1} of saline) were bound to α-1-lipoprotein and at higher concentrations to albumin (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation marginally positive (10).

In vitro primary rat hepatocytes, DNA repair assay weakly positive (11).

Other comments

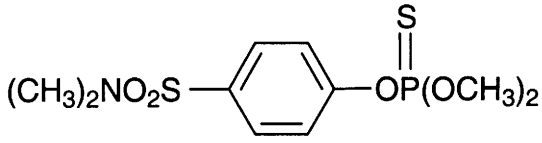
Physical properties, use, carcinogenicity and metabolism reviewed (12,13).

Evans Blue may be prepared using *o*-toluidine, a suspected cancer agent which may be a possible impurity (12).

References

1. *Br. Heart J.* 1959, **21**, 492.
2. *Arch. Surg.* 1944, **48**, 17.
3. *IARC Monograph* 1987, **Suppl. 7**, 63.
4. Marshall, A. H. E. *Acta Pathol. Microbiol. Scand.* 1953, **33**, 1-9.
5. Ruttner, J. R. et al *Schweiz. Z. Allg. Pathol. Bakteriol.* 1956, **19**, 436-455.
6. Beaudoin, A. R. *Proc. Soc. Exp. Biol. Med.* 1968, **127**, 215-219.
7. Stoelinga, G. B. A. et al *Acta Physiol. Pharmacol. Neerl.* 1967, **14**, 391-409.
8. Wilde, W. S. et al *Am. J. Physiol.* 1971, **220**, 1991-1999.
9. Schen, R. J. et al *Clin. Chim. Acta* 1967, **16**, 445-448.
10. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
11. Kornbrust, D. et al *Environ. Mutagen.* 1985, **7**(1), 101-120.
12. *IARC Monograph* 1975, **8**, 151-156.
13. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F1 famphur



$C_{10}H_{16}NO_5PS_2$ **Mol. Wt.** 325.35 **CAS Registry No.** 52-85-7

Synonyms phosphorothioic acid *O*-[4-[(dimethylamino)sulfonyl]phenyl] *O,O*-dimethyl ester; phosphorothioic acid *O,O*-dimethyl ester, *O*-ester with *p*-hydroxy-*N,N*-dimethyl benzenesulfonamide; Famophos; Warbex; ENT 25644; Bo-Ana

EINECS No. 200-154-0 **RTECS No.** TF 7650000

Uses Insecticide, particularly for cattle and reindeer, for lice infestation.

Physical properties

M. Pt. 52.5-53.5°C

Solubility Organic solvents: acetone, carbon tetrachloride, chloroform

Ecotoxicity

Bioaccumulation

Calculated bioconcentration factor of 31.8 (based on log K_{ow} of 2.28) suggests that bioconcentration in fish and aquatic organisms is not expected to be a significant process (1).

Biotransfer factor (log B_6) –4.11 (2).

Environmental fate

Abiotic removal

Under neutral conditions, hydrolysis $t_{1/2}$ 115 days and, under basic conditions, $t_{1/2}$ 6 days (pH 11) and 60 days (pH 10) (3).

Adsorption and retention

Calculated K_{oc} 419 suggests that moderate mobility and adsorption can occur (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 1.78, 4.2 mg kg^{-1}, respectively (5).

LD_{50} oral ♂ mouse 27 mg kg^{-1} (6).

LD_{50} oral ♂, ♀ rat 35, 62 mg kg^{-1}, respectively (6).

LD_{50} dermal rabbit 2.7 g kg^{-1} (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (7).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

WHO Toxicity Class Ib (9).

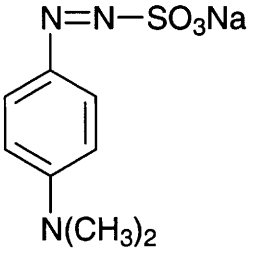
Other comments

Toxicity reviewed (10).

References

1. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, **5**, 1-30, McGraw-Hill, New York, NY, USA.
2. Travis, C. C. *Environ. Sci. Technol.* 1988, **22**(3), 271-274.
3. Ellington, J. J. et al *Measurement of Hydrolysis Rate Constants for Evaluation of Hazardous Waste Land Disposal* 1988, **3**, NTIS P888-234042, US Environ. Res. Lab., Athens, GA, USA.
4. Suraan, R. L. et al *Residue. Rev.* 1983, **85**, 17-28.
5. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
6. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *S.I. 1991 No. 472 The Environment Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
9. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.2.
10. *Dangerous Prop. Ind. Mater. Rep.* 1987, 7(3), 91-92

F2 fenaminosulf



$C_8H_{10}N_3NaO_3S$ **Mol. Wt.** 251.24 **CAS Registry No.** 140-56-7

Synonyms sodium 4-dimethylaminobenzenediazosulfonate; sodium *p*-(dimethylamino)benzenediazosulfonate; Le san; Phenaminosulf; Dexon

EINECS No. 205-419-4 **RTECS No.** CZ 1750000

Uses Superseded seed and soil fungicide.

Physical properties

Solubility Water: 40 g l^{-1} at 20°C. Organic solvents: dimethyl formamide

Occupational exposure

Supply classification toxic

Risk phrases Harmful in contact with skin – Toxic if swallowed (R21, R25)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) goldfish >10 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} (estimated) oral redwing blackbird, starling 17.8 mg kg^{-1} (2).
LD_{50} oral rat, guinea pig 60, 150 mg kg^{-1}, respectively (1).
LD_{50} oral dog, rabbit 5-20 mg kg^{-1} (3).
LD_{50} dermal rat >100 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, insufficient evidence of carcinogenicity to animals, IARC classification group 3 (4).
National Toxicology Program conducted feeding studies in rats and mice. No evidence of carcinogenicity was found in either sex of the two species (5).
Oral rats (12 month) 1 g kg^{-1} diet developed liver tumours (3).
Oral rats (15 month) 340 or 1000 mg kg^{-1} diet developed no liver tumours (6).

Genotoxicity

Saccharomyces cerevisiae D7 mutagenicity assay weakly positive (7).
Salmonella typhimurium TA97, TA98, TA100, TA1535 with metabolic activation positive (8).

Other effects

Any other adverse effects

Compound altered feeding behaviour of house sparrows as a result of illness-induced aversion (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No.472, 1991 (11).
WHO Toxicity Class II (12).

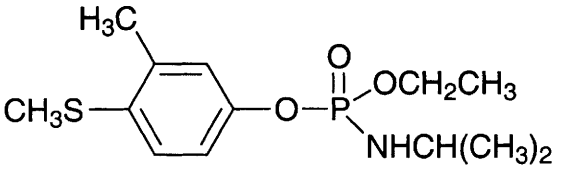
Other comments

Pollutant in soil and water.
Carcinogenicity and mutagenicity reviewed (13,14).
Reviews on experimental toxicology, human health effects and physico-chemical properties listed (15).

References

1. *The Pesticide Manual* 8th ed., 1987, British Crop Protection Council, Farnham, UK.
2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
3. Herrmann, R. C. et al *J. Pharmacol. Exp. Ther.* 1949, **95**, 272-285.
4. *IARC Monograph* 1987, **Suppl. 7**, 62.
5. *National Toxicology Program Research and Testing Division* 1992, Report No. TR101, NIEHS, Research Triangle Park, NC, USA.
6. Miller, J. A. et al *Cancer Res.* 1957, **17**, 387-398.
7. Zhang, W. et al *Zhonghua Laodong Weisheng Zhiyebing Zazhi* 1988, **6**(3), 142-146 (Ch.) (*Chem. Abstr.* **112**, 113939n).
8. Zeiger, E. *Environ. Mol. Mutagen.* 1988, **11**, 1-157.
9. Babu, T. H. *Pavo* 1988, **26**(1-2), 17-23.
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
13. *IARC Monograph* 1975, **8**, 147.
14. Ashby, J. et al *Mutat. Res.* 1991, **257**(3), 229-306.
15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F3 fenamiphos



$C_{13}H_{22}NO_3PS$ **Mol. Wt.** 303.36 **CAS Registry No.** 22224-92-6

Synonyms (1-methylethyl)phosphoramidic acid ethyl 3-methyl-4-(methylthio)phenyl ester; isopropyl phosphoramidic acid ethyl 4-(methylthio)-*m*-tolyl ester; Bay 68138; Nemacur

EINECS No. 244-848-1 **RTECS No.** TB 3675000

Uses Nematicide.

Physical properties

M. Pt. 49°C **Specific gravity** 1.15 at 20°C **Partition coefficient** log P_{ow} 3.30
Solubility Water: 700 mg l^{-1} at 20°C. Organic solvents: dichloromethane, isopropanol

Occupational exposure

FR-VME 0.1 mg m^{-3}
US-TWA 0.1 mg m^{-3}
Supply classification very toxic
Risk phrases Toxic in contact with skin – Very toxic if swallowed (R24, R28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S28, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout 9.6, 72.1 μg l^{-1}, respectively (1).

Invertebrate toxicity
Compound has no effect on soil bacteria (1).

Environmental fate

Degradation studies
In soil it is oxidised to sulfoxide and sulfone and then hydrolysed (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral duck, hen 2, 12 mg kg^{-1}, respectively (2,3).
LD_{50} dermal duck 24 mg kg^{-1} (4).
LD_{50} oral dog, rat 10, 25 mg kg^{-1}, respectively (2,5).
LD_{50} oral guinea pig 75-100 mg kg^{-1} (2).
LD_{50} dermal rat 500 mg kg^{-1} (2).

Metabolism and toxicokinetics
In mammals, rapidly metabolised to sulfoxide and sulfone, hydrolysed, conjugated and excreted in urine (1).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (6).

Other effects

Any other adverse effects

Compound is an inhibitor of cholinesterase activity and thus affects nervous function in a variety of species (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (8).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Log P_{ow} exceeds European Union limit of 3.0.

WHO Toxicity Class Ib (10).

EPA Toxicity Class I (formulation) (1).

ADI 0.0005 mg kg^{-1} (1).

Other comments

Compound inhibits cellulose decomposition in soil (11).

The hazards posed by the use of the compound reviewed (12).

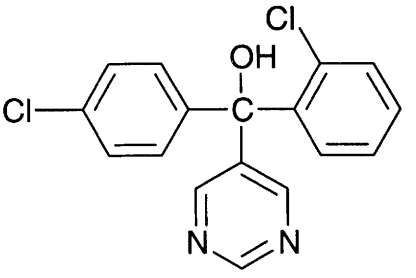
Toxicity to earthworms assessed (13).

When used by dripping in irrigation procedures, the compound can leach into the groundwater of a shallow water table (2).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. *Toxicol. Appl. Pharmacol.* 1979, **47**, 451.
4. Hill, E. F. et al *Ecotoxicol. Environ. Saf.* 1984, **8**, 551.
5. Waggoner, T. B. et al *Residue. Rev.* 1974, **53**, 79-97.
6. Zeiger E., *Environ. Mol. Mutagen* 1988, **11**, 1-157.
7. Weaver, D. J. *Gov. Rep. Announce. Index (U. S.)* 1990, **90**(22), Abstr. No. 057, 781.
8. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
9. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
10. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
11. Zamorski, R. *Zesz. Probl. Postepow Nauk Roln.* 1986, **297**, 81-89 (Pol.) (*Chem. Abstr.* **106**, 151583a).
12. *Dangerous Prop. Ind. Mater. Rep.* 1990, **10**(2), 54-61.
13. Martin, N. A. *J. Agric. Res.* 1986, **29**(4), 699-706

F4 fenarimol



$C_{17}H_{12}Cl_2N_2O$ **Mol. Wt.** 331.20 **CAS Registry No.** 60168-88-9

Synonyms α-(2-chlorophenyl)-α-(4-chlorophenyl)-5-pyrimidinemethanol; 2,4'-dichloro-α-(pyrimidin-5-yl)benzhydryl alcohol; EL-222; Rimidine; Rubigan; Bloc; Curol; Drawisan; Fenasip; Rimidin; Transflo

EINECS No. 262-095-7 **RTECS No.** UV 9279400

Uses Plant fungicide.

Physical properties

M. Pt. 117-119°C **Partition coefficient** log P_{ow} 3.69 at pH 7 and 25°C
Solubility Water: 13.7 mg l^{-1} at 25°C and pH 7. Organic solvents: acetone, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 0.91 mg l^{-1} (1).
LC_{50} (96 hr) rainbow trout 1.8 mg l^{-1} (1).

Environmental fate

Degradation studies
Microbial degradation is accelerated by light (2).

Mammalian & avian toxicity

Acute data
LD_{50} bobwhite quail >2 g kg^{-1} (1).
LD_{50} oral rat, mouse 2.5, 4.5 g kg^{-1}, respectively (3).
LD_{50} oral dog >200 mg kg^{-1} (1).
LD_{50} dermal rabbit >2 g kg^{-1} (1).

Teratogenicity and reproductive effects
Compound exhibits an inhibitory effect on the fertility of ♂ rats after administration to dams, possibly due to inhibition of aromatase activities in the central nervous system. The compound is not antioestrogenic or antiandrogenic (4).
The effect is dose-related and is manifest as producing an absence of ♂ sexual behaviour. Within the brain it is preferentially accumulated in the hypothalamus (5).
♀ sheep fed 0.01-0.05 × LD_{50} for 2 months showed no effect to ovarian cycle, but the mortality of newborn lambs was increased. No malformations were seen (6).

Metabolism and toxicokinetics

Does not cross the placenta in rats, but is excreted in breast milk (5).

Irritancy

Application of 2 g kg^{-1} to rabbit skin for unspecified duration caused no irritation (1).
68 mg instilled into rabbit eye (duration unspecified) caused mild irritation (1).
Mild eye irritant (species unspecified) (2).

Genotoxicity

In vitro Crepis capillaris, fibroblasts tests for chromosome abnormalities positive on 3rd mitosis (7).
In vitro human embryonic diploid fibroblasts non-specific cytotoxicity 400 μg ml^{-1} (8).

Other effects

Any other adverse effects

Single or multiple doses of 250 mg kg^{-1} day^{-1} to rats caused degenerative changes in liver. Signs of regeneration such as increased DNA synthesis were also noted (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
Log P_{ow} exceeds European Union limit of 3.0.
WHO Toxicity Class Table 5 (12).
EPA Toxicity Class III (formulation) (1).
ADI 0.1 mg kg^{-1} body weight (1).

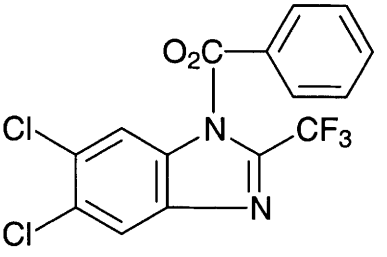
Other comments

Environmental pollutant. Food contaminant.
Non-toxic to bees (2).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Beraud, J. M. *Def. Veg.* 1980, **34**, 17.
4. Hirsch, K. S. et al *Toxicol. Appl. Pharmacol.* 1987, **91**(2), 235-245.
5. Hirsch, K. S. et al *Toxicol. Appl. Pharmacol.* 1986, **86**(3), 391-399.
6. Savov, A. et al *Biol. Immunol. Reprod.* 1987, **13**, 56-61 (Bulg.) (*Chem. Abstr.* **108**, 1849u).
7. Popov, P. *Nauchni Tr. – Plovdivski Univ.* 1986, **24**, 233-240 (Bulg.) (*Chem. Abstr.* **107**, 170371s).
8. Popov, P. *Nauchni Tr. – Plovdivski Univ.* 1985, **23**, 181-188 (Bulg.) (*Chem. Abstr.* **107**, 170239e).
9. Palut, D. et al *Rocz. Panstw. Zakl. Hig.* 1990, **41**(5-6), 253-261.
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F5 fenazaflor



$C_{15}H_7Cl_2F_3N_2O_2$ **Mol. Wt.** 375.13 **CAS Registry No.** 14255-88-0

Synonyms phenyl-5,6-dichloro-2-(trifluoromethyl)benzimidazole-1-carboxylate; phenyl-5,6-dichloro-2-(trifluoromethyl)-1*H*-benzimidazole-1-carboxylate; Lovozal; NC5016; Tarzol

EINECS No. 238-134-9 **RTECS No.** DD 6650000

Uses Superseded acaricide.

Physical properties

M. Pt. 103-104°C

Occupational exposure

Supply classification harmful

Risk phrases Harmful in contact with skin and if swallowed (R21/22)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 283 mg kg^{-1} (1).

LD_{50} oral mouse 1.6 g kg^{-1} (2).

LD_{50} oral dog, chicken 50 mg kg^{-1} (3).

LD_{50} dermal rat 700 mg kg^{-1} (4).

Legislation

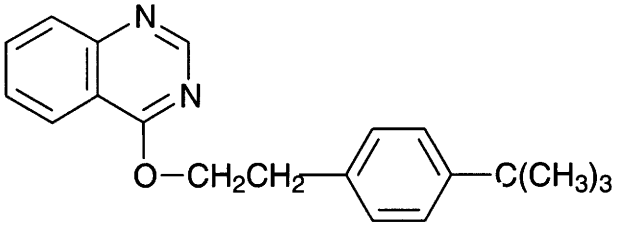
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

References

1. *Farm Chemicals Handbook* 1983, **C103**, 1983, Meister Publishing Co., Willoughby, OH, USA.
2. *Commun. State Univ. Agric. Sci. Ghent* 1968, **33**, 839.
3. *Wirksubstanzen der Pflanzenschutz- und Schaedlingsbekaempfungsmittel* 1971-1976, Werner Perkow, Berlin, Germany.
4. *World Rev. Pest Control* 1970, **9**, 119.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F6 fenazaquin



$C_{20}H_{22}N_2O$ **Mol. Wt.** 306.41 **CAS Registry No.** 120928-09-8

Synonyms 4-*tert*-butylphenethyl quinazolin-4-yl ether; 4-[[4-(1,1-dimethylethyl)phenyl]ethoxy]quinazoline; Boramae; Demitan; Magister; Magus; Pride

Uses Contact acaricide used against *Eutetranychus*, *Panonychus*, and *Tetranychus* spp. and *Brevipalpus phoenicis* on almonds, apples, citrus, cotton, grapes, and ornamentals.

Physical properties

M. Pt. 77.5-80°C **Partition coefficient** log P_{ow} 5.51 **Volatility** v.p. 2.6×10^{-8} Pa

Solubility Water: 0.22 mg l^{-1} at 20°C. Organic solvents: acetone, acetonitrile, chloroform, hexane, isopropanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) trout, bluegill sunfish 3.8, 34.1 μg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} *Daphnia magna* (48 hr) 4.1 μg l^{-1} (1).

LD_{50} (contact) 8.18 μg bee^{-1} (1).

Environmental fate

Abiotic removal

DT_{50} of aqueous solution exposed to sunlight 15 days (pH 7, 25°C) (1).

Adsorption and retention

Soil DT_{50} ≈45 days. K_{oc} 15800 (sandy loam), 42100 (clay loam). K_D 54 (sand), 487 (clay loam) (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail, mallard ducks 1747, >2000 mg kg^{-1}, respectively (1).

LD_{50} oral rats, ♂ 134, ♀ 138 mg kg^{-1} (1).

LD_{50} oral mice, ♂ 2449, ♀ 1480 mg kg^{-1} (1).

LD_{50} dermal rabbits >5000 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rats 1.9 mg l^{-1} (1).

Carcinogenicity and chronic effects

No evidence of carcinogenicity (1).

Teratogenicity and reproductive effects

No evidence of teratogenicity (1).

Irritancy

Slightly irritating to rabbit eyes, non-irritating to skin (1).

Sensitisation

Not a skin sensitiser (1).

Genotoxicity

No evidence of mutagenicity (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
Acceptable daily intake 0.005 mg kg^{-1} (1).
WHO Toxicity Class II (4).

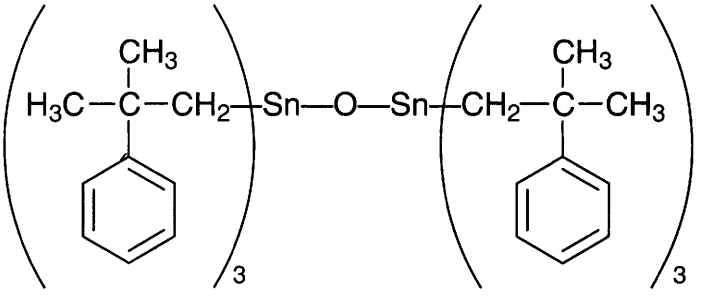
Other comments

Affects the metabolism of mites, inhibiting the mitochondrial electron transport chain by binding with Complex 1 at co-enzyme site Q (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F7 fenbutatin oxide



$C_{60}H_{78}OSn_2$ **Mol. Wt.** 1052.70 **CAS Registry No.** 13356-08-6

Synonyms distannoxane, hexakis(2-methyl-2-phenylpropyl)-; di-[tris(2-methyl-2-phenylpropyl)tin] oxide; hexabis(β,β-dimethylphenethyl)distannoxane; bis[tris(2-methyl-2-phenylpropyl)tin] oxide; Acanor; Neopec; Norvan; Osadan; Vendex; Torque

EINECS No. 236-407-7 **RTECS No.** JN 8770000

Uses Acaricide.

Physical properties

M. Pt. 138-139°C **Specific gravity** 1290-1330 kg m^{-3} at 20°C **Partition coefficient** log P_{ow} 5.2
Volatility v.p. 8.5 × 10^{-5} mPa at 20°C
Solubility Water: 5 μg l^{-1} at 23°C. Organic solvents: acetone, benzene, dichloromethane

Occupational exposure

SE-LEVL 0.1 mg m^{-3} (as Sn)
SE-STEL 0.2 mg m^{-3} (as Sn)
UK-LTEL 0.1 mg m^{-3} (as Sn)
UK-STEL 0.2 mg m^{-3} (as Sn)
US-TWA 0.1 mg m^{-3} (as Sn)
US-STEL 0.2 mg m^{-3} (as Sn)
Supply classification harmful
Risk phrases Harmful in contact with skin – Irritating to eyes and skin (R21, R36/38)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) rainbow trout 0.27 mg l^{-1} (1).

Invertebrate toxicity
Tetranychus urticae (48 hr) challenged 2, 4, 6 or 15 × gave LC_{50} 0.04-0.24 ppm (2).
Tetranychus urticae (48 hr) slide-dip method, LC_{50} 75 ppm (3).
EC_{50} (30 min) *Photobacterium phosphoreum* >6 mg l^{-1} Microtox test (4).
LD_{50} oral bee >0.1 mg bee^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, starling >100 mg kg^{-1} (5).
LD_{50} oral mouse, dog, rat 1500, >1500, 2630 mg kg^{-1}, respectively (1).
LD_{50} dermal rat, rabbit >1000, 2000 mg kg^{-1}, respectively (1,6).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail 5065 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) 100 mg kg^{-1} in diet and oral dog (2 yr) 15 mg kg^{-1} day^{-1} caused no adverse effects (1).

Irritancy
Severe irritant to the eyes and skin (7).

Genotoxicity

A medical survey of 55 Hungarian agrochemical sprayers showed no increase in chromosome aberrations in those working in closed spaces, but there was an increase in those working in open fields (8).

Other effects

Other adverse effects (human)
In vitro human lymphocyte cells of agricultural workers exposed to fenbutatin oxide decreased pseudo-cholinesterase activity by 25% of normal value (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).
WHO Toxicity Class Table 5 (11).
EPA Toxicity Class III (1).
ADI 0.03 mg kg^{-1} body weight (1).

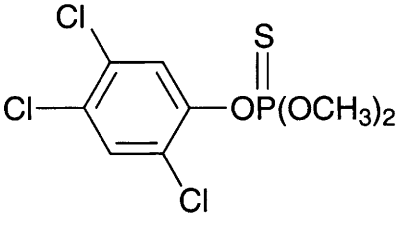
Other comments

Toxic to fish (12).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Hoy, M. A. et al *J. Econ. Entomol.* 1987, **80**(1), 221-225.
3. Knowles, C. O. et al *J. Econ. Entomol.* 1988, **81**(6), 1586-1591.
4. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
5. Shafer, E. W. *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-383.
6. *Tin Its Uses* 1976, (110), 6.
7. Arena, J. M. *Poisoning* 4th ed., 1979, Charles C. Thomas, Springfields, IL, USA.
8. Nehez, M. et al *Regul. Toxicol. Pharmacol.* 1988, **8**(1), 37-44.
9. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.2.
12. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

F8 fenchlorfos



$C_8H_8Cl_3O_3PS$ **Mol. Wt.** 321.55 **CAS Registry No.** 299-84-3

Synonyms *O,O*-dimethyl *O*-2,4,5-trichlorophenyl phosphorothioate; Blitex; Dermafos; Ectoral; Etrolene; Korlan; Navchor; Trichlormetaphos; Trolene; Ronnel

EINECS No. 206-082-6 **RTECS No.** TG 0525000

Uses Superseded pesticide.

Physical properties

M. Pt. 41°C **Specific gravity** 1.485 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 4.88 (1)
Volatility v.p. 8×10^{-4} mmHg at 25°C
Solubility Water: 1.08 mg l^{-1} at 20°C. Organic solvents: acetone, carbon tetrachloride, diethyl ether, kerosene, methylene chloride, toluene

Occupational exposure

FR-VME 10 mg m^{-3}
UK-LTEL 10 mg m^{-3}
US-TWA 10 mg m^{-3}
Supply classification harmful
Risk phrases Harmful in contact with skin and if swallowed (R21/22)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the eyes – Wear suitable protective clothing and gloves (S2, S25, S36/37)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 305 μg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 75-375 mg kg^{-1} (3).
LD_{50} oral rat, mouse 625, 2630 mg kg^{-1}, respectively (4-6).
LD_{50} dermal rabbit, rat 1000, 2000 mg kg^{-1}, respectively (7,8).
LD_{50} intraperitoneal mouse, rat 118, 2823 mg kg^{-1}, respectively (9).

Sub-acute and sub-chronic data

Oral rat (105 day) 15 mg kg^{-1} day^{-1} did not cause any fatalities (10).

Teratogenicity and reproductive effects

Oral rat (6-15 days gestation) 0, 100, 600, 800 mg kg^{-1} in single daily doses increased incidence of extra-rib recorded (11).
Oral rabbits (6-18 days of gestation) 0, 12.5, 25, 50 mg kg^{-1} caused no effect on implantation efficacy, number of live foetuses or foetal weight. The incidence of major malformations, cardiovascular and brain anomalies was increased in all treated groups (12).
Oral blue fox during different (unspecified) periods of gestation (concentrations unspecified) caused head malformations, including incomplete ossification of the skull bones, cleft palate, hydrocephalus internus and externus. Skeletal variants increased substantially. The study suggests fenchlorfos has both embryotoxic and teratogenic potential (13).

Metabolism and toxicokinetics

Found in milk of cattle following oral administration (14).
In rats undergoes hydrolysis and is excreted in the urine as phenylphosphoric acid and phosphorothioic acid (15).

Other effects

Any other adverse effects

Inhibits cholinesterase activity (16).

Legislation

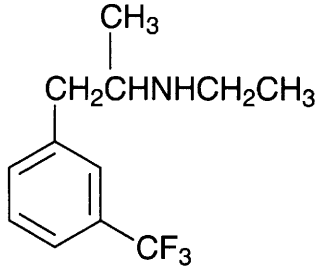
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (17).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (19).
WHO Toxicity Class II (20).

References

1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed. 1983, 1045-1046, Van Nostrand Reinhold, New York, NY, USA.
2. Solon, J. M. et al *Bull. Environ. Contam. Toxicol.* 1970, **5**(5), 408-413.
3. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
4. Gaines, T. B. et al *Toxicol. Appl. Pharmacol.* 1969, **14**, 515.
5. *Gig. Sanit.* 1980, **45**(6), 14.
6. *Pesticide Chemicals Official Compendium* 1966, 965, Assoc. Am. Pesticide Control Officials, Inc., Topeka, KS, USA.
7. *Farm Chemicals Handbook* 1989, C252, Meister Publishing Co., Willoughby, OH, USA.
8. *World Rev. Pest. Control* 1970, **9**, 119.

9. *Proc. Soc. Exp. Biol. Med.* 1968, **129**, 699.
10. *The Agrochemicals Handbook* 1st ed., 1983, The Royal Society of Chemistry, London, UK.
11. Khera, K. S. et al *J. Toxicol. Environ. Health* 1982, **10**(1), 111-119.
12. Nafstad, I. et al *Acta Vet. Scand.* 1983, **24**(3), 295-304.
13. Berse, G. N. et al *Acta Vet. Scand.* 1983, **24**(1), 99-112.
14. Clarke, M. L. et al *Veterinary Toxicology* 2nd ed., 1981, Bailliere Tindall, London, UK.
15. Menzie, C. M. *Metabolism of Pesticides* 1969, 329, U.S. Department of the Interior, Bureau of Sport, Fisheries and Wildlife, Publication No. 127, Washington, DC, USA.
16. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
17. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
18. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
19. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
20. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F9 fenfluramine



$C_{12}H_{16}F_3N$ **Mol. Wt.** 231.26 **CAS Registry No.** 458-24-2

Synonyms *N*-ethyl-α-methyl-3-(trifluoromethyl) phenylethylamine

EINECS No. 207-276-3 **RTECS No.** SH 6820000

Uses Orally active anorexic, particularly for short-term use. Usually administered as hydrochloride salt.

Physical properties

M. Pt. 168-172°C **B. Pt.** 98-100°C at 10 mmHg

Solubility Water: 50 g l^{-1}. Organic solvents: ethanol, chloroform

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 170-238 mg kg^{-1} (1,2).

LD_{50} oral dog, cat, rabbit 50-100 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 53 mg kg^{-1} (2).

Minimum toxic dose reported for oral administration to humans 4.3 mg kg^{-1}. Symptoms were those of stimulation of the autonomic nervous system, and central nervous system effects including hallucinations and distorted perception (3).

Sub-acute and sub-chronic data

Intraperitoneal rats administered 11.5 mg kg^{-1} on day-8 after birth followed by regular 30-min exposures (10-30 day postnatally), caused behavioural effects relating to mobility, exploration and grooming, suggestive of involvement of central nervous system serotonin activity (4).

Metabolism and toxicokinetics

The compound in its hydrochloride form is readily absorbed from the gastro-intestinal tract of humans. It is extensively metabolised to its active metabolite norfenfluramine by de-ethylation. Penetrates most tissue and crosses the blood-brain barrier. Excretion is via urine, both as unchanged compound and metabolites (5).

Other effects

Other adverse effects (human)

Common adverse effects include those related to altered central nervous system activity, such as drowsiness, dizziness, headache, irritability, elevated mood, lethargy, dreams, depression, dependence and psychotic reactions, along with those of a peripheral nature, such as gastro-intestinal disturbance, cardiovascular effects, impotence, urinary frequency and skin rashes (5).

Pulmonary hypertension has been the cause of several fatalities (6).

The risk of drug abuse is regarded as small, but abuse with high doses has occurred (5,7).

Any other adverse effects

Subcutaneous rats 10 mg kg^{-1} single dose caused a decrease in the number of serotonin terminals in the brain, suggestive of some neurotoxicity (8).

Other comments

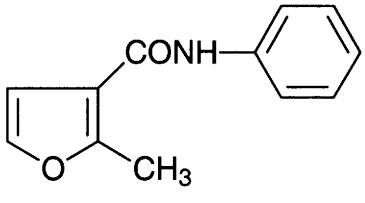
The compound is a mimetic of catecholamines and serotonin. The anorexic action is thought to be associated with actions on central and peripheral serotonin receptors (9-11).

Biochemical pharmacology reviewed (9).

References

1. Le Dovarec, J. C. et al *Arch. Int. Pharmacodyn. Ther.* 1966, **161**, 206.
2. Costa, E. (Ed.) *Amphetamines and Related Compounds* 1970, Proc. Mario Negri Institute, Raven Press, Milan, Italy.
3. *Therapie* 1979, **34**, 205.
4. Goeb, R. et al *Biomed. Biochem. Acta* 1987, **46**(4), 189-198.
5. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
6. Committee on Safety of Medicines *Current Problems* 1992, **34**.
7. Rosenvinge, H. P. *Br. Med. J.* 1975, **1**, 735.
8. Wagner, J. *Neuropsychopharmacology* 1990, **3**(3), 219-220.
9. Garrattini, S. et al *Curr. Med. Res. Opin.* 1979, **6** (Suppl.1), 15-27.
10. Horowitz, M. et al *Br. J. Clin. Pharmacol.* 1985, **19**, 849-851.
11. Turner, P. *Curr. Med. Res. Opin.* 1979, **6** (Suppl.1), 101-106

F10 fenfuram



$C_{12}H_{11}NO_2$ **Mol. Wt.** 201.22 **CAS Registry No.** 24691-80-3

Synonyms 2-methyl-*N*-phenyl-3-furancarboxamide; 2-methyl-3-furanilide; fenfurame; Panoram; WL2236

EINECS No. 246-421-5 **RTECS No.** LT 8506000

Uses Fungicide.

Physical properties

M. Pt. 109-110°C (tech. grade) **Volatility** v.p. 1.5×10^{-7} mmHg at 20°C
Solubility Water: 100 mg l^{-1} at 20°C. Organic solvents: acetone, cyclohexanone, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) guppy 11 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral cat, rat 2450, 12,900 mg kg^{-1}, respectively (2).
LC_{50} (4 hr) inhalation rat >10.3 mg l^{-1} (1).
LD_{50} intraperitoneal rat 1.5 g kg^{-1} (1)

Sub-acute and sub-chronic data
Oral dog (90 day) 300 mg kg^{-1} in diet, no adverse effects reported (2).

Carcinogenicity and chronic effects
Oral rat (2 yr) feeding study 10 mg kg^{-1} day^{-1}, no adverse effects reported (2).

Other effects

Any other adverse effects
House sparrows receiving the compound showed abnormalities of feeding behaviour due to illness-induced aversion (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum permissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
WHO Toxicity Class Table 5 (6).
EPA Toxicity Class IV (formulation) (2).

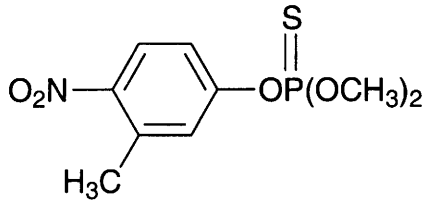
Other comments

Non-toxic to bees (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Babu, T. H. *Pavo* 1988, **26**(1-2), 17-23.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F11 fenitrothion



$C_9H_{12}NO_5PS$ **Mol. Wt.** 277.24 **CAS Registry No.** 122-14-5

Synonyms *O,O*-dimethyl *O*-(3-methyl-4-nitrophenyl) phosphorothioate; BAY 41831; MEP; phosphorothioic acid, *O,O*-dimethyl *O*-(3-methyl-4-nitrophenyl) ester; Accothion; Chemition; Demise; Etalene; Fenion; Galation

EINECS No. 204-524-2 **RTECS No.** TG 0350000

Uses Non-systemic organophosphorus insecticide with contact and stomach action.

Physical properties

M. Pt. 3.4°C **B. Pt.** 140-145°C (decomp.) at 0.1 mmHg **Flash point** 157°C **Specific gravity** 1.3227 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.4314 at 20°C (1) **Volatility** v.p. 6×10^{-6} mmHg at 20°C

Solubility Water: 30 mg l^{-1} at 21°C. Organic solvents: acetone, diethyl ether, dichloromethane, ethanol, hexane, isopropanol, methanol, toluene, xylene

Occupational exposure

JP-OEL 1 mg m^{-3}

Supply classification harmful, dangerous for the environment

Risk phrases Harmful if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 4.1 mg l^{-1} (1).

LC_{50} (96 hr) brook trout, bluegill sunfish 1.7, 3.8 mg l^{-1}, respectively (1).

LC_{50} (48 hr) killifish 0.59 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (48 hr) red snail, marsh snail 6, 15 mg l^{-1}, respectively (3).

LC_{50} (3 hr) *Daphnia pulex* 0.05 mg l^{-1} (3).

LC_{50} (48 hr) *Daphnia magna* 0.0086 mg l^{-1} (4).

LC_{50} (96 hr) brown shrimp, blue crab 0.0015-0.0086 mg l^{-1} at 22-29°C (5,6).

LD_{50} contact bee 0.12 μg bee^{-1} (7).

Bioaccumulation

Bioconcentration factor carp 36-157 plateaus after 12-48 hr exposure, with highest concentration in liver and kidneys (8).

Rainbow trout and southern top-mouthed minnow exposed to 0.1 or 0.02 mg l^{-1}, bioaccumulation ratio 200-250, independent of fenitrothion concentration in water. Depuration occurred rapidly in fresh water (9).

Lake trout were exposed to two applications of 280 g ha^{-1} with a 9-day interval, accumulation peaked within 2-4 days. Residues were detected in fat, muscle, intestine, liver and ovary. Residues persisted in tissues for 8 days (10).
Bioaccumulation factors in marine clam, mussel and freshwater clam were 19-35, 78-130 and 9, respectively (11).
Bioconcentrated by cyanobacteria, but not metabolised after uptake (12).
Bioaccumulation factor for killifish (whole body) 122 (2).
Excretion rate constant for killifish (whole body) 0.11 hr^{-1} (2).
European eels (*Anguilla anguilla*) were exposed in a flow-through test system to 0.04 mg fenitrothion l^{-1} for 96 hr and then transferred to clean water for 72 hr. The pesticide bioconcentrated selectively in the tissues. The highest accumulation was in the brain and a steady-state was observed in the blood within a few hr of the start of exposure. Elimination started rapidly in blood and brain during the recovery period. Calculated elimination kinetics adjusted to a one-compartment model were K_2 of 0.015 hr^{-1} for blood and 0.044 hr^{-1} for brain (13).

Environmental fate

Degradation studies

10 mg kg^{-1} on a dry weight basis incubated in soils with various physical and chemical properties, upland or submerged conditions, in the dark at 25°C. Adsorption and decomposition were variable, depending on the properties of the soils and incubation conditions. Under upland conditions, $t_{1/2}$ 12-28 days and submerged $t_{1/2}$ 4-20 days. No direct relationship was observed between the decomposition in soil and clay content, organic matter content, ion exchange capacity and pH. 3-Methyl-4-nitrophenol and carbon dioxide were identified as decomposition products (14).
Under submerged conditions, the major decomposition product was aminofenitrothion; maximum amounts detected were 18-66% of initial fenitrothion concentration (14).
Several species of soil and water bacteria, *Bacillus subtilis*, *Escherichia coli*, *Escherichia freundii*, *Pseudomonas rephilovora*, and *Pseudomonas aeruginosa* can metabolise fenitrothion (15).
Applied as sole source of carbon, stability is greater under aerobic conditions, 77% of the initial dose being recovered after 164 hr incubation (16).
In a study on the removal of pollutants in rivers by aquatic plants, fenitrothion was reported not to be removed (17).
Readily degraded under anaerobic cometabolic conditions, $t_{1/2}$ 1 day (16).

Abiotic removal

Undergoes hydrolysis in the absence of light through a pH-independent process below pH 7 and a base-catalysed process above pH 10, while both processes occur between pH 7 and pH 10. In natural water, $t_{1/2}$ 200-630 days at 15°C, 17-61 days at 30°C and 4-8 days at 45°C (18).
Photodegradation is very slow in seawater, where hydrolysis predominates (19).
5-14% lost by evaporation from model surface (glass beads) under laboratory conditions (20).
Fenitrothion degradation in fresh water at pH 8.0-pH 8.2 was 2.5, 78, 90 and 93% in 2 hr, 7 days, 14 days and 21 days, respectively (21).
Products of hydrolysis are phosphorothioic acid, phosphoric acid and 3-methyl-4-nitrophenol (1).

Adsorption and retention

In a laboratory leaching study, no movement occurred with water in three loam soils. In sand containing 0.2% clay and <0.1% organic matter, 15% of applied fenitrothion was eluted from the soil column. Preincubation for 60 days in sandy soil decreased the degree of mobility (22).
Persistence in seawater was affected by water quality, sunlight, temperature, but not suspended solid or vaporisation. After 72 hr, persistence in seawater was 56-97% of original concentration (23).

Mammalian & avian toxicity

Acute data

LD_{50} oral starling, redwing blackbird, quail 11-56 mg kg^{-1} (24).
LD_{50} oral rat, mouse, guinea pig 250, 715, 870 mg kg^{-1}, respectively (1,25).

LC_{50} (4 hr) inhalation rat 378 mg m^{-3} (26).
LD_{50} dermal rat, mouse 750, 2500 mg kg^{-1}, respectively (27,28).
LD_{50} subcutaneous mouse 1000 mg kg^{-1} (27).
LD_{50} intravenous rat 33 mg kg^{-1} (27).
LD_{50} intraperitoneal rat, mouse 300, 410 mg kg^{-1} (values for fenitrothion following degradation under sunlight 60, 120 mg kg^{-1}), respectively (29,30).

Sub-acute and sub-chronic data
LC_{50} (5 day) oral bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck 157-2500 mg kg^{-1} diet (31).
Sprague-Dawley rats (1 hr) 15% aerosol, after 3 days mild inflammation was detected including interstitial oedema, cellular infiltration and increased numbers of alveolar macrophages. After 7 days, irritation was minimal and tissues were normal at 21 and 60 days (32).
Oral rat (40 day) 10, 20 or 40 mg kg^{-1}, high doses caused >50% mortality. Symptoms of toxicity induced transient loss of reflexes, changes in motor activity and ataxia indices (33).
Oral chick (7 day) 3 mg kg^{-1} day^{-1}, no neurotoxicity observed (34).
Mice exposed subchronically (dose and duration unspecified) exhibited suppressed humoral immune function and moderate histological changes of lymph organs (35).

Carcinogenicity and chronic effects
Oral rat (21 month) no-adverse-effect level 5 mg kg^{-1} diet (1).
ICR Swiss mice (78 wk) 0, 30, 100 or 200 mg kg^{-1} in diet caused no observable effects to weight gain, food intake, mortality, or ophthalmological and gross/histopathological findings (36).

Teratogenicity and reproductive effects
Oral ♂, ♀ rats 200 mg kg^{-1} in diet before mating and during gestation period in a one-generation study. No effect to fertility, gestation and live births (37).
Prenatal exposure of rats induced long-lasting effects on behavioural parameters related to learning. A no-effect level of 5 mg kg^{-1} was established (38).

Metabolism and toxicokinetics
Following ingestion in a suicide attempt, $t_{1/2}$ in blood was ≈4.5 hr. Urinary metabolites identified were 3-methyl-4-nitrophenol, aminofenitrothion, aminofenitrooxon, acetylamino-fenitrooxon and *S*-methylfenitrothion (39).
Following dermal application to monkeys 49% ($t_{1/2}$ 14 hr) was absorbed from the forehead whereas 21% ($t_{1/2}$ 17 hr) was absorbed from the forearm. For rats, 84% ($t_{1/2}$ 20 hr) was absorbed from the mid-dorsal region (40).
In animals and *in vitro* systems metabolised to fenitrooxon, which is more acutely toxic (37).
Oral rats, mice, rabbits, dogs readily absorbed from the gastro-intestinal tract and distributed to various tissues, maximum concentrations 0.093-0.144 mg kg^{-1} after 1-3 hr. Rapidly and completely eliminated in urine 89-95% (rats), >90% (mice), 86-94% (rabbits) and 88% (dogs). Metabolites were demethylated products, free 3-methyl-4-nitrophenol or sulfuric/glucuronic acid conjugates (41).
Extrahepatic activation of the compound accounts for toxicity in mice, but in rats hepatic activation also contributes to toxicity (42).
Sex differences occur in ability of rat liver to metabolise fenitrothion, viz. ♀ produced lower amounts of fenitrooxon than ♂, but this does not account for differing toxicity (higher in ♀) between the sexes. Metabolism does not occur to any significant degree by glutathione-mediated biotransformation (43).

Irritancy
0.1 ml instilled into rabbit eye caused slight hyperaemia of the conjunctiva 1 hr after application. Eyes were normal after 48 hr. Dermal rabbit, 0.5 ml no irritation observed (37).

Sensitisation
Contact dermatitis in humans has been attributed to exposure to fenitrothion (37).
Landsteiner-Draize test, guinea pigs 10 and 5% solution in corn oil, applied intradermally every other day for 20 days. Allergic reactions were not observed (37).
Hartley guinea pigs maximisation test, 5% intradermal and 25% topical. Challenge concentrations of 0.05% showed potential for allergy (44).

Genotoxicity

Salmonella typhimurium TA98, TA1535 with metabolic activation positive, without metabolic activation negative (45).
Drosophila melanogaster sex-linked recessive lethal assay negative (46).
In vitro human lymphocytes, sister chromatid exchanges positive (47).
In vivo rat bone marrow cells, chromosomal aberrations negative (48).
Did not increase the frequency of somatic mutations in a heterozygous chlorophyll mutant of *Nicotiana tabacum* var. *xanthi* (49).

Other effects

Other adverse effects (human)

Signs and symptoms of poisoning are those of parasympathetic stimulation. In a few cases, the toxic manifestations were delayed in onset and recurred for up to a few months, perhaps because of slow release from adipose tissue. No evidence of delayed neurotoxicity or of an association with Reye's syndrome (37).

Any other adverse effects

Sub-chronic exposure of rats (unspecified duration) resulted in a marked suppression of the humoral immune function and moderate histological changes of lymphoid organs without any significant clinical effects (50).
Intratracheal rat, single injection of 30 mg kg^{-1} increased lactate dehydrogenase activity in the bronchoalveolar lavage fluid, indicating significant pulmonary injury (51).
Oral calf, single doses of 100-260 mg kg^{-1} induced a dose-dependent reduction in cholinesterase activity, 2 hr no-effect level was 85 mg kg^{-1} (52).
In experimental animals, major toxic signs are salivation, tremor, exophthalmos, urinary incontinence, piloerection and dyspnoea (53).

Legislation

WHO Toxicity Class II (54).
EPA Toxicity Class II (formulation) (55).
Tolerable daily intake (TDI) human 0.005 mg kg^{-1} day^{-1} (55).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (56).
Pesticides are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (57).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (58).
EEC maximum residue level, citrus fruit 2 ppm; other fruit and vegetables 0.5 ppm (1).

Other comments

Acetylcholinesterase inhibitor (53).
Residues have been isolated from water and crops (21,59).
Acute poisoning in humans reviewed (60).
Degradation in soil reviewed (61).
Side-effects on beneficial organisms based on field and semi-field tests reviewed (62).
Comprehensive review on the ocular effects to humans of exposure to organophosphates (63).

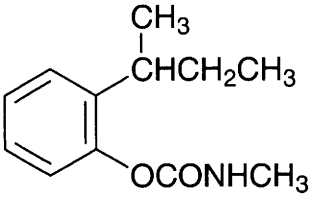
References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Tsuda, T. et al *Chemosphere* 1997, **35**(5), 939-949.
3. Hashimoto, Y. et al *J. Pestic. Sci.* 1981, **6**, 257-264.
4. Forbis, A. D. *Acute Toxicity of Fenitrothion to Daphnia magna* 1987, Technical Report No. HW-70-0234, Sumitomo Chemical, Japan.
5. Johnson, J. J. et al *Comp. Biochem. Physiol.* 1985, **80**, 181-188.
6. Mayer, F. L. *Acute Toxicity Handbook of Chemicals to Estuarine Organisms* 1987, US EPA600/8-87/017, Gulf Breeze, FL, USA.

7. Niijima, K. et al *Tamagawa Daigaku Nogakubu Kenkyu Hokoku* 1985, (25), 83-90 (Japan.) (*Chem. Abstr.* **106**, 14397d).
8. Tsuda, T. et al *Comp. Biochem. Physiol., C: Comp. Pharmacol. Toxicol.* 1990, **96C**(1). 23-26.
9. Takimoto, Y. et al *J. Pestic. Sci.* 1976, **1**, 261-271.
10. Holmes, S. B. et al *Bull. Environ. Contam. Toxicol.* 1984, **33**, 468-475.
11. McLeese, D. W. et al *Bull. Environ. Contam. Toxicol.* 1979, **22**, 800-806.
12. Lal, S. et al *Environ. Pollut.* 1987, **46**(3), 187-196.
13. Sancho, E. et al *J. Environ. Sci. Health, Part B* 1997, **B32**(6), 901-914.
14. Miyamoto, J. et al *J. Pestic. Sci.* 1978, **3**, 35-41.
15. *Fenitrothion: The Effects of its Use of Environmental Quality and its Chemistry* 1975, National Research Council of Canada No. 14104, Ottawa, Canada.
16. Liu, D. et al *Environ. Sci. Technol.* 1981, **15**, 788-793.
17. Kameoka, H. et al *Kinki Daigaku Kenkyo Kagaku Kenkyusho Kankyu Hokoku* 1985, **13**, 31-36 (Japan.) (*Chem. Abstr.* **107**, 27825n).
18. Mikami, N. et al *J. Pestic. Sci.* 1985, **10**, 263-272.
19. Durand, G. et al *Toxicol. Environ. Chem.* 1991, **31-32**, 55-62.
20. Neuruner, H. et al *Bodenkultur* 1991, **42**(1), 57-70 (Ger.) (*Chem. Abstr.* **115**, 34704r).
21. Dayananda, S. et al *Pollut. Res.* 1986, **5**(1), 19-21.
22. Takimoto, Y. et al *J. Pestic. Sci.* 1976, **1**, 131-143.
23. Kodama, T. et al *J. Pestic. Sci.* 1980, **5**, 351-355.
24. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
25. Schrader, G. *Angew. Chem.* 1961, **73**, 331.
26. *Egeszsegtudomany* 1980, **24**, 173.
27. *Agric. Biol. Chem.* 1961, **25**, 605.
28. Krishna, C. R. *Scientific Report* 1977, 101.
29. Hiraoka, Y. et al *Hiroshima J. Med. Sci.* 1989, **38**(4), 209-212 (*Chem. Abstr.* **113**, 167145q).
30. *Toxicol. Appl. Pharmacol.* 1982, **63**, 91.
31. Hill, E. F. et al *Lethal Dietary Toxicities of Environmental Pollutants to Birds* 1975, US Fish and Wildlife Service, Report Wildlife No. 191, Washington, DC, USA.
32. Chevalier, G. et al *Toxicol. Appl. Pharmacol.* 1984, **76**, 349-355.
33. Rondeau, D. B. et al *Neurobehav. Toxicol. Terabiol.* 1981, **3**, 313-319.
34. Farage-Elawar, M. et al *J. Toxicol. Environ. Health* 1988, **23**(2), 217-228.
35. Moon, C. K. et al *Arch. Pharmacol. Res.* 1986, **9**(3), 175-181.
36. *IPCS Environmental Health Criteria 133: Fenitrothion* 1992, WHO, Geneva, Switzerland.
37. Gowda, H. et al *Indian J. Pharmacol.* 1979, **11**(4), 287.
38. Lehotzky, K. et al *Neurotoxicol. Teratol.* 1989, **1**, 321-342.
39. Kojima, T. et al *Forensic Sci. Int.* 1989, **41**(3), 245-253.
40. Moody, R. P. et al *J. Toxicol. Environ. Health* 1987, **20**(1-2), 209-218.
41. Miyamoto, J. et al *J. Pestic. Sci.* 1976, **1**, 9-21.
42. Becker, J. *Pestic. Biochem. Physiol.* 1990, **38**(1), 34-40.
43. Sultatos, L. G. et al *Toxicology* 1991, **68**(1), 1-9.
44. Matsushita, T. et al *Ind. Health* 1985, **23**, 145-153.
45. Wong, P. K. et al *Chemosphere* 1989, **18**(11-12), 2413-2422.
46. Velazquez, A. et al *Mutagenesis* 1987, **2**(5), 333-336.
47. Yu, Y. et al *Zhonghua Yufang Yixue Zazhi* 1986, **20**(6), 354-356 (Ch.) (*Chem. Abstr.* **106**, 170813s).
48. Malki, P. K. et al *Mutat. Res.* 1987, **188**(1), 45-51.
49. Briza, J. *Biol. Plant.* 1989, **31**(2), 145-151.
50. Moon, C. K. et al *Arch. Pharmacol. Res.* 1986, **9**(3), 175-181.
51. Khan, M. F. et al *Bull. Environ. Contam. Toxicol.* 1990, **45**(4), 598-603.
52. Korolev, B. et al *Dokl. Vses. Akad. S-kh. Nauk im. V. I. Lenina* 1986, (7), 33-35 (Russ.) (*Chem. Abstr.* **106**, 28653w).
53. Namba, T. *Bull. W.H.O.* 1971, **44**, 289-307.
54. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
55. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
56. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
57. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
58. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
59. Gurderson, E. L. *J. Assoc. Off. Anal. Chem.* 1988, **71**(6), 1200-1209.

60. Hayes, W. J. *Fenitrothion: Handbook of Pesticide Toxicology* 1991, 1020-1023, Academic Press, London, UK.
61. Hassan, S. A. et al *J. Appl. Entomol.* 1987, **103**(1), 92-107.
62. Schoen, S. R. *J. Environ. Sci. Health, Part B* 1987, **B22**(3), 347-377.
63. Dementi, B. *J. Appl. Toxicol.* 1994, **14**(2), 119-129

F12 fenobucarb



$C_{12}H_{17}NO_2$ **Mol. Wt.** 207.27 **CAS Registry No.** 3766-81-2

Synonyms 2-*sec*-butylphenyl methylcarbamate; 2-(1-methylpropyl) phenylmethylcarbamate; Bassa; Baycarb; BPMC; Carvil; Osbac

EINECS No. 223-188-8 **RTECS No.** FB 5425000

Uses Insecticide.

Physical properties

M. Pt. 31-32°C **Flash point** 142°C (closed) **Specific gravity** 1.035 at 30°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.79 **Volatility** v.p. 3.6×10^{-4} mmHg at 20°C
Solubility Water: 610 mg l^{-1} at 30°C. Organic solvents: acetone, benzene, toluene

Occupational exposure

JP-OEL 5 mg m^{-3}
Supply classification harmful, dangerous for the environment
Risk phrases Harmful if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 12.6 mg l^{-1} (1).
Carp 50-100 mg kg^{-1} reduced levels of cytochrome P_{450} and raised levels of UDP glucuronyl transferase activity (2).

Invertebrate toxicity
LC_{50} (48 hr) shrimp 1.15 μg l^{-1} (3).
LC_{50} (48 hr) *Moina macrocopa* 37.8 μg l^{-1} (3).

Environmental fate

Degradation studies
Degradation occurs more rapidly in flooded than non-flooded soils, and in alkaline rather than acid soils (4).

When sprayed onto paddy fields it disappeared from water in 10 days, but from soil more quickly. The compound was reduced to <5% original level on plants within 13 days (5).
In soil, $t_{1/2}$ 14-23 days; $t_{1/2}$ in water 7-9 days (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral duck 323 mg kg^{-1} (7).
LD_{50} oral ♂, ♀ rat 623-657 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >0.366 mg tech. l^{-1} air (1).
LD_{50} dermal rat 75 g kg^{-1} (1).
LD_{50} intraperitoneal mouse 140 mg kg^{-1} (8).
LD_{50} intravenous mouse 42 mg kg^{-1} (8).

Sub-acute and sub-chronic data
LC_{50} (5 day) oral duck, quail >5.5 g kg^{-1} diet (7).
Subcutaneous mice 50 mg kg^{-1} single dose or for 10 days caused reversible central nervous system effects on behaviour (9).

Carcinogenicity and chronic effects
2-yr feeding study with rats established a no-effect level of 100 mg kg^{-1} diet (7).

Other effects

Any other adverse effects
Metabolic activation in the liver leading to toxicity of the compound can be potentiated by insecticides such as fenthion (10).
Dogs receiving 100 mg kg^{-1} orally show no symptoms of cholinergic overactivity unless predosed with a compound such as fenthion (11).

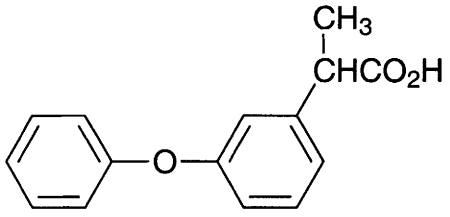
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (12).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).
WHO Toxicity Class II (14).
EPA Toxicity Class II (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Ariyoshi, T. et al *Bull. Environ. Contam. Toxicol.* 1990, **44**(2), 189-196.
3. Hatakeyama, S. *Environ. Pollut.* 1989, **59**(4), 325-336.
4. Varca, L. M. *Philipp. Entomol.* 1987, **7**(2), 177-189.
5. Tsukabayashi, H. *Ishikawa-ken Eisei Kogai Kekyusho Nenpo* 1988, **25**, 301-307 (*Chem. Abstr.* **111**, 35113b).
6. Garg, P. K. et al *Indian J. Plant Prot.* 1986, **14**(1), 29-32.
7. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
8. *Fund. Appl. Toxicol.* 1984, **4**, 724.
9. Kobayashi, H. et al *Jpn. J. Vet. Sci.* 1989, **51**(4), 789-795.
10. Miyaoka, T. et al *J. Pharmacobiodyn.* 1986, **9**(9), 697-703.
11. Miyaoka, T. et al *Jpn. J. Vet. Sci.* 1987, **49**(1), 173-175.
12. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
13. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
14. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F13 fenoprofen



$C_{15}H_{14}O_3$ **Mol. Wt.** 242.27 **CAS Registry No.** 31879-05-7

Synonyms α-methyl-3-phenoxybenzeneacetic acid; (±)-*m*-phenoxyhydratropic acid; Lilly 53838; Nalfon (calcium salt)

EINECS No. 250-850-3 **RTECS No.** MU 6646000

Uses Used in treatment of rheumatic diseases, mild to moderate pain and fever. The compound usually administered as the calcium salt.

Physical properties

B. Pt. 168-171°C at 0.11 mmHg

Mammalian & avian toxicity

Metabolism and toxicokinetics

When administered to humans as the calcium salt, the compound is readily absorbed from the gastro-intestinal tract with peak concentrations reached 1-2 hr after dosing, $t_{1/2}$ 2.5 hr; >99% is bound to plasma proteins, 95% excreted over 24 hr, principally as the glucuronide of hydroxylated fenoprofen, and 2% is eliminated in faeces (1). In mammals, including humans, after dosing with racemate, chiral conversion is unidirectional with the *R*-isomer converting to the active antipode. In humans, conversion is probably presystemic but may be hepatic in rat (2). Partial conversion from *R*- to *S*-isomers also occurs in rabbit, where glucuronidation of the *S* form is potentiated by phenobarbitone pretreatment but glucuronidation of the *R* form is not (3).
Similar phenomena are seen in humans (4).

Other effects

Other adverse effects (human)

Compound can cause irritation of gastro-intestinal tract, but the compound is less irritating than aspirin (5). There have been numerous reports of thrombocytopenia (6,7).

Other comments

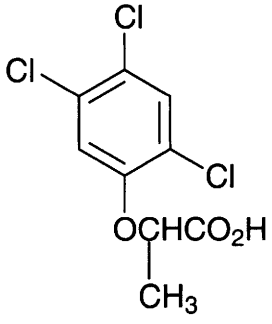
Compound is a non-steroidal anti-inflammatory drug. It is excreted in breast milk of nursing mothers taking the drug, but quantities are considered too small to be harmful (8).
Compound occurs as a racemate of *R* and *S* forms, and is normally used clinically as a racemic mixture (2).
Toxicology reviewed (9).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
2. Berry, B. N. et al *J. Pharmacol. Exp. Ther.* 1991, **258**(2), 695.
3. Hayball, P. J. *J. Pharmacol. Exp. Ther.* 1987, **240**(2), 631-636.
4. Volland, C. et al *Pharmacology* 1991, **43**(2), 53-60.
5. Ridolfo, A. S. et al *Clin. Pharm. Ther.* 1973, **14**, 226.
6. Simpson, R. E. et al *New Engl. J. Med.* 1978, **298**, 629.

7. Katz, M. G. et al *Ann. Intern. Med.* 1980, **92**, 262.
8. *British National Formulary* 1992, British Medical Association, London, UK.
9. Emmerson, J. L. et al *Toxicol. Appl. Pharmacol.* 1973, **25**, 444

F14 fenoprop



$C_9H_7Cl_3O_3$ **Mol. Wt.** 269.51 **CAS Registry No.** 93-72-1

Synonyms α-(2,4,5-trichlorophenoxy)propionic acid; Kuran; Propen; Silvex; Fenormone

EINECS No. 202-271-2 **RTECS No.** UF 8225000

Uses A superseded hormonal-type herbicide which mimics the action of indoleacetic acid. Herbicide for woody plants.

Physical properties

M. Pt. 181.6°C

Solubility Water: 140 mg l^{-1}. Organic solvents: acetone, diethyl ether, methanol

Occupational exposure

Supply classification harmful, dangerous for the environment

Risk phrases Harmful if swallowed – Irritating to the skin – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R38, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable gloves – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S37, S60, S61)

Environmental fate

Degradation studies

Mechanisms of interactions with humic substances from different sources have been reviewed (1).

Degradation by anaerobic sludge has been reported (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 650 mg kg^{-1} (3).

LD_{50} dermal rabbit >3.2 g kg^{-1} (4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification 2B (5).

Metabolism and toxicokinetics

When an oral dose of 1 mg kg^{-1} was given to human volunteers, peak plasma levels were reached in 2-4 hr. Within 144 hr, ≥95% of dose had been eliminated in urine, either unchanged or (≥70%) as acid or base labile conjugates. ≤3% of dose was detected in faeces (6).

Other effects

Any other adverse effects

Compound is a peroxisome proliferator and when rat hepatocytes are exposed to the compound, catalase activity is induced (7).

In rat liver mitochondria the compound reduces respiration and increases oxidative phosphorylation (8).

Legislation

EPA terminated all registrations for use on rice fields, orchards, sugar cane, rangeland and non-crop sites in March, 1985 (9).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).

Included in Schedule 6 (Release Into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

WHO Toxicity Class III (12).

Other comments

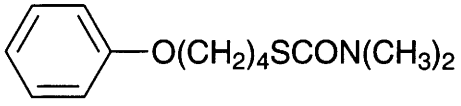
Chlorophenoxy herbicides have been studied extensively for carcinogenic activity (5,13).

Toxicity reviewed (14).

References

1. Senesi, N. et al *Stud. Environ. Sci.* 1986, **29**, 183-196.
2. Kirk, P. et al *Environ. Technol. Lett.* 1989, **10**(4), 405-414.
3. *The Pesticide Manual* 8th ed., 1987, British Crop Protection Council, Farnham, UK.
4. *Arch. Environ. Contam. Toxicol.* 1977, **6**, 33.
5. *IARC Monograph* 1987, **Suppl. 7**, 156.
6. Sauerhoff, *J. Toxicol. Environ. Health* 1977, **3**, 941-952.
7. Lake, B. G. et al *Arch. Toxicol., Suppl.* 1988, **12**, 217-224.
8. Zychlinski, L. et al *Toxicol. Lett.* 1990, **52**(1), 25-34.
9. *Chem. Eng. News* 1985, **636** (Mar. 25).
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S.I. 1991 No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21
13. *IARC Monograph* 1986, **41**, 357-406.
14. Baily, G. W. et al *Residue Rev.* 1965, **10**, 97

F15 fenothiocarb



$C_{13}H_{19}NO_2S$ **Mol. Wt.** 253.37 **CAS Registry No.** 62850-32-2

Synonyms *S*-4-phenoxybutyl *N,N*-dimethylthiocarbamate; *S*-(4-phenoxybutyl)dimethylthiocarbamate; Panocon; KCO-3001; BI-5452

RTECS No. FD 3825000

Uses Acaricide.

Physical properties

M. Pt. 40-41°C **B. Pt.** 155°C at 0.02 mmHg **Partition coefficient** log P_{ow} 3.28
Solubility Water: 30 mg l^{-1} at 20°C. Organic solvents: acetone, acetonitrile, cyclohexanone, n-hexane, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp >7.9 mg l^{-1} (1).

Invertebrate toxicity
LD_{50} topical bees 0.2-0.4 mg bee^{-1} (1).

Environmental fate

Degradation studies
In sterilised soil the compound degraded more slowly than in non-sterilised soil, $t_{1/2}$ 8-15 days, nine degradation products identified (2).

Abiotic removal
Photodegradation under artificial conditions by sunlight yielded products including *S*-4-phenoxybutyl *N*-formyl-*N*-methylthiocarbamate, *N*-methylthiocarbamate, bis(4-phenoxybutyl)thiosulfinate and thiosulfonate, and fenothiocarb sulfoxide. The primary photodegradation step is presumed to be sulfur oxidation to fenothiocarb sulfoxide followed by cleavage of the ester linkage and oxidation or dimerisation (3).

Adsorption and retention
Fenothiocarb sulfoxide is more readily bound to soil residues than the parent compound (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♀, ♂ quail, duck 0.88, 1, 2 g kg^{-1}, respectively (5).
LD_{50} oral rat 1.15-1.2 g kg^{-1} (1).
LD_{50} oral ♀, ♂ mouse 4.8, 7 g kg^{-1}, respectively (1).
LD_{50} dermal mouse 8 g kg^{-1} (1).

Carcinogenicity and chronic effects
2-yr studies established the following no-effect levels: ♂ rats 1.8 mg kg^{-1} day^{-1}, ♀ rats 1.94 mg kg^{-1} day^{-1}, ♂ mice 14 mg kg^{-1} day^{-1}, ♀ mice 17.3 mg kg^{-1} day^{-1}, ♂ dogs 1.5 mg kg^{-1} day^{-1} and ♀ dogs 3.0 mg kg^{-1} day^{-1} (5).

Legislation

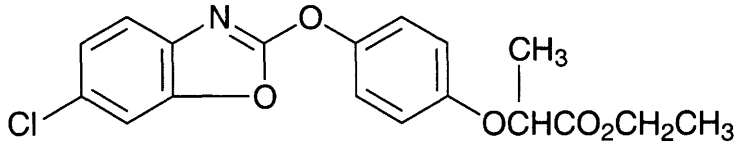
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (8).
WHO Toxicity Class III (9).
ADI 0.0075 mg kg^{-1} (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Unai, T. *Nippon Noyaku Gakkaishi* 1986, **11**(3), 335-345.
3. Unai, T. *Nippon Noyaku Gakkaishi* 1986, **11**(3), 363-367.
4. *Nippon Noyaku Gakkaishi* 1986, **11**(3), 357-361.
5. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S.I. 1991 No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
9. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F16 fenoxaprop-ethyl



$C_{18}H_{16}ClNO_5$ **Mol. Wt.** 361.78 **CAS Registry No.** 66441-23-4

Synonyms (±)-ethyl 2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoate; Acclaim; Cheetah R; Furore; Puma; Whip

EINECS No. 266-362-9 **RTECS No.** UA 2454000

Uses Superseded herbicide.

Physical properties

M. Pt. 85°C **B. Pt.** 300°C **Specific gravity** 1.3 at 20°C **Partition coefficient** log P_{ow} 4.12 (1)
Volatility v.p. 1.43×10^{-10} mmHg at 20°C
Solubility Water: 0.9 mg l^{-1} at pH 7.0 and 25°C. Organic solvents: acetone, cyclohexane, ethanol, ethyl acetate, *n*-octanol

Occupational exposure

Supply classification irritant, dangerous for the environment
Risk phrases May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R43, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin –Wear suitable gloves – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S24, S37, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) river trout, bluegill sunfish 0.31-0.48 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} contact bee >0.02 μg bee^{-1} (2).

Environmental fate

Degradation studies

$t_{1/2}$ in water <4 hr. In soil, residues were below limit of detection within 6 days. Photolysis in sterile water, $t_{1/2}$ 269 hr, and for combined photolysis and microbial degradation, $t_{1/2}$ 29 hr. Products of degradation include the corresponding acid; 6-chlorobenzoxazolinone; ethyl 2-(4-hydroxyphenoxy)propanoate; and 2-(4-hydroxyphenoxy)propanoic acid (3).

Metabolised via fenoxaprop to 6-chloro-2,3-dihydrobenzoxazol-2-one (1).

Abiotic removal

Hydrolysis at pH 9.1, $t_{1/2}$ ≈8 hr. Hydrolysis was slower at lower pHs (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail >2510 mg kg^{-1} (2).

LD_{50} oral Japanese quail >5000 mg kg^{-1} (1).

LD_{50} oral ♂, ♀ rat, ♂, ♀ mouse 2357, 2500, 4670, 5490 mg kg^{-1}, respectively (1).

LC_{50} (4 hr) inhalation rat 510 mg m^{-3} (4).

LD_{50} dermal rabbit >1000 mg kg^{-1}, ♀ rat >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral rat, dog (90 day) no-adverse-effect level for rats 80 mg kg^{-1} diet, for dogs 16 mg kg^{-1} diet (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Tolerance under Federal Food, Drug and Cosmetic Act 0.05 ppm for combined residues of fenoxaprop-ethyl and its metabolites 2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy] propanoic acid and 6-chloro-2,3-dihydrobenzoxazol-2-one in or on cotton seed, peanuts and peanut husks (7).

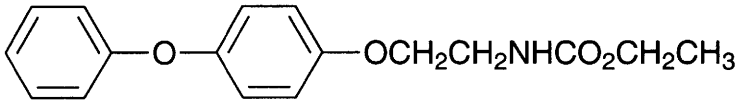
WHO Toxicity Class Table 5 (8).

Partition coefficient exceeds the European Union limit of 3.0.

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, 373, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 9th ed., 1991, British Crop Protection Council, Farnham, UK.
3. Toole, A. P. et al *Environ. Toxicol. Chem.* 1989, **8**(12), 1171-1176.
4. *Farm Chemicals Handbook* 1991, **C136**, Meister Publishing, Willoughby, OH, USA.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *Fed. Reg.* 24 May 1989, **54**(99), 22438-22439, US EPA, Washington, DC, USA.
8. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F17 fenoxycarb



$C_{17}H_{19}NO_4$ **Mol. Wt.** 301.34 **CAS Registry No.** 79127-80-3

Synonyms ethyl 2-(4-phenoxyphenoxy)ethylcarbamate; Comply; Eclipse; Insegar; Logic; Precision; Torus

EINECS No. 276-696-7 **RTECS No.** FD 0423000

Uses Insecticide with a strong juvenile hormone activity.

Physical properties

M. Pt. 53-54°C **Specific gravity** 1.23 at 20°C **Partition coefficient** log P_{ow} 4.07 at 25°C (1)
Volatility v.p. 2.87×10^{-8} mmHg at 20°C
Solubility Water: 6 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, diethyl ether, ethanol, ethyl acetate, hexane, isopropanol, methanol

Occupational exposure

Supply classification dangerous for the environment
Risk phrases Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R50/53)
Safety phrases This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, carp 1.6, 10.3 mg l^{-1}, respectively (1,2).

Environmental fate

Abiotic removal
Stable to light. Stable to hydrolysis in aqueous solution at pH 3, 7 and 9 at 35 and 50°C (1,2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >10,000 mg kg^{-1} (1,2).
LD_{50} oral Japanese quail >7000 mg kg^{-1} (1,2).
LD_{50} dermal rat >2000 mg kg^{-1} (1,2).

Metabolism and toxicokinetics
In rats the major metabolic pathway is ring hydroxylation to form ethyl [2-[*p*(*p*-hydroxyphenoxy)-phenoxy]ethyl]carbamate (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
The log P_{ow} exceeds the European Community recommended level 3.0 (6th and 7th amendments) (5).
ADI 0.04 mg kg^{-1} body weight (2).

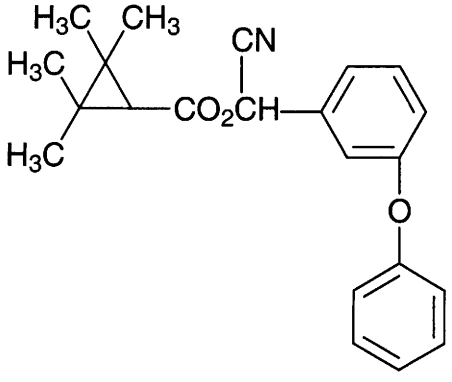
Other comments

Attributed endocrine disruption effects in wildlife. Arthropod moult inhibition (6).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
6. *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* 1997, EPA/630/R-96/012, Risk Assessment Forum, US Environmental Agency, Washington, DC 20460, USA

F18 fenpropathrin



$C_{22}H_{23}NO_3$ **Mol. Wt.** 349.43 **CAS Registry No.** 64257-84-7

Synonyms cyano(3-phenoxyphenyl)methyl-2,2,3,3-tetramethylcyclopropanecarboxylate; Danitol; fenpropanate; Kilumal; Meothrin; phenpropanage; Rody; Smash; Tame; Herald; Randal

EINECS No. 254-485-0 **RTECS No.** GZ 2090000

Uses Acaricide. Insecticide.

Physical properties

M. Pt. 45-50°C **Specific gravity** 1.150 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.03 (6.0 at 20°C) (1,2) **Volatility** v.p. 5.49×10^{-6} mmHg at 20°C

Solubility Water: 0.026 mg l^{-1} at 20°C. Organic solvents: cyclohexanone, methanol, xylene

Occupational exposure

Supply classification Very toxic, dangerous for the environment

Risk phrases Harmful in contact with skin – Toxic if swallowed – Very toxic by inhalation – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21, R25, R26, R50/53)

Safety phrases Keep locked up and out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous

waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S38, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) bluegill sunfish 1.95 μg l^{-1} (2).

LC_{50} (24 hr) rainbow trout 8.6-77 μg l^{-1} static bioassay (1).

Environmental fate

Degradation studies

Degraded by aerobic microbes, undergoing ester hydrolysis and hydroxylation. In soil, $t_{1/2}$ 11-17 days (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck 1090 mg kg^{-1} (4).

LD_{50} oral rat 18-70 mg kg^{-1} (2,5,4).

LD_{50} dermal rat, rabbit 870, 2000 mg kg^{-1}, respectively (2,5).

LC_{Lo} intravenous rat 2.5 mg kg^{-1} (6).

Sub-acute and sub-chronic data

Oral (8 day) mallard duck, bobwhite quail >10,000 mg kg^{-1} diet (2).

Metabolism and toxicokinetics

Following oral administration of 27 mg kg^{-1} to rats of ^{14}C-labelled fenpropathrin, labelled at the α-position of the benzyl radical or the 1-position of the cyclopropane ring, the label was almost completely eliminated in the faeces and urine within 7 days. 0.4-1.4 mg kg^{-1} was found in the fat after 7 days. Most of the faecal metabolites retained the ester linkage, whereas urinary metabolites were ester-cleaved (7).

Sensitisation

Reported to be non-sensitising to skin (species unspecified) (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (8).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (10).

WHO Toxicity Class II (11).

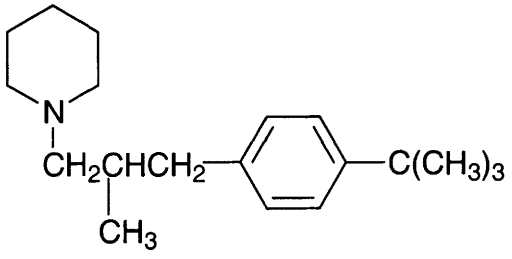
EPA Toxicity Class II (formulation) (2).

ADI 0.03 mg kg^{-1} body weight (2).

References

1. Coates, J. R. et al *Bull. Environ. Contam. Toxicol.* 1979, **23**, 250-255.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Sakata, S. et al *Nippon Noyaku Gakkaishi* 1990, **15**(3), 363-373.
4. Crawford, M. J. et al *Pestic. Sci.* 1977, **8**, 579.
5. *Farm Chemicals Handbook* 1983, **C70**, Meister Publishing Co., Willoughby, OH, USA.
6. Vershoyle, R. D. et al *Arch. Toxicol.* 1980, **45**, 325.
7. Kaneko, H. et al *Nippon Noyaku Gakkaishi* 1987, **12**(3), 385-395 (Eng.) (*Chem. Abstr.* **108**, 1850n).
8. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
10. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
11. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F19 fenpropidin



$C_{19}H_{31}N$ **Mol. Wt.** 273.46 **CAS Registry No.** 67306-00-7

Synonyms (*RS*)-1-[3-[4-(1,1-dimethylethyl)phenyl]-2-methylpropyl]piperidine; (±)-1-[3-(*p-tert*-butylphenyl)-2-methylpropyl]piperidine; Sorilan; Mallard; Patrol; Tern

RTECS No. TM 7292000

Uses Fungicide.

Physical properties

B. Pt. 117°C at 0.2 mmHg **Flash point** >100°C **Specific gravity** 0.91 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.0 (1) **Volatility** v.p. 1.58×10^{-4} mmHg at 20°C
Solubility Water: 0.35 g l^{-1} at pH 7 and 25°C. Organic solvents: acetone, chloroform, ethanol, ethyl acetate, heptane, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish, mirror carp 1.9-3.6 mg l^{-1} (1,2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* 0.5 mg l^{-1} (1).
LD_{50} (48 hr) oral bee >0.1 mg bee^{-1} (2).
LD_{50} (48 hr) contact bee 0.046 mg bee^{-1} (2).

Environmental fate

Abiotic removal
Stable to hydrolysis at 80°C at pH 4, 7 and 10 (1).
Stable to UV light in aqueous solution (1).

Adsorption and retention
Strongly adsorbed by soils (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral pheasant, mallard duck 370, 1900 mg kg^{-1}, respectively (2).
LD_{50} oral rat, mouse >1447, >3200 mg kg^{-1}, respectively (1,2).
LD_{50} dermal rat >1800 mg kg^{-1} (1,2).
LD_{50} intraperitoneal rat 350 mg kg^{-1} (1,2).

Metabolism and toxicokinetics
Following oral administration to rats, fenpropidin is rapidly absorbed, distributed, metabolised and excreted completely in the urine and faeces (1).

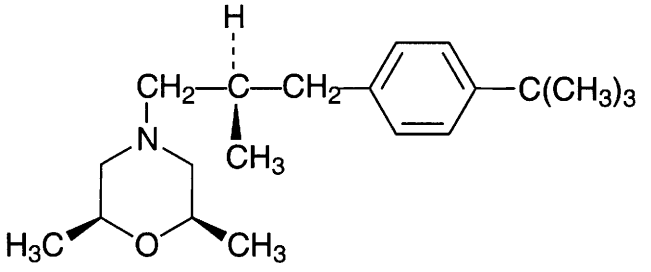
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class II (5).
ADI 0.005 mg kg^{-1} (2).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F20 fenpropimorph



$C_{20}H_{33}NO$ **Mol. Wt.** 303.49 **CAS Registry No.** 67564-91-4

Synonyms 4-[3-[4-(1,1-dimethylethyl)phenyl]-2-methylpropyl]-2,6-dimethylmorpholine; *cis*-4-[3-(4-*tert*-butylphenyl)-2-methylpropyl]-2,6-dimethylmorpholine; Corbel; Forbel; Mistral; Task; Aura; Keetak

EINECS No. 266-719-9 **RTECS No.** QE 1940000

Uses Fungicide.

Physical properties

B. Pt. 120°C at 0.05 mmHg **Flash point** ≈105°C **Specific gravity** 0.931 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 4.061 (1) **Volatility** v.p. 2.5×10^{-5} mmHg at 20°C
Solubility Water: 4.3 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, cyclohexane, diethyl ether, ethanol, ethyl acetate, toluene

Occupational exposure

Supply classification harmful, dangerous for the environment
Risk phrases Harmful by inhalation – Irritating to the skin – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R20, R38, R51/53)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing, gloves and eye/face protection – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S36/37/39, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) carp, bluegill sunfish, rainbow trout 3.2, 3.2-4.2, 9.5 mg l^{-1}, respectively (1,2).

Environmental fate

Degradation studies

Degraded in soil by oxidation of the tertiary butyl group, in addition to oxidation and opening of the dimethylmorpholine ring. In soil, $t_{1/2}$ 15 days for moderately humous loamy soil, and 93 days in very humous loamy soil (1).

Abiotic removal

Stable to hydrolysis at 50°C at pH 3, 7 and 9 (1).
Stable to photodegradation (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3420-3650 mg kg^{-1} (1,2).
LC_{50} (4 hr) inhalation rat ≈2900 mg m^{-3} (3).
LD_{50} dermal rat 4200-4380 mg kg^{-1} (1,2).
LD_{50} intraperitoneal mouse 1180-1270 mg kg^{-1} (1,2).

Carcinogenicity and chronic effects

Oral rat, mouse. No-adverse-effect level for rat 0.3-0.4 mg kg^{-1} diet, and for mouse 3.0-3.5 mg kg^{-1} diet. No carcinogenic effects were observed in these feeding trials (exposure duration unspecified) (1,2).

Irritancy

Inhalation rat (4 hr) LD_{50} concentration of 2900 mg m^{-3} caused moderate irritation of the respiratory organs (1).

Sensitisation

Non-sensitising in guinea pigs (1).

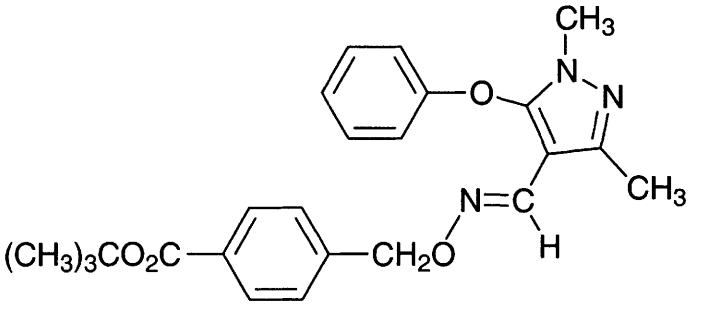
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
Partition coefficient exceeds European Union limit of 3.0.
WHO Toxicity Class Table 5 (6).
ADI 0.003 mg kg^{-1} body weight (2).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Bohren, K. et al *Proc. Br. Crop. Prot. Conf. – Pests Dis.* 1979, 541-548.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F21 fenpyroximate



$C_{24}H_{27}N_3O_4$ **Mol. Wt.** 421.50 **CAS Registry No.** 111812-58-9

Synonyms *t*-butyl (*E*)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneamino-oxy)-*p*-toluate; (*E*)-1,1-dimethylethyl 4-[[[[(1,3-dimethyl-5-phenoxy-1*H*-pyrazol-4-yl)methylene]amino]oxy]methyl]benzoate; Asalto; Danitron; Manhao; Naja; Ortus; Pamanrin

Uses Acaricide.

Physical properties

M. Pt. 101.1-102.4°C **Specific gravity** 1.25 **Partition coefficient** log P_{ow} 5.0 (1) **Volatility** v.p. 0.0075 mPa at 25°C

Solubility *Water:* 0.0146 mg l^{-1} at 20°C. *Organic solvents:* acetone, chloroform, dichloromethane, methanol, tetrahydrofuran

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, carp 0.079, 0.29 mg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} (24 hr) *Daphnia* 0.204 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail, mallard duck >2000 mg kg^{-1} (1).
LD_{50} oral ♂, ♀ rat 7193, 6798 mg kg^{-1}, respectively (1).
LC_{50} inhalation (duration unspecified) ♂ rat 1.9 mg l^{-1} (1).
LD_{50} percutaneous ♂, ♀ rats >4000 mg kg^{-1} (1).

Irritancy

Non-irritating to skin but slightly irritating to eyes of rabbits (1).

Genotoxicity

Non-mutagenic in Ames and DNA repair tests (1).
In vitro chromosomal aberrations and mouse micronucleus tests both negative (1).

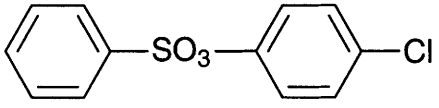
Legislation

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (2).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (3).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations*, 1991, HMSO, London, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

F22 fenson



$C_{12}H_9ClO_3S$ **Mol. Wt.** 268.72 **CAS Registry No.** 80-38-6

Synonyms 4-chlorophenyl benzenesulfonate; benzenesulfonic acid, 4-chlorophenyl ester; Murvis; Trifenson

EINECS No. 201-274-6

Uses Superseded acaricide.

Physical properties

M. Pt. 62°C

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to the eyes (R22, R36)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S24, S26)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1550 mg kg^{-1} (1).
LD_{50} dermal rat, rabbit >2000 mg kg^{-1} (2).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye caused moderate irritation (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

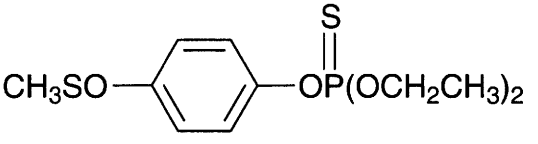
Other comments

Believed to be no longer manufactured or marketed for crop protection use.
Residual toxicity to *Phytoseiulus persimilis* (Athias-Henriot), a predator used in the control of the two-spotted spider mite *Tetranychus urticae* (Koch), estimated (6).

References

1. *Agricultural Research Service. USDA Information Memorandum* 1966, **20**, 10.
2. *The Pesticide Manual* 8th ed., 1987, British Crop Protection Council, Farnham, UK.
3. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 197, Prague, Czechoslovakia.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. Malezieux, S. et al *J. Econ. Entomol.* 1992, **85**(6), 2077-2081

F23 fensulfothion



$C_{11}H_{17}O_4PS_2$ **Mol. Wt.** 308.36 **CAS Registry No.** 115-90-2

Synonyms *O,O*-diethyl *O*-(4-methylsulfinyl)phenyl phosphorothioate; phosphorothioic acid, *O,O*-diethyl *O*-[(*p*-methylsulfinyl)phenyl] ester; Agricur; Dasonit; DMSP

EINECS No. 204-114-3 **RTECS No.** TF 3850000

Uses Superseded nematicide and insecticide.

Physical properties

B. Pt. 138-141°C at 0.01 mmHg **Specific gravity** 1.202 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.23 (1) **Volatility** v.p. 6.82×10^{-7} mmHg at 20°C
Solubility Water: 1.54 g l^{-1} at 25°C. Organic solvents: acetone, dichloromethane, ethanol, xylene

Occupational exposure

FR-VME 0.1 mg m^{-3}
US-TWA 0.1 mg m^{-3}
Supply classification very toxic, dangerous for the environment
Risk phrases Very toxic in contact with skin and if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R27/28, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S23, S28, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 0.12 mg l^{-1} (2).
LC_{50} (96 hr) rainbow trout, golden orfe 6.8-8.6 mg l^{-1} (2).

Invertebrate toxicity
LD_{50} *Gammarus fasciatus* 7-14 μg l^{-1} (3).

Environmental fate

Degradation studies

Biodegradation in surface and groundwater samples resulted in reduction in concentration from 50 to 0.1 μg in 164 day (4).

Pseudomonas alcaligenes C1, NC3 used >80% within 120 hr when supplemented as a carbon source.

p-(Methylsulfinyl)phenol and diethyl phosphorothioic acid were detected as degradation products (5).

Incubation with a mixed culture of soil microorganisms from sandy loam soil, $t_{1/2}$ 16 wk. Trace amounts of fensulfothion sulfide were detected (6).

Abiotic removal

Removal from water reported by UV irradiation at 254 nm. Degradation efficiency was increased by the addition of hydrogen peroxide (7).

Hydrolysis $t_{1/2}$ 58-87 days at 25°C and pH 4.5-8.0 (8).

Reacts with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2} \approx 7$ hr (9).

Easily oxidised to the sulfone, and isomerises readily to the *O,S*-diethyl isomer (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral quail 1.8 mg kg^{-1} (11).

LD_{50} oral redwing blackbird, starling 0.24-0.56 mg kg^{-1} (12).

LD_{50} oral rat, guinea pig 2.2, 10.5 mg kg^{-1}, respectively (2,12).

LC_{50} (1 hr) inhalation rat 113 mg m^{-3} (2).

LD_{50} dermal rat 3.0-30 mg l^{-1} (2,13).

LD_{Lo} intraperitoneal guinea pig, mouse 5.4, 7.0 mg kg^{-1}, respectively (14).

Sub-acute and sub-chronic data

LD_{50} (5 day) oral bobwhite quail, mallard duck 35-43 mg kg^{-1} (2).

Oral rat (16 month) 1 mg kg^{-1} diet caused no ill-effects (2).

Captive house sparrows were offered granular pesticide (0.3 mg kg^{-1} $granule^{-1}$) in bands on soil surfaces at application rates of 50, 100, 200, 400, 800, 1200, 1600 or 2000 LD_{50} ft^{-2}. A significant negative correlation between brain cholinesterase activity and the natural log of application rate was observed. This suggests an asymptotic, not linear relationship (15).

Teratogenicity and reproductive effects

Oral mouse, three-generation study, 5 mg kg^{-1} diet caused no embryotoxic or teratogenic effects (16).

Metabolism and toxicokinetics

Following oral administration to sheep, rapid adsorption occurred. Peak blood levels were reached 1-2 hr after dosing, 65% excreted in urine within 24 hr, 95% in 7 days. Negligible concentrations of fensulfothion and its oxidation and hydrolysis products were detected in organs on autopsy (16).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (17).

Escherichia coli WP2 *uvr-A* reverse mutation, without metabolic activation negative (18).

Saccharomyces cerevisiae without recombination assay negative (17).

Other effects

Any other adverse effects

Inhibits cholinesterase activity after conversion into the oxygen analogue fensulfoxon (19).

In mammals (unspecified), rapidly absorbed from the gastro-intestinal tract and by inhalation. Dermal absorption is slower, although dermal toxicity is relatively high (20).

No residues of fensulfothion or its oxidation products were found in fat, muscle or liver of sheep after oral administration.
No residues detected in cows grazing on treated land 28 days after treatment.
Traces (0.02 ppm) were detected in the butterfat of cows that grazed 14 days after treatment (21).
Good absorption via lungs demonstrated following inhalation of aerosols (22).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (23).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (24).
WHO Toxicity Class Ia (25).
Tolerable daily intake (TDI) humans 0.0003 $mg\ kg^{-1}$ (1).

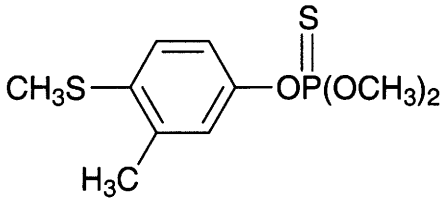
Other comments

Residues have been isolated from surface wastes (26).
Environmental fate reviewed (26).
In cotton plants, metabolism occurred within 4-9 days. The majority remained as the unchanged compound with minor amounts of the oxygen analogue and the oxygen analogue sulfone (27).

References

1. Bowman, B. T. et al *J. Environ. Sci. Health, Part B* 1983, **B18**, 667-684.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. *Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates* 1980, 83, US Dept. Interior, Fish and Wildlife Service, Publ. No. 137, Washington, DC, USA.
4. Frank, R. et al *Bull. Environ. Contam. Toxicol.* 1991, **47**(3), 374-380.
5. Sheela, S. et al *Appl. Environ. Microbiol.* 1983, **46**(2), 475-479.
6. Miles, J. R. W. et al *J. Environ. Sci. Health, Part B* 1982, **B17**(6), 675-682.
7. Thiermann, W. et al *DVGW-Schriftenr., Wasser* 1988, **107**, 129-146 (Ger.) (*Chem. Abstr.* **110**, 101421h).
8. Chapman, R. A. et al *J. Environ. Sci. Health, Part B* 1982, **B17**, 487.
9. *GEMS: Graphical Exposure Modeling System, Fate of Atmospheric Pollutants Database* 1986, US EPA, Office of Toxic Substances.
10. Benjamini, E. et al *J. Econ. Entomol.* 1959, **52**, 94-99.
11. Schafer, E. W. *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
12. Schafer, E. W. *Toxicol. Appl. Pharmacol.* 1972, **21**, 315-330.
13. *World Rev. Pest Control* 1970, **9**, 119.
14. *Toxicol. Appl. Pharmacol.* 1964, **6**, 78.
15. Stafford, T. R. et al *Environ. Toxicol. Chem.* 1998, **17**(3), 526-529.
16. Hayes, W. J. *Pesticides Studies in Man* 1982, 402, Williams and Wilkins, Baltimore, MD, USA.
17. Poole, D. C. et al *Toxicol. Appl. Pharmacol.* 1977, **41**(1), 196.
18. *GENE-Tox Program: Current Status of Bioassay in Genetic Toxicology* USEPA, Washington, DC, USA.
19. *Documentation of Threshold Limit Values* 4th ed., 1980, 191, ACGIH, Cincinnati, OH, USA.
20. *FAO Data Sheet on Pesticides: No. 44 Fensulfothion* 1980, WHO, Geneva, Switzerland.
21. Menzie, C. M. *Metabolism of Pesticides: Update* 1974, 201, US Dept. of Interior, Fish, Wildlife Report No. 184, Washington DC, USA.
22. *Documentation of Threshold Limit Values* 4th ed., 1980, ACGIH, Cincinnati, OH, USA.
23. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
24. *S. I. 1991 No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
25. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
26. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, Lewis Publishers, Chelsea, MI, USA.
27. Katague, D. B. et al *Bull. Environ. Contam. Toxicol.* 1967, **2**(4), 228-235

F24 fenthion



$C_{10}H_{15}O_3PS_2$ **Mol. Wt.** 278.33 **CAS Registry No.** 55-38-9

Synonyms phosphorothioic acid, *O,O*-dimethyl *O*-[4-(methylthio)-*m*-tolyl] ester; Baycid; Baytex; Fenthion-methyl; Mercaptophos; MPP; Queletox; Spotton; Sulfidophos; Talodex; Tiguvon; Cidalina; Lebaycid; Pilartex

EINECS No. 200-231-9 **RTECS No.** TF 9625000

Uses Insecticide. Acaricide. Veterinary ectoparasiticide.

Physical properties

M. Pt. 7.5°C **B. Pt.** 87°C at 0.01 mmHg **Specific gravity** 1.246 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.1753 (1) **Volatility** v.p. 3×10^{-5} mmHg at 20°C
Solubility Water: 2 mg l^{-1} at 20°C. Organic solvents: acetone, carbon tetrachloride, chloroform, dichloromethane, diethyl ether, dimethyl sulfoxide, ethanol, methanol, toluene

Occupational exposure

DE-MAK 0.2 mg m^{-3} (inhalable fraction of aerosol)
JP-OEL 0.2 mg m^{-3}
US-TWA 0.2 mg m^{-3}
Supply classification toxic, dangerous for the environment
Risk phrases Harmful in contact with skin – Toxic if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21, R25, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) mosquito fish 2.9 ppm (2).
LC_{50} (96 hr) bluegill sunfish, rainbow trout, bass, carp, goldfish 0.7-3.3 mg l^{-1} (3,4).
LC_{50} (48 hr) goldfish 1.9 mg l^{-1} (3).

Invertebrate toxicity
LC_{50} (48 hr) freshwater shrimp 0.04 μg l^{-1} (5).
EC_{50} (48 hr) *Daphnia magna* 0.88 μg l^{-1} (6).

Toxicity to other species
Tadpoles (*Rana catesbeiana*) concentrated fenthion ~60 times from water when exposed to an initial concentration of 5 ppm. The tadpoles were lethal when subsequently fed to mallard ducks (7).

Bioaccumulation
The average bioaccumulation factor in whole body of carp 24-168 hr after exposure to an unspecified concentration was 26, excretion rate constant 0.34 hr^{-1} (8).
Bioconcentration factor in whole body of willow shiner after 24-168 hr exposure was 481, excretion rate 0.07 hr^{-1} (9).

Environmental fate

Degradation studies

Utilised as a sole carbon source by *Pseudomonas aeruginosa* and *Bacillus megaterium* (10).

Intact sediment cores, with and without a salt marsh plant (*Juncus roemerianus*) were placed in microcosm vessels to simulate an undisturbed sediment bed of a salt marsh. In a formalin-sterilised microcosm without plants, exponential disappearance was recorded, $t_{1/2}$ 105 hr. In a non-sterile microcosm without plants $t_{1/2}$ ≈35 hr; with plants $t_{1/2}$ ≈33 hr. Biodegradation occurred principally in the upper (1-7 mm) sediment layers (11).

Abiotic removal

Stability of and uptake by water plants and fish was detected in experimental ecosystems containing water alone or water and sediment, aquatic plants and fish. Fenthion was particularly stable in water alone, $t_{1/2}$ ≥20 days (12).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling, quail 1.7-17.8 mg kg^{-1} (15).

LD_{50} oral mouse, rat 88, 615 mg kg^{-1}, respectively (3,13,14).

LC_{50} (4 hr) inhalation rat 0.22-1.84 g m^{-3} (16).

LD_{50} dermal rat, mouse 330, 500 mg kg^{-1}, respectively (13,17).

LD_{50} intraperitoneal mouse 125 mg kg^{-1} (13).

LD_{50} intravenous mouse 320 mg kg^{-1} (18).

Sub-acute and sub-chronic data

LC_{50} (5 day) oral bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck 30-230 mg kg^{-1} diet·(19).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via feed. No evidence of carcinogenicity in rats and ♀ mice, equivocal results for ♂ mice (20).

Oral rat (2 yr) no-adverse-effect level was 3 mg kg^{-1} diet (3).

Metabolism and toxicokinetics

In mammals, following oral administration metabolites are eliminated principally as hydrolysis products in the urine (3).

Metabolism in plants and animals give five major metabolites: fenthion sulfoxide, fenthion sulfone, the oxygen analogue fenoxon, fenoxon sulfoxide, and fenoxon sulfone (21).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with and without metabolic activation negative (22).

In vitro rat hepatocytes, unscheduled DNA synthesis negative (23).

In vitro human lymphocytes, chromosomal aberrations positive (24).

Other effects

Any other adverse effects

Sub-chronic exposure of rodents resulted in a marked suppression of the humoral immune function and moderate changes of lymphoid organs without any significant effect in clinical status (dose and duration unspecified) (25).

Cholinesterase activity inhibitor (26).

Legislation

EEC maximum residue level for fruit and vegetables 0.2 ppm (3).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (27).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (28).

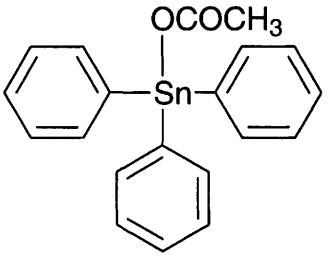
Partition coefficient exceeds European Union limit of 3.0.

WHO Toxicity Class Ib (29).
EPA Toxicity Class II (30).
ADI 0.007 mg kg^{-1} (30).

References

1. McCoy, G. D. et al *Carcinogenesis (London)* 1990, **11**(7), 1111-1117.
2. Tietze, N. S. et al *J. Am. Mosquito Control Assoc.* 1991, **7**(2), 290-293.
3. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
4. Macek, K. J. et al *Trans. Am. Fish Soc.* 1970, **99**(1), 20-27.
5. Hatakeyama, S. et al *Environ. Pollut.* 1989, **59**(4), 325-336.
6. Vighi, M. et al *Chemosphere* 1987, **16**(5), 1043-1051.
7. Hall, R. J. et al *J. Toxicol. Environ. Health* 1980, **6**(4), 853-860.
8. Tsuda, T. et al *Comp. Biochem. Physiol., C: Comp. Pharmacol. Toxicol.* 1993, **104C**(2), 275-278.
9. Tsuda, T. et al *Chemosphere* 1992, **25**(12), 1945-1951.
10. Selvenayagam, M. et al *J. Environ. Biol.* 1989, **10**(4), 399-407.
11. O'Neill, E. J. et al *Environ. Toxicol. Chem.* 1989, **8**(9), 759-768.
12. Vrochinskii, K. K. *Izv. Gos. Nauchno-Issled. Inst. Ozern. Rechn. Rybn. Khoz.* 1976, **109**, 88-93 (Russ.) (*Chem Abstr.* **87**, 128431e).
13. Gaines, T. B. et al *Toxicol. Appl. Pharmacol.* 1960, **2**, 88.
14. *Hokkaidoritsu Eisei Kenkyushoho* 1980, **30**, 53.
15. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
16. Iwasaka, M. et al *Jpn. J. Vet. Sci.* 1988, **50**(1), 23-30 (*Chem. Abstr.* **109**, 2065t).
17. *Oyo Yakuri* 1967, **1**, 74.
18. *US Army Armament Research and Development Command, Chemical Systems Laboratory Report No. NX 00142,* NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA.
19. Hill, E. F. et al *Lethal Dietary Toxicities of Environmental Pollutants to Birds* 1975, US Fish and Wildlife Service, Report Wildlife No. 191, Washington, DC, USA.
20. *National Toxicology Program Research and Testing Division Report No. TR-103* 1992, NIEHS, Research Triangle Park, NC, USA.
21. Cabras, P. et al *J. Chromatogr.* 1991, **540**(1-2), 406-410.
22. Zeiger, E. et al *Cancer Res.* 1987, **47**, 1287-1296.
23. Ennever, F. K. et al *Environ. Mutagen.* 1986, **8**(6), 849-865.
24. Rani, M. V. U. et al *Bull. Environ. Contam. Toxicol.* 1991, **47**(2), 316-320.
25. Moon, C. K. et al *Arch. Pharmacol. Res.* 1986, **9**(3), 175-181.
26. *The Pesticide Manual* 9th ed., 1991, 383, British Crop Protection Council, Farnham, UK.
27. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
28. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
29. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
30. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

F25 fentin acetate



$C_{20}H_{18}O_2Sn$ **Mol. Wt.** 409.07 **CAS Registry No.** 900-95-8

Synonyms triphenyltin acetate; stannane, acetyloxytriphenyl-; acetatotriphenylstannane; Batasan; Brestan 60; Lirostanol; tintriphenyl acetate; VP 19-40; TPTA

EINECS No. 212-984-0 **RTECS No.** WH 6650000

Uses Fungicide. Molluscicide. Algicide.

Physical properties

M. Pt. 124-126°C **Specific gravity** 1.5 at 20°C **Partition coefficient** log P_{ow} 3.43 (1)
Volatility v.p. 1.42×10^{-5} mmHg at 60°C
Solubility Water: 9 mg l^{-1} at 20°C. Organic solvents: ethanol, ethyl acetate, *n*-hexane, dichloromethane, toluene

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Sn) (total dust)
FR-VME 0.1 mg m^{-3} (as Sn) **FR-VLE** 0.2 mg m^{-3} (as Sn)
SE-LEVL 0.1 mg m^{-3} (as Sn) **SE-STEL** 0.2 mg m^{-3} (as Sn)
UK-LTEL 0.1 mg m^{-3} (as Sn) **UK-STEL** 0.2 mg m^{-3} (as Sn)
US-TWA 0.1 mg m^{-3} (as Sn) **US-STEL** 0.2 mg m^{-3} (as Sn)

UN No. 2788 (liquid)

UN No. 3146 (solid) **HAZCHEM Code** 2X (solid) **Conveyance classification** toxic substance
Supply classification very toxic, dangerous for the environment
Risk phrases Toxic in contact with skin and if swallowed – Very toxic by inhalation – Irritating to eyes and skin – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R26, R36/38, R43, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 0.32 mg l^{-1} (2).
LC_{50} (2 day) goldfish 0.62 mg l^{-1} (3).

Invertebrate toxicity
LC_{50} (1 day) *Chironomus riparius* 0.070 mg l^{-1} (3).
LC_{50} (2 day) *Chironomus riparius* 0.050 mg l^{-1} (3).
EC_{50} *Daphnia pulex* 0.023 mg l^{-1} (5).

LC_{50} (1 day) *Asellus aquaticus* 3 mg l^{-1} (3).
Survival percentages of *Asellus aquaticus* (48 hr) 40% at 3 mg l^{-1} (3).
EC_{50} *Thalassiosira pseudonana* 1.2 μg l^{-1} (6).

Environmental fate

Nitrification inhibition

Jack bean urease was inhibited competitively by 0.016 mg l^{-1}; 43% inhibition of soil urease by 4.09 mg l^{-1}; 100% inhibition of soil nitrification by 4.09 mg l^{-1} (7).
Concentrations between 100 and 250 μg l^{-1} inhibited nitrification (8).

Degradation studies

In soil degraded to inorganic tin via di- and monophenyltin compounds (2).
The $t_{1/2}$ in soil with 1% organic C was 47-70 days and 115-140 days in soil with 2% organic C (9).
Degradation of 80 mg kg^{-1} occurred in 3-10 days (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, rabbit, mouse, rat 21, 80, 81, 125 mg kg^{-1}, respectively (11-14).
LD_{50} dermal rat 450 mg kg^{-1} (15).
LD_{50} subcutaneous mouse 44 mg kg^{-1} (16).
LD_{50} intraperitoneal rat, mouse, rabbit 8.5, 10, 719 mg kg^{-1} (13,17,15).
LD_{50} intravenous rat, mouse 18 mg kg^{-1} (16,18).
LD_{50} oral redwing blackbird, coturnix 100-117 mg kg^{-1} (19).

Sub-acute and sub-chronic data

Oral rat (duration unspecified) 5, 10 or 100 mg kg^{-1} showed histopathogical lesions in lungs, liver, intestine and kidney, a reduction in mean lymphocyte count and monocyte count were also observed (20).
Dermal rat (duration unspecified), applications of 50 mg TPTA kg^{-1} to nuchal skin caused no mortality but some signs of irritation. Five applications of 200 mg kg^{-1} were lethal to rat (21).
Oral (30 day) 10 ♂ and 10 ♀ rat 0, 37.5, 150 or 625 ppm in diet, no effects were found on haematology and urinalysis. Seven rats from each sex in the 625 ppm group died during the study. Piloerection and deterioration of the general condition was observed in the 625 ppm group. Histopathology showed gastro-intestinal haemorrhages and hepatic changes in the 625 ppm group (21).

Carcinogenicity and chronic effects

Oral mice (18 month) 0.46 mg kg^{-1} day^{-1} between the ages of 7-28 days and thereafter a dietary level of 1206 mg kg^{-1}. No statistically significant increase in tumours was observed compared with a control group (22).

Teratogenicity and reproductive effects

It is an experimental teratogen (23).
Oral rat 0, 4 or 8 mg kg^{-1} day^{-1} on days 6-20 of gestation. In dams the body weight of the 8 mg kg^{-1} group was significantly lower than in the controls, 2 of 4 rats died on the expected day of delivery (24).
Oral Wistar rats 0, 1.5, 3, 6, 9 or 12 mg kg^{-1} day^{-1} on days 7-17 of gestation. Vaginal bleeding, bloody mouth and nose, somnolence and depression of body weight gain and food intake were observed. Increase in embryonic and foetal deaths and resorption of foetuses occurred above 6 mg kg^{-1}. No teratogenic effect in rats (25).
Oral 15 pregnant rabbits 0, 0.1, 0.32 or 1.0 mg kg^{-1} day^{-1} on days 6-18 of gestation and sacrificed on day 29 of gestation. In the 1.0 mg kg^{-1} group 1 dam died, 3 aborted and 1 was sacrificed to a premature delivery. Three dams showed vaginal haemorrhages. Water and food consumption of dams at 1 mg kg^{-1} decreased. The number of implantations and of live foetuses decreased, mean foetal weight, mean crown/rump length and mean placental weight decreased in pups at 1 mg kg^{-1}. There was an increase in the number of foetuses with fewer than 13 ossified caudal vertebrae and some foetuses showed weak ossification of the hyoid bone or non-ossification or only slight ossification of the *os pubis* (21).
Four groups of 12 pregnant rats, 0, 5, 10 or 15 mg kg^{-1} body weight day^{-1} from day 6-15 of gestation and then sacrificed on day 21 of gestation. Average maternal weight gain decreased at 5 mg kg^{-1}, 10 mg kg^{-1} and

15 mg kg^{-1}. Post-implantation centres, mainly at the level of the metacarpus and caudal vertebrae, were seen in all groups (21).
Oral pregnant Wistar rats 0, 1.25, 3.2 or 8 mg kg^{-1} day^{-1} on day 7-16 of gestation and then sacrificed on day 21 of gestation. Ten dams at 8 mg kg^{-1} had abortions and showed signs of clinical intolerance as piloerection, bloody nose secretion, local hair loss accompanied by scab formation (21).

Metabolism and toxicokinetics
Subcutaneous guinea pig 2 mg [^{113}Sn]-TPTA, 21% remained in the body after 20 days. The biological $t_{1/2}$ was 9.4 days. Radioactivity was mainly excreted in the faeces. About 18.5%, 4.3% and 0.1% of the dose remained at the injection site after 5, 10 and 20 days, respectively. The highest concentration of radioactivity was noted in the liver, adrenal glands, kidneys and brain (22).

Irritancy
Five applications of 0.5 ml to depilated and irritant rabbit skin caused slight local irritation (21).
Dermal 6 New Zealand white rabbits (54 hr) 500 mg moistened with saline solution caused no irritation after 72 hr (21).
A 20% solution produced irritation of the skin and the mucous membrane of the upper respiratory tract in humans (26).

Other effects

Other adverse effects (human)
Symptoms of poisoning include severe headache, nausea, vomiting, abdominal pain, dizziness, transient loss of consciousness, convulsions, photophobia and blurred vision (27).

Any other adverse effects
Oral guinea pig 15 mg kg^{-1} for 77 days caused a decrease in plasma cells in the spleen and in the mesenteric, cervical, auxillary, and popliteal lymph nodes (28).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (29).
Included in Schedules 4 and 5 (Release into Air/Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (30).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (31).

Other comments

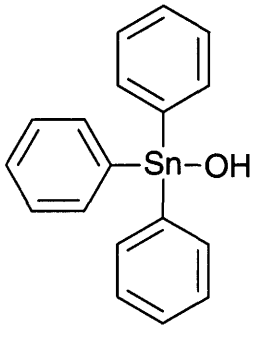
Human health effects, environmental toxicity, environmental effects, ecotoxicology, exposure levels and hazard assessment reviewed (32).
Organotins (unspecified) enhanced the induction of chromatid aberrations by clastogenic pollutants in chlorinated tap water, indicating a potential increased risk to health (33).

References

1. *The Pesticide Manual* 11th ed., 1997, British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Cotta'-Ramusino, M. et al *Bull. Environ. Contam. Toxicol.* 1987, **38**, 647.
4. Walsh, G. E. et al *Chemosphere* 1985, **14**, 383-392.
5. Hashimoto, Y. et al *J. Pestic. Sci.* 1981, **6**, 257.
6. Walsh, G. E. et al *Environ. Toxicol. Chem.* 1987, **6**, 767-770.
7. D'Arrigo, C. M. et al *Agrochimica* 1989, **33** (1-2), 69-74.
8. Kuthubutheen, A. J. et al *Appl. Organometallic Chem.* 1989, **3**, 319-333.
9. Loch, J. P. G. et al *Water, Air, Soil Pollut.* 1990, **53**(1-2), 119-129.
10. Cenci, P. et al *Ind. Sac. Ital.* 1969, **69**, 313-316.
11. Klimier, O. R. *Pflanzenschutz- und Schaedlingsbekaempfungsmittel: Abriss einer Toxikologie und Therapie von Vergiftungen* 2nd ed., 1971, 127, Hundt-Verlag, Hattingen, Germany.

12. Perkow, W. *Wirksubstanzen der Pflanzenschutz- und Schaedlingsbekaempfungsmittel* Verlag Paul Parey, Berlin, Germany.
13. *Br. J. Ind. Med.* 1966, **23**, 22.
14. *Tin and its Uses* 1958, **43**, 9.
15. *Arzneim.-Forsch.* 1969, **19**, 934.
16. *Guide to the Chemicals used in Crop Protection* 1973, Information Canada, 171 Slater St., Ottawa, ON, Canada.
17. *Arzneim.-Forsch.* 1963, **13**, 432.
18. *Report* NX 00648, US Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA.
19. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
20. Attahiru, U. S. et al *Vet. Hum. Toxicol.* 1991, **33**(5), 499-502.
21. *IPCS Pesticide Residues in Food – 1991, Evaluations* 1991, **Part II Toxicology**, WHO, Geneva, Switzerland.
22. Innes, J. R. M. et al *J. Natl. Cancer Inst.* 1969, **42**, 1101-1114.
23. *Sax's Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY. USA.
24. Miyake, K. et al *Nippon Eiseigaku Zasshi* 1991, **46**(3), 169-176.
25. Noda, T. et al *Toxicol. Lett.* 1991, **56**(1-2), 207-212.
26. *Environmental Health Criteria 15. Tin and Organotin Compounds* 1980, WHO, Geneva, Switzerland.
27. Manzo, L. et al *Clin. Toxicol.* 1981, **18**(11), 1345-1353.
28. *Evaluation of Some Pesticide Residues in Food* 1971, 327-366, FAO/WHO, Rome, Italy.
29. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
30. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
31. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
32. *ECETOC Technical Report No. 71* 1996, European Chemical Industry Ecology and Toxicology Centre, B-1160 Brussels, Belgium.
33. Sasaki, Y. F. *Mutat. Res.* 1993, **300**(1), 5-14

F26 fentin hydroxide



$C_{18}H_{16}OSn$ **Mol. Wt.** 367.03 **CAS Registry No.** 76-87-9

Synonyms Fenolovo; Du-Ter; hydroxytriphenylstannane; triphenyltin hydroxide; TPTH; Tubotin; Anticercospora; Brestan; EndSpray; Fermatin; Haitin; Sanatir

EINECS No. 200-990-6 **RTECS No.** WH 8575000

Uses Fungicide. Antifouling agent. Catalyst.

Physical properties

M. Pt. 118-120°C **Specific gravity** 1.54 at 20°C **Partition coefficient** log P_{ow} 3.43 (1)
Volatility v.p. 3.5×10^{-7} mmHg at 50°C
Solubility Water: ~1 mg l^{-1} at 20°C and pH 7. Organic solvents: acetone, dichloromethane, diethyl ether, ethanol, toluene

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Sn) (total dust)
FR-VME 0.1 mg m^{-3} (as Sn) **FR-VLE** 0.2 mg m^{-3} (as Sn)
SE-LEVL 0.1 mg m^{-3} (as Sn) **SE-STEL** 0.2 mg m^{-3} (as Sn)
UK-LTEL 0.1 mg m^{-3} (as Sn) **UK-STEL** 0.2 mg m^{-3} (as Sn)
US-TWA 0.1 mg m^{-3} (as Sn) **US-STEL** 0.2 mg m^{-3} (as Sn)

UN No. 2788 (liquid)

UN No. 3146 (solid) **HAZCHEM Code** 2X (solid) **Conveyance classification** toxic substance
Supply classification very toxic, dangerous for the environment
Risk phrases Toxic in contact with skin and if swallowed – Very toxic by inhalation – Irritating to eyes and skin – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R26, R36/38, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) harlequin fish, rainbow trout, golden orfe, guppy, carp 0.03-0.11 mg l^{-1} (1,2).
LC_{50} (48 hr) red killifish 0.66 mg l^{-1} (3).
LC_{50} (96 hr) fathead minnow 7.1 μg l^{-1} (4).
LC_{50} (30 day) fathead minnow 0.23 μg l^{-1} (4).

Invertebrate toxicity
EC_{50} *Skeletonema costatum, Thalassiosira pseudonana* 0.66-1.2 μg l^{-1} (exposure duration unspecified) (5).

Environmental fate

Abiotic removal
Dehydration occurs at temperatures >45°C yielding bis(triphenyltin) oxide which is stable up to 250°C (1).
Slowly decomposed by sunlight, and more rapidly by UV light to give inorganic tin via di- and mono-phenyltin compounds (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >100 mg kg^{-1} (6).
LD_{50} oral rat 46 mg kg^{-1} (7).
LD_{50} oral mouse 171-268 mg kg^{-1} (8,9).
LD_{Lo} intraperitoneal mouse 8.5 mg kg^{-1} (10).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail 38.5 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 2 mg kg^{-1} diet (1).
National Toxicology Program tested rats and mice via feed. Negative results were reported in ♂ and ♀ rats and mice (11).

Teratogenicity and reproductive effects
TD_{Lo} oral rat 105 mg kg^{-1} day^{-1} on days 8-14 of gestation, no teratogenic effects observed (11).

Irritancy
Caused severe irritation in contact with guinea pig eye for 2 sec (12).

Sensitisation
Negative in patch tests on agricultural workers (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (14).
In vitro mouse lymphoma L5178Y, tk^+/tk^- point mutation assay positive (15).
In vitro Chinese hamster ovary cells, hypoxanthine-guanine phosphoriboxyl transferase assay negative, induction of micronuclei positive (15).

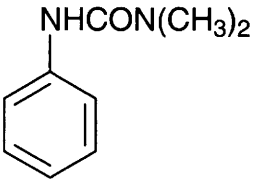
Legislation

EEC maximum residue levels celery 1 ppm, carrots 0.1 ppm, other fruit and vegetables 0.05 ppm (1).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (16).
Pesticides and organometallic compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (17).
Partition coefficient exceeds European Union limit of 3.0.
WHO Toxicity Class II (18).
EPA Toxicity Class II (19).
ADI humans 0.0005 mg kg^{-1} (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Tooby, T. E. et al *Chem. Ind. (London)* 21 June 1975.
3. Nagase, H. et al *Appl. Organomet. Chem.* 1991, **5**, 91-97.
4. Jarvinen, A. W. et al *Environ. Pollut.* 1988, **52**(4), 289-301.
5. Walsh, G. E. et al *Environ. Toxicol. Chem.* 1987, **6**(10), 767-770.
6. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
7. *Litton Bionetics Progress Report* 1972, Contract No. NIH-NCI-E-C-72-3252, Bethesda, MD, USA.
8. *Yakkyoku* 1979, **30**, 505.
9. *Clin. Toxicol.* 1978, **13**(2), 281- 296.
10. *Toxicol. Appl. Pharmacol.* 1972, **23**, 288.
11. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-139, NIEHS, Research Triangle Park, NC, USA.
12. *Toxicol. Appl. Pharmacol.* 1969, **14**, 628.
13. Lisi, P. et al *Contact Dermatitis* 1986, **15**(5), 266-269.
14. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19** (Suppl. 21), 2-141.
15. Oshiro, Y. et al *J. Appl. Toxicol.* 1991, **11**(3), 167-177.
16. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
17. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
18. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
19. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

F27 fenuron



$C_9H_{12}N_2O$ **Mol. Wt.** 164.21 **CAS Registry No.** 101-42-8

Synonyms *N,N*-dimethyl-*N'*-phenylurea; 1,1-dimethyl-3-phenylurea; Dibar; Fenidin; Ferulon; PDU; 3-phenyl-1,1-dimethylurea

EINECS No. 202-941-4 **RTECS No.** YT 1450000

Uses Catalyst. Herbicide.

Physical properties

M. Pt. 133-134°C **Specific gravity** 1.08 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} 0.87 (1) **Volatility** v.p. 1.6×10^{-4} mmHg at 60°C
Solubility Water: 3.85 g l^{-1} at 25°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, *n*-hexane, groundnut oil

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) guppy 610 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (10 day) *Chlorococcum* sp., *Dunaliella tertiolecta, Isochrysis galbana* and *Phaeodactylum tricornutum* 750-1500 µg l^{-1} (3).

Bioaccumulation
Calculated bioconcentration factor range 1-6 (4).

Environmental fate

Degradation studies
Biodegradation is a step-by-step demethylation process in soil and water (5).
Rhizoctonia solani degraded 10% (initial concentration unspecified) after 6 days in a pure culture study (6).

Abiotic removal
Oxidised by ozone at concentrations of 1.5-2.3 mg l^{-1} ozone at pH 8.0-8.5. Levels were reduced from 0.6 mg l^{-1} to <0.1 µg l^{-1} after 8-12 min contact (7).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 2.3 hr (8).
Freundlich adsorption parameter, K, for activated carbon 0.029. Carbon concentration to reduce 5 mg l^{-1} fenuron to 0.1 mg l^{-1}, 500 mg carbon l^{-1} (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit, guinea pig 3200-7500 mg kg^{-1} (10,11).

Sub-acute and sub-chronic data
Oral rat (90 day) 500 mg kg^{-1} diet caused no apparent adverse effects (2).
LC_{50} (5 day) oral bobwhite quail, Japanese quail, ringnecked pheasant, mallard duck >5000 mg kg^{-1} diet (12).

Teratogenicity and reproductive effects
Gavage rat 20, 75, 1500 mg kg^{-1} day^{-1} on days 6-15 of gestation caused dose-related foetal and maternal toxicity, characterised by defects in circulation, the stomach, intestine and heart. The brain showed disruption of haemodynamics and dystrophic alterations (13).

Metabolism and toxicokinetics
Metabolised by microorganisms, plants and animals by *N*-demethylation and *N*-demethoxylation (14).

Genotoxicity

In vitro mouse, inhibition of testicular DNA synthesis positive (15).
In vitro mouse bone marrow, induction of micronuclei negative (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (16).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (17).
WHO Toxicity Class Table 5 (18).

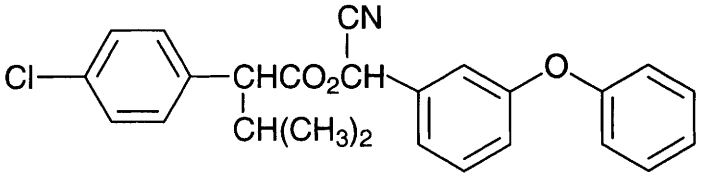
Other comments

Residues have been isolated from crops (14).

References

1. Nendza, M. *Chemosphere* 1991, **23**(4), 497-506.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Walsh, G. E. *Hyacinth Control J.* 1972, **10**, 45-48.
4. Kenaga, E. E. *Ecotoxicol. Environ. Saf.* 1980, **4**, 26-38.
5. Abel, A. L. et al *World Crops* 1957, 328-330.
6. Weinberger, M. et al *Appl. Microbiol.* 1972, **24**, 750-754.
7. Konyk, L. V. et al *Khim. Tekhnol. Vody*.1987, **9**(2), 145-147 (Russ.) (*Chem. Abstr.* **107**, 12549b).
8. Atkinson, R. *Environ. Toxicol. Chem.* 1988, **7**, 435-442.
9. Sforzolini, G. S. et al *Boll. – Soc. Ital. Biol. Sper.* 1970, **46**, 903-906.
10. *Farm Chemicals Handbook* 1980, **D137**, Meister Publishing, Willoughby, OH, USA.
11. Bailey, J. L. et al *Residue Rev.* 1965, **10**, 97.
12. Hill, E. F. et al *Lethal Dietary Toxicities of Environmental Pollutants to Birds* 1975, US Fish and Wildlife Service, Wildlife Report No. 191, Washington, DC, USA.
13. Talakin, Y. N. et al *Gig. Sanit.* 1989, (9), 73-75.
14. Kolbe, A. et al *Biochem. Physiol. Pflanz.* 1987, **182**(4), 267-283.
15. Seiler, J. P. *Mutat. Res.* 1978, **58**(2-3), 353-359.
16. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
17. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
18. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F28 fenvalerate



$C_{25}H_{22}ClNO_3$ **Mol. Wt.** 419.91 **CAS Registry No.** 51630-58-1

Synonyms α-cyano-3-phenoxybenzyl-2-(4-chlorophenyl)-3-methylbutyrate; cyano(3-phenoxyphenyl)methyl-4-chloro-α-(1-methylethyl)benzeneacetate; Ectrin; Sumicidin; Fenbaz; Kayvalerate; Lyder; Pydrin; Tribute

EINECS No. 257-326-3 **RTECS No.** CY 1576350

Uses Insecticide. Acaricide.

Physical properties

B. Pt. 300°C at 37 mmHg **Specific gravity** 1.175 at 25°C with respect to water at 25°C
Partition coefficient log P_{ow} 5.01 at 23°C (1) **Volatility** v.p. 1.1×10^{-8} mmHg at 25°C
Solubility Water: <1 mg l^{-1} at 20°C. Organic solvents: acetone, chloroform, cyclohexanone, ethanol, hexane, methanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) rainbow trout, carp 20, 76 μg l^{-1}, respectively (1,2).
Inhibited magnesium and sodium-potassium ATPases in the gill, brain, liver and muscle of carp after exposure to 10 μg l^{-1} for 6-48 hr (3).

Invertebrate toxicity

LC_{50} (96 hr) grass shrimp 0.007-0.071 μg l^{-1} (4).
LC_{50} contact bee 0.02-0.30 μg bee^{-1} (5).

Bioaccumulation

Bioconcentration factors for sheepshead minnow, fathead minnow, carp, eastern oyster 600-3000 (6-9).

Environmental fate

Carbonaceous inhibition

The cyanobacteria *Nostoc linckia* and *Scenedesmus bijugatus* growth inhibited at concentrations of 10-50 μg l^{-1}. *Phormidium tenue* and *Synechococcus elongatus* showed stimulated gogenase (25).

Metabolism and toxicokinetics

9% of a 1.18 μg dose was absorbed though human skin *in vitro* (26).
Following oral administration of carbonyl-[^{14}C] fenvalerate to chickens, 85% of the dose was eliminated in 24 hr, followed by an additional 3% after 48 hr and a further 0.2% after 6 days. Eggs layed within 24 hr contained radiocarbon, mainly in the albumen. Residue in the yolk peaked in 4-5 days. In the hen, radiocarbon residues were detected mainly in the liver and kidney. Metabolism occurred rapidly by hydrolytic cleavage of the ester bond followed by extensive hydroxylation of the acid moiety at the carbon adjacent to carboxyl group, the methyl group, or both (27).
Following administration to mice by gavage of ^{14}C-labelled fenvalerate, radioactivity was distributed mainly in the liver, kidneys, lung, skin and hair. Elimination occurred principally via the urine (28).
A lipophilic metabolite, cholesteryl (2*R*)-2-(4-chlorophenyl)isovalerate has been detected in several tissues, notably the adrenal glands, liver and mesenteric lymph nodes, of rats and mice. In the mouse, this metabolite was

produced in the brain, kidney and spleen, and to a lesser extent in liver microsomes. This metabolite has been indicated as the causative agent for microgranulomatous changes following administration of fenvalerate (29-31).

Irritancy

Dermal rabbit (3 wk) 100 mg kg^{-1} 5 day wk^{-1} caused mild irritation (14).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA104, TA1535, TA1537, TA1538 with and without metabolic activation negative (32).
Drosophila melanogaster sex-linked recessive lethal assay, sex-chromosome loss and nondisjunction negative (33).
In vitro human lymphocytes, sister chromatid exchanges and chromosomal aberrations positive (34).
In vivo mouse bone marrow, chromosome aberrations, induction of polychromatic erythrocytes, micronuclei and sperm abnormalities positive (35).
In vivo oral administration to mice and rats 25, 50 or 100 mg kg^{-1} day^{-1}, dominant lethal assay and fertility effects negative (15).

Legislation

EEC maximum residue level for pome and stone fruit, grapes 0.5 ppm (14).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (36).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (37).
EPA Toxicity Class II (14).
WHO Toxicity Class II (38).
Tolerable daily intake (TDI) human 0.02 mg kg^{-1} (14).

Other comments

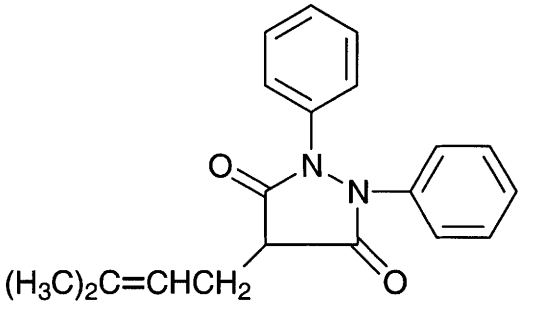
Residues have been detected on crops (22).
Mode of action, mammalian toxicity, metabolism and environmental fate of pyrethroid insecticides reviewed (6,39).
Physical properties, use, occurrence, analysis, regulations, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (22).

References

1. Coats, J. R. et al *Bull. Environ. Contam. Toxicol.* 1979, **23**, 250-255.
2. Jagan, P. et al *J. Environ. Biol.* 1989, **10**(2), 135-138.
3. Reddy, P. M. et al *Biochem. Int.* 1991, **23**(4), 715-721.
4. Baughman, D. S. et al *Environ. Toxicol. Chem.* 1989, **8**(5), 417-429.
5. Leahy, J. P. (Ed.) *The Pyrethroid Insecticides* 1985, Taylor Francis, London, UK.
6. Schimmel, S. C. et al *J. Agric. Food. Chem.* 1983, **31**, 104-113.
7. Hansen, D. J. et al *Environ. Toxicol. Chem.* 1983, **2**, 251-258.
8. Spehar, R. L. et al *Aquat. Toxicol.* 1983, **3**, 171-182.
9. Ohkawa, H. et al *J. Pestic. Sci.* 1980, **5**, 11-22.
10. Megharaj, M. et al *Ecotoxicol. Environ. Saf.* 1987, **14**(2), 142-146.
11. Cotham, W. E. Jr. et al *J. Agric. Food Chem.* 1989, **37**(3), 824-828.
12. Sun, J. et al *Yuanzineng Nongye Yingyong* 1986, (3), 8-14 (Ch.) (*Chem. Abstr.* **107**, 149201b).
13. Mikami, N. et al *J. Pestic. Sci.* 1980, **5**, 225-236.
14. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
15. *Pesticide Residues in Food-1979 Evaluations* 1980, FAO Plant Production and Protection Paper No. 20, Suppl. FAO, United Nations, Rome, Italy.
16. *Farm Chemicals Handbook* 1983, **C104**, Meister Publishing Co., Willoughby, OH, USA.
17. *Arch. Toxicol.* 1980, **45**, 325.
18. *Toxicol. Appl. Pharmacol.* 1982, **66**, 290.
19. Majumder, S. et al *Toxicol. Environ. Chem.* 1996, **55**(1-4), 103-113.

20. Parker, C. M. et al *Fundam. Appl. Toxicol.* 1984, **4**, 577-586.
21. Cabral, J. R. P. et al *Cancer Lett. (Shannon, Irel.)* 1990, **49**, 13-18.
22. *IARC Monograph* 1991, **53**, 309-328.
23. *Pesticide Residues in Food – 1981 Evaluations* 1982, FAO Plant Production and Protection, Paper No. 42, FAO, United Nations, Rome, Italy.
24. Parker, C. M. et al *Fundam. Appl. Toxicol.* 1983, **3**, 114-120.
25. Ghosh, T. K. *Environ. Ecol.* 1990, **8**(IA), 63-67.
26. Shehata-Keram, H. et al *Toxicol. Lett.* 1988, **40**(3), 233-239.
27. Akhtar, M. H. et al *J. Agric. Food Chem.* 1989, **37**(1), 190-196.
28. Gong, Z. et al *Shanghai Yike Daxue Xuebao* 1989, **16**(4), 269-272 (Ch.) (*Chem. Abstr.* **112**, 15904c).
29. Keneko, H. et al *Toxicol. Appl. Pharmacol.* 1986, **83**, 148-156.
30. Okuno, Y. et al *Toxicol. Appl. Pharmacol.* 1986, **83**, 157-169.
31. Tokamatsu, Y. et al *J. Pestic. Sci.* 1987, **12**, 397-404.
32. Herrera, A. et al *Mutagenesis* 1988, **3**(6), 509-514.
33. Batiste-Alentorn, M. et al *Mutagenesis* 1987, **2**(1), 7-10.
34. Ping, M. et al *Mutagenesis* 1989, **4**, 72-74.
35. Pati, P. C. et al *Mutat. Res.* 1989, **222**(3), 149-154.
36. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
37. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
38. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999*, WHO/PCS/98.21.
39. *IPCS Environmental Health Criteria 95: Fenvalerate* 1990, WHO, Geneva, Switzerland

F29 feprazone



$C_{20}H_{20}N_2O_2$ **Mol. Wt.** 320.39 **CAS Registry No.** 30748-29-9

Synonyms 4-(β-isoamylenyl)-1,2-diphenyl-3,5-pyrazolidenedione; 4-(2-isopentenyl)-1,2-diphenyl-3,5-pyrazolidinedione; Methrazone; 4-(3-methyl-2-butenyl)-1,2-diphenyl-3,5-pyrazolidinedione; Analud; Fenilphrenzone; Methrazone; Prenazone; Zepelin

EINECS No. 250-324-3 **RTECS No.** UQ 8530000

Uses Anti-inflammatory drug.

Physical properties

M. Pt. 156.5°C

Solubility Organic solvents: acetone, benzene, chloroform, diethyl ether, dimethyl formamide, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1070, 1340 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal mouse, rat 270, 360 mg kg^{-1}, respectively (1).
LD_{50} intravenous mouse 180 mg kg^{-1} (2).

Teratogenicity and reproductive effects

TD_{Lo} oral rat 2840 mg kg^{-1} on days 7-17 of gestation, teratogenic effects (skeletal effects) (1).

Other effects

Other adverse effects (human)

Gastro-intestinal disturbances, rashes, jaundice, nephropathy, blood disorders, oedema, headache and tinnitus have been reported among patients (4).

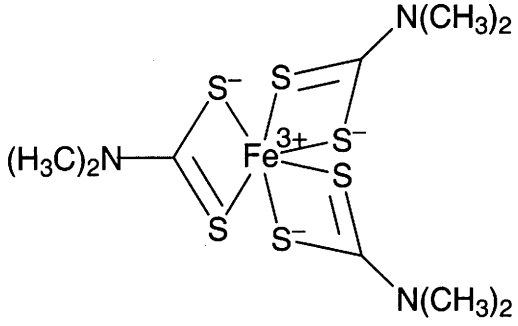
Any other adverse effects

An inducer of the rat hepatic mixed-function oxidase system, showing selectivity toward the P_{450} IIB family of proteins (5).

References

1. *Iyakuhin Kenkyu* 1979, **10**, 149.
2. Biarchi, C. et al *Arzneim.-Forsch.* 1972, **22**, 196.
3. Berry, D. et al *Xenobiotica* 1988, **18**(7), 857-868.
4. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
5. Smith, J. N. et al *J. Biochem. Toxicol.* 1990, **5**(1), 9-12

F30 ferbam



$C_9H_{18}FeN_3S_6$ **Mol. Wt.** 416.51 **CAS Registry No.** 14484-64-1

Synonyms ferric dimethyldithiocarbamate; iron dimethyldithiocarbamate; tris(dimethylcarbamodithioato-*S,S'*)iron; tris(*N, N*-dimethyldithiocarbamato)iron(III); Fermate; Ferradow; Hexaferb; Trifungol

EINECS No. 238-484-2 **RTECS No.** NO 8750000

Uses Fungicide. Vulcanisation accelerator.

Physical properties

M. Pt. 180°C (decomp.) **Partition coefficient** log P_{ow} –1.6
Solubility Water: 120 mg l^{-1} at 20°C. Organic solvents: acetone, acetonitrile, chloroform, pyridine

Occupational exposure

DE-MAK 15 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 10 mg m^{-3}
UK-LTEL 10 mg m^{-3} **UK-STEL** 20 mg m^{-3}
US-TWA 10 mg m^{-3}
Supply classification irritant
Risk phrases Irritating to eyes, respiratory system and skin (R36/37/38)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) freshwater catfish 2.2 mg l^{-1} (1).
LC_{50} (24, 48 hr) killifish 1.0, 0.8 mg l^{-1}, respectively (2,3).

Invertebrate toxicity
EC_{50} (96 hr) eastern oyster 0.075 mg l^{-1} (3).
EC_{50} (15 min) *Photobacterium phosphoreum* 0.199 ppm Microtox test (4).

Environmental fate

Nitrification inhibition
Threshold of inhibition of nitrification, rotating disc 0.5 mg l^{-1}. 80% inhibition of nitrification/denitrification in activated sludge process (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 1130, 3400 mg kg^{-1}, respectively (6,7).
LD_{50} intraperitoneal rat 2700 mg kg^{-1} (8).

Carcinogenicity and chronic effects
No adequate data for evaluation of carcinogenicity to humans, insufficient evidence of carcinogenicity to animals, IARC classification group 3 (9).
Gavage mouse (78 wk) 10 mg kg^{-1} day^{-1} for 3 wk, followed by oral administration of 32 mg kg^{-1} diet did not cause a significantly greater tumour incidence (10).
Oral rat (2 yr) 0, 25, 250 or 2500 mg kg^{-1} diet did not cause a significant increase in treatment-related tumours. The median length of survival for the high-dose group was reduced to 430 days compared with 600-700 days for controls (11).
Subcutaneous mouse (18 month) single dose of 100 mg kg^{-1} at 28 days of age, did not cause an increased incidence of tumours (12).

Teratogenicity and reproductive effects
Oral mouse 1000 mg kg^{-1} day^{-1} for 5 days caused a significant increase in abnormal sperm. No adverse effects were observed following intraperitoneal administration. The study concluded that oral administration succeeded in producing active metabolites able to interfere with the differentiation process of spermatogenesis (13).
Oral rat 150 mg kg^{-1} day^{-1} on days 6-15 of gestation caused some foetal deaths, increased resorption, decreased foetal weight and produced a slight increase in the number of animals with soft and skeletal tissue abnormalities (14).

Metabolism and toxicokinetics

40-70% of an oral dose to rats was absorbed from the gastro-intestinal tract. 18% of the dose was exhaled via the lungs as carbon disulfide and 23-43% in the urine (15).

When pregnant rats were dosed with [dimethyl-^{14}C]ferbam, a small amount of radioactivity crossed the placenta and accumulated in the foetuses. Radioactivity was also secreted in the milk of lactating rats and was in turn excreted in the urine of the pups (15,16).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with metabolic activation positive (17).

Bacillus subtilis H17 rec$^+$ M45 rec$^-$ DNA damage positive (18).

Escherichia coli microtitration SOS chromotest without metabolic activation positive (19).

Aspergillus niger and *Allium cepa* chromosome aberrations and gene conversions positive (20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (21).

Pesticides and organometallic compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (22).

Regulated in the USA (23,24).

WHO Toxicity Class Table 5 (25).

EPA Toxicity Class IV (26).

Tolerable daily intake (TDI) human 0.02 $mg\ kg^{-1}$ (26).

Other comments

Residues have previously been detected in crops (27).

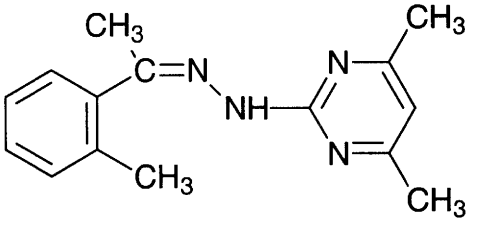
Physical properties, use, occurrence, carcinogenicity, genotoxicity and mammalian toxicity reviewed (27,28,29).

References

1. A. D. Little Inc. *Relationship Between Organic Chemical Pollution of Fresh Water and Health* 1970, FWQA.
2. Lowe, J. I. *Selected Data Presented at Pesticides Ecology Seminar 1970, Athens, Georgia* 1970, Bureau of Commercial Fisheries, Pesticide Field Station, Gulf Breeze, FL, USA.
3. Pimental, D. *Ecological Effects of Pesticides on Non-Target Species* June 1971, Presidential Report, Office of Science and Technology.
4. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
5. Kroetze, C. *Water Report* 1979, (9), 5-6.
6. *Farmakol. Toksikol. (Moscow)* 1969, **32**, 356.
7. *J. Toxicol. Environ. Health* 1978, **4**, 93.
8. Hodge, H. C. et al *J. Am. Pharm. Soc.* 1952, **41**, 662.
9. *IARC Monograph* 1987, **Suppl. 7**, 63.
10. Innes, J. R. M. et al *J. Natl. Cancer Inst.* 1969, **42**, 1101-1114.
11. Hodge, H. C. et al *J. Pharmacol. Exp. Ther.* 1956, **118**, 174-181.
12. *Evaluation of Carcinogenic, Teratogenic and Mutagenic Activities of Selected Pesticides and Industrial Chemicals* 1968, **1**, National Technical Information Service, US Dept. Commerce, Washington, DC, USA.
13. Quinto, I. et al *Mutat. Res.* 1989, **224**(4), 405-408.
14. Minor, J. L. et al *Toxicol. Appl. Pharmacol.* 1974, **29**, 120.
15. Hodgson, J. R. et al *Toxicol. Appl. Pharmacol.* 1975, **33**, 503-513.
16. Hodgson, J. R. et al *Fed. Proc.* 1974, **33**, 537.
17. Remondelli, P. et al *Med., Biol., Environ.* 1986, **14**(1), 377-386.
18. Shirasu, Y. et al *Mutat. Res.* 1976, **40**, 19-30.
19. Xu, H. H. et al *Toxic. Assess.* 1990, **5**(1), 1-14.
20. Prasad, I. et al *Phytopathology* 1968, **58**, 1188-1189.
21. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.

22. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
23. *US Code of Federal Regulations: Protection of Environment* 1974, **40**(180.114), 248-249, Washington, DC, USA.
24. *US Code of Regulations: Air Contaminants* 1975, **29**(1910.1000), 61, Washington, DC, USA.
25. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
26. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
27. *IARC Monograph* 1976, **12**, 121-129.
28. *Dangerous Prop. Ind. Mater. Rep.* 1988, **8**(6), 57-63.
29. Richardson, M. L. (Ed.) *Chemical Safety International Reference Manual* 1994, 141- 156, VCH Publishers, Weinheim, Germany

F31 ferimzone



$C_{15}H_{18}N_4$ **Mol. Wt.** 254.33 **CAS Registry No.** 89269-64-7

Synonyms (Z)-2'-methylacetophenone 4,6-dimethylpyrimidin-2-ylhydrazone; (Z)-4,6-dimethyl-2(1*H*)-pyrimidinone[1-(2-methylphenyl)ethylidene]hydrazone

Uses Fungicide.

Physical properties

M. Pt. 175-176°C **Specific gravity** 1.185 **Partition coefficient** log P_{ow} 2.89 at 25°C

Volatility v.p. 4.11×10^{-3} mPa at 20°C

Solubility Water: 162 mg l^{-1} at 30°C. Organic solvents: acetonitrile, chloroform, ethanol, ethyl acetate, xylene

Ecotoxicity

Fish toxicity

LC_{50} (72 hr) carp 10 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} oral bee >140 μg bee^{-1} (1).

Environmental fate

Abiotic removal

Stable to sunlight. Stable in neutral and alkaline aqueous solutions (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail, mallard ducks >2250, >292 mg kg^{-1}, respectively (1).

LD_{50} oral ♂ rats 725, ♀ rats 642, ♂ mice 590, ♀ mice 542 mg kg^{-1} (1).

LD_{50} dermal rats >2000 mg kg^{-1} (1).

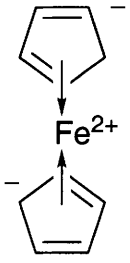
Legislation

WHO Toxicity Class III (2).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (3).
Included in Schedules 5 and 6 (Release into Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F32 ferrocene



$C_{10}H_{10}Fe$ **Mol. Wt.** 186.04 **CAS Registry No.** 102-54-5

Synonyms bis(cyclopentadienyl)iron; di-2,4-cyclopentadien-1-yliron

EINECS No. 203-039-3 **RTECS No.** LK 0700000

Uses Anti-knock additive for gasoline. Catalyst. Fireproofing agent. Photoimaging agent.

Physical properties

M. Pt. 174-176°C **B. Pt.** 249°C
Solubility Organic solvents: benzene, diethyl ether, ethanol, petroleum ether

Occupational exposure

FR-VME 10 mg m^{-3}
UK-LTEL 10 mg m^{-3} **UK-STEL** 20 mg m^{-3}
US-TWA 10 mg m^{-3}

Environmental fate

Degradation studies
Used as substrate by *Rhus vernicifera* (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 832, 1320 mg kg^{-1}, respectively (2,3).
LD_{50} intraperitoneal mouse, rat 335, 500 mg kg^{-1}, respectively (4).
LD_{50} intravenous mouse 178 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Oral administration of 30, 100, 300, 1000 mg kg^{-1} day^{-1}. Animals were killed at 12 wk, 6 months or observed for 1 yr or 26 months after 6-month treatment period. It was concluded that ferrocene induced cirrhotic liver changes, affected erythrocytes and produced testicular hypoplasia (6).
Inhalation rat, mouse (2 wk) 0-40 mg m^{-3} 6-hr day^{-1}. No fatalities or signs of clinical toxicity were observed. ♂ rats, mice were found to have exposure-related decreases in body, liver and spleen weights and an increase in thymus weight. ♀ mice had decreased brain, liver and spleen weights. Histopathological examination revealed only lesions in the nasal turbinates of both species. *In vitro* studies showed that nasal tissue, particularly the olfactory epithelium had ≈10 × higher ferrocene hydroxylase activity than the liver tissue (7).
Oral dog (1 wk) 300 mg kg^{-1} day^{-1} produced haemosiderosis, with a dose-related decrease in haemoglobin, packed-cell volume and erythrocyte count (8).

Metabolism and toxicokinetics

Metabolism of ferrocene was studied in rats following inhalation exposure to 88 μg ferrocene labelled with ^{59}Fe for 17 min. 2 hr after exposure 55% was deposited in nasopharyngeal region and 30% in bronchopulmonary region. Clearance $t_{1/2}$ was 200 days in bronchopulmonary region and 70 days in nasopharyngeal region (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with metabolic activation positive (10).
In vitro Chinese hamster ovary cells with metabolic activation sister chromatid exchanges positive (11).
Drosophila melanogaster 100 ppm, sex chromosome loss and nondisjunction positive; parental 100 ppm, heritable translocation test positive (12).

Other effects

Other adverse effects (human)

Biological effects of exposure were described, including target organs, acute, sub-acute, chronic and human effects. Primarily affects gastro-intestinal system and central nervous system; carcinogenic effects are possible (13).

Other comments

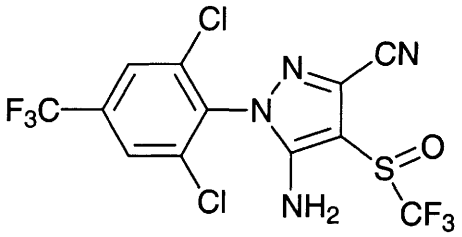
Toxicology and occupational hazard reviewed (14,15).
Properties and toxicological effects of ferrocene reviewed (16,17).

References

1. Ji, L. et al *Zuran Zazhi*, 1990, **13**(3), 189-190 (Ch.) (*Chem. Abstr.* **113**, 128511m).
2. *Shell Chemical Company Report* 1961, 5, San Roman, CA, USA.
3. *Br. J. Pharmacol. Chemother.* 1965, **24**, 352.
4. *Progress Report PH-43-64-886 to Natl. Cancer Inst.* 1965, Inst. Chem. Biol., San Francisco, CA, USA.
5. *US Army, Armament Res. Dev. Command* NX. 02382, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA.
6. Yeary, R. A. *Toxicol. Appl. Pharmacol.* 1969, **15**, 666-676.
7. Sun, J. D. et al *Fundam. Appl. Toxicol.* 1991, **17**(1), 150-158.
8. Osal, A. et al (Ed.) *Remmington's Pharmaceutical Sciences* 15th ed., 1975, 177, Mack Publishing Co., Easton, PA, USA.
9. Dahl, A. R. et al *Toxicol. Appl. Pharmacol.* 1980, **56**(2), 232-239.
10. Haworth, S. et al *Environ. Mutagen.* 1983, **5**(Suppl. 1), 3-143.
11. Galloway, S. M. et al *Environ. Mutagen.* 1985, **7**, 1-5.
12. Zimmering, S. et al *Environ. Mutagen.* 1985, **7**(1), 87-100.

13. *NIOSH Info. Profiles on Potential Occup. Hazards* 1977, 210-77-0120, 143-156.
14. *Info. Profiles in Potential Occup. Hazards Metallocenes* 1981, SRC TR81-623,210-79-0030, 1-25.
15. *Tox-Tips Ferrocene* 1987, 130-23, National Toxicology Program, Bethesda, MD, USA.
16. Levis, C. E. *J. Occup. Med.* 1960, 225-228.
17. Sullivan, R. J. *Natl. Air Pollut. Control Admin.* 1969 APTO 69-38, 1-94 Consumer Protection and Environmental Health Service

F33 fipronil



$C_{12}H_4Cl_2F_6N_4OS$ **Mol. Wt.** 437.15 **CAS Registry No.** 120068-37-3

Synonyms (±)-5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile; (±)-5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl)sulfinyl]-1*H*-pyrazole-3-carbonitrile; Regent; Prince

Uses Pyrazole insecticide used in the control of many soil and foliar insects on a variety of crops and non-crops.

Physical properties

M. Pt. 200-201°C **Partition coefficient** log P_{ow} 4.0 **Volatility** v.p. 2.8×10^{-12} mmHg at 20°C
Solubility Water: 2 mg l^{-1}. Organic solvents: acetone, corn oil

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) Japanese carp 0.34 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} *Daphnia magna* (48 hr) 0.19 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral pheasants, mallard ducks 31, >2000 mg kg^{-1}, respectively (1).
LD_{50} oral rats 100 mg kg^{-1} (1).
LD_{50} dermal rabbit >354 mg kg^{-1} (1).

Irritancy
Non-irritating to skin, slightly irritating to eyes (1).

Genotoxicity

Not genotoxic in the Ames and chromosome aberration tests (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).
WHO Toxicity Class II (4).

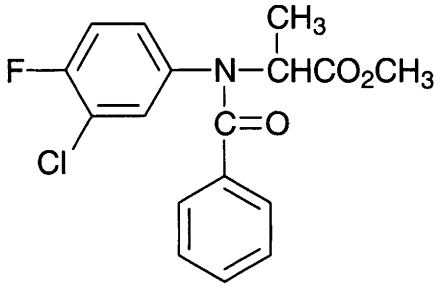
Other comments

Fipronil acts as a potent blocker of the GABA-regulated chloride channel in insects (5).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
5. Cole, L. M. et al *Pestic. Sci.* 1994, **42**(1), 59-63

F34 flamprop-methyl



$C_{17}H_{15}ClFNO_3$ **Mol. Wt.** 335.76 **CAS Registry No.** 52756-25-9

Synonyms methyl *N*-benzoyl-*N*-(3-chloro-4-fluorophenyl)alaninate

EINECS No. 258-155-7 **RTECS No.** UE 8900000

Uses Superseded herbicide.

Physical properties

M. Pt. 84-86°C

Solubility Water: 35 mg l^{-1} at 20°C. Organic solvents: acetone, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 4.7 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 720, 1200 mg kg^{-1}, respectively (2,3).

Metabolism and toxicokinetics

A single oral dose of 4 mg kg^{-1} to rats was rapidly metabolised and 90% of the dose eliminated in the urine and faeces within 48 hr. After 4 days, tissue residues were highest in the kidneys at 0.22 mg kg^{-1}. In other tissues residues were <0.10 mg kg^{-1}. The major metabolic routes were ester hydrolysis to the corresponding acid, hydroxylation of the benzoyl aromatic rings and conjugation. (*R*)-flamprop-methyl isomer was partially converted into the (*S*)-form (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

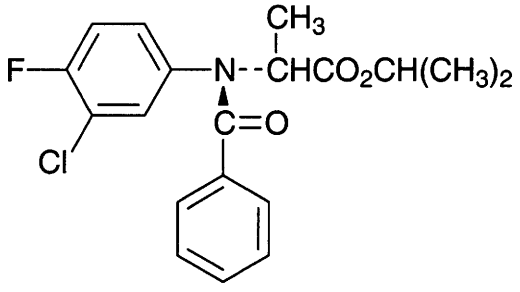
Other comments

Metabolic pathways reviewed (7).

References

1. Fiedler, H. et al *Toxicol. Environ. Chem.* 1990, **26**(1-4), 157-160.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *Farm Chemicals Handbook* 1991, **C190**, Meister Publishing Co., Willoughby, OH, USA.
4. Hutson, D. H. et al *Pestic. Sci.* 1991, **31**(2), 151-152.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

F35 flamprop-M-isopropyl



$C_{19}H_{19}ClFNO_3$ **Mol. Wt.** 363.82 **CAS Registry No.** 63782-90-1

Synonyms (*R*)-1-methylethyl *N*-benzoyl-*N*-(3-chloro-4-fluorophenyl)alaninate; (*R*)-isopropyl *N*-benzoyl-*N*-(3-chloro-4-fluorophenyl)alaninate; Barnon; Cartouche; Commando; Cossack; Gunner; Suffix BW

EINECS No. 261-051-4

Uses Herbicide.

Physical properties

M. Pt. 72.5-74.5°C **Partition coefficient** log P_{ow} 3.69 **Volatility** v.p. 2.4×10^{-7} mmHg at 20°C

Solubility Water: ~12 mg l^{-1} at 20°C. Organic solvents: acetone, cyclohexanone, ethanol, hexane, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 3.3 mg l^{-1} (1).

Environmental fate

Abiotic removal

Undergoes hydrolysis to propan-2-ol and flamprop-M at pH >8.0 (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse >4000 mg kg^{-1} (1,2).
LD_{50} dermal rat >1600 mg kg^{-1} (1,2).
LD_{50} intraperitoneal rat >1200 mg kg^{-1} (1,2).

Sub-acute and sub-chronic data

Oral rat, dog (90 day) 50 mg kg^{-1} diet caused no adverse effects to rats, 30 mg kg^{-1} diet caused no adverse effects to dogs (1,2).

Metabolism and toxicokinetics

Following oral administration to mammals, metabolism and elimination occur within 4 days (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
Partition coefficient exceeds European Union limit of 3.0.

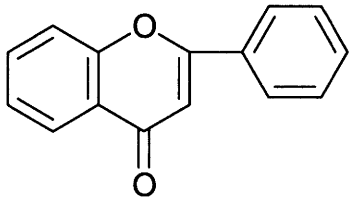
Other comments

In plants, flamprop-M-isopropyl is hydrolysed to the biologically active flamprop-M which then undergoes conversion into a biologically inactive conjugate (1).
Metabolic pathways reviewed (5).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

F36 flavone



$C_{15}H_{10}O_2$ **Mol. Wt.** 222.24 **CAS Registry No.** 525-82-6

Synonyms 2-phenyl-4*H*-1-benzopyran-4-one; 2-phenylchromone; asmacoril; chromocor; cromaril

EINECS No. 208-383-8 **RTECS No.** DJ 3100630

Occurrence Plant flavanoid.

Physical properties

M. Pt. 99-100°C

Solubility Organic solvents: soluble in most organic solvents

Ecotoxicity

Invertebrate toxicity

Minimal inhibitory concentration *Staphylococcus epidermidis* 50 μg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling >100 mg kg^{-1} (2).

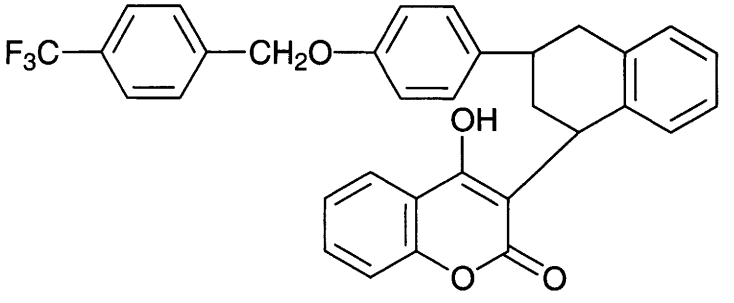
Other comments

Strongly inhibited Epstein-Barr virus activation (3).

References

1. Nishino, C. et al *Agric. Biol. Chem.* 1987, **51**(1), 139-143.
2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
3. Konoshima, T. et al *Shoyakugaku Zasshi* 1989, **43**(2), 135-141

F37 flocoumafen



$C_{33}H_{25}F_3O_4$ **Mol. Wt.** 542.55 **CAS Registry No.** 90035-08-8

Synonyms 4-hydroxy-3-[1,2,3,4-tetrahydro-3-[4-(4-trifluoromethylbenzyloxy)phenyl]-1-naphthyl]coumarin; 4-hydroxy-3-[1,2,3,4-tetrahydro-3-[4-[[4-(trifluoromethyl)phenyl]methoxy]phenyl]-1-naphthalenyl]-2*H*-1-benzopyran-2-one; Storm; Stratagem

RTECS No. DJ 3100300

Uses Rodenticide.

Physical properties

M. Pt. 181-191°C (*cis*-isomer); 163-166°C (*trans*-isomer) **Partition coefficient** log P_{ow} 4.7
Volatility v.p. 1×10^{-12} mmHg at 25°C
Solubility Water: 1.1 mg l^{-1}. Organic solvents: acetone, chloroform, dichloromethane, ethanol

Ecotoxicity

Fish toxicity
Non-toxic to aquatic species (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken, Japanese quail >100 mg kg^{-1} (1).
LD_{50} oral rat, mouse, rabbit 0.2-0.8 mg kg^{-1} (1).
LD_{50} oral cat, goat >10 mg kg^{-1} (1).
LD_{50} oral pig 60 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (5 day) oral Japanese quail 37 mg kg^{-1} diet, oral mallard duck 1.7 mg kg^{-1} diet (1).

Metabolism and toxicokinetics
Appreciable penetration of radioactivity occurred through rat skin following dermal application of ^{14}C-flocoumafen. After 7 days 12% radioactivity remained at the site of application while 25% was located in the liver as unchanged flocoumafen. Unchanged flocoumafen comprised the major product detected in the faeces. Biliary excretion was a very minor route of excretion. Considerable amounts of unchanged flocoumafen associated with the contents of the large intestine after intraperitoneal administration to rats fitted with biliary fistulae indicated that flocoumafen enters the intestine by a non-biliary route (2).
Following oral administration to rats, residues accumulated in the liver, principally as unchanged flocoumafen with a minor polar metabolite. The study suggested the presence in rat liver of a saturable high-affinity binding site and a second binding site of lower affinity. Lethal anticoagulant action occurs only when the binding sites have become saturated. Flocoumafen was not extensively metabolised, with 30-60% being eliminated unchanged in the faeces. Polar metabolites and a lipophilic compound were minor products in the faeces (3).

Other effects

Any other adverse effects

Mode of rodenticidal action is as an indirect anticoagulant. Inhibits the metabolism of vitamin K_1, and thus depletes vitamin K_1-dependent clotting factors in plasma. Blocks formation of prothrombin (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
Partition coefficient exceeds European Union limit of 3.0.
EPA Toxicity Class Ia (4).
WHO Toxicity Class Ia (7).

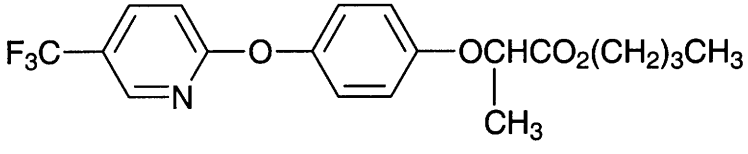
Other comments

Mixture of *cis* and *trans* isomers in the ratio range 60:40 to 40:60 (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Huckle, K. R. et al *Xenobiotica* 1989, **19**(1), 63-74.
3. Huckle, K. R. et al *Xenobiotica* 1988, **18**(12), 1465-1479.
4. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F38 fluazifop-butyl



$C_{19}H_{20}F_3NO_4$ **Mol. Wt.** 383.37 **CAS Registry No.** 69806-50-4

Synonyms (±)-butyl 2-[4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoate; butyl-(*RS*)-2-[4-(5-trifluoromethyl-2-pyridyloxy)phenoxy]propanoate; Fusilade; Halokon; Onecide; Hache Uno Super; Onecide

EINECS No. 274-125-6 **RTECS No.** UA 3000000

Uses Herbicide.

Physical properties

M. Pt. 13°C **B. Pt.** 167°C at 0.05 mmHg **Specific gravity** 1.21 at 20°C **Partition coefficient** log P_{ow} 4.5 (1)
Volatility v.p. 4.1×10^{-6} mmHg at 20°C
Solubility Water: 2 mg l^{-1} at 20°C. Organic solvents: acetone, cyclohexanone, dichloromethane, hexane, methanol, propylene glycol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, mirror carp, rainbow trout 0.53-1.37 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 10.6 ppm, Microtox test (2).

Environmental fate

Degradation studies

Undergoes hydrolysis in soil to yield fluazifop with $t_{1/2}$ <3 days. Fluazifop undergoes further degradation with a $t_{1/2}$ 5-20 wk (1).

Abiotic removal

Photodegradation $t_{1/2}$ 10 days under laboratory conditions. Degradation products included a dimer, a free acid and hydroxylated derivatives (3).

Adsorption and retention

No adsorption was detected in silty clay loam, silt loam or Bloomfield sand (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit 620 mg kg^{-1} (1).
LD_{50} oral rat, mouse, guinea pig 1500-3330 mg kg^{-1} (1).
LD_{50} dermal rabbit >2420 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 1760 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LD_{50} (5 day) oral mallard duck >2500 mg kg^{-1}, ring necked pheasants >18,500 mg kg^{-1} (1).
Oral rat (90 day) no toxicological effects were observed at 100 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects

Oral mouse (2 yr) no toxicological effects were observed at 5 mg kg^{-1} diet (1).
Oral dog (1 yr) no toxicological effects were observed at 5 mg kg^{-1} day^{-1} (1).

Sensitisation

Reported not to cause skin sensitisation (species unspecified) (1).

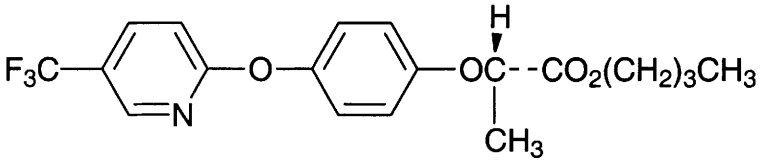
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (7).
EPA Toxicity Class II (8).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Mel'nikora, N. P. et al *Izv. Timiryazevsk. S-kh. Akad.* 1990, (1), 183-186 (Russ.) (*Chem. Abstr.* **112**, 212383h).
4. Rick S. K. et al *Weed Sci.* 1987, **35**(2), 282-288.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
8. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

F39 fluazifop-P-butyl



$C_{19}H_{20}F_3NO_4$ **Mol. Wt.** 383.37 **CAS Registry No.** 79241-46-6

Synonyms butyl (*R*)-2-[4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoate; Barclay Winner; Chorus; Citadel; Fusilade; Grapple; Wizzard

RTECS No. UA 2950000

Uses Herbicide.

Physical properties

M. Pt. 5°C **B. Pt.** 164°C at 0.02 mmHg **Flash point** >50°C **Partition coefficient** log P_{ow} 4.50 (1)
Volatility v.p. 4×10^{-7} mmHg at 20°C
Solubility Water: 1 mg l^{-1}. Organic solvents: acetone, dichloromethane, ethyl acetate, hexane, methanol, toluene, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, mirror carp, rainbow trout 0.53-1.37 mg l^{-1} (the compound stereochemistry was unspecified) (1).

Invertebrate toxicity
LD_{50} oral and contact bee >0.2 mg bee^{-1} (1).

Environmental fate

Degradation studies
In moist soil $t_{1/2}$ for hydrolysis to fluazfop-P <1 wk. Fluazfop-P undergoes further degradation with a $t_{1/2}$ of ~3 wk (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck >3500 mg kg^{-1} (1).
LD_{50} oral rat 2450-3680 mg kg^{-1} (1).
LD_{50} dermal rabbit >2400 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral rat (90 day) no-adverse-effect level 10 mg kg^{-1} (1).

Irritancy
Mild skin and eye irritant to rabbits (1).

Sensitisation
Reported to cause no skin sensitisation (1).

Legislation

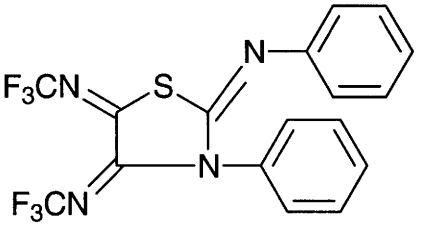
Maximum residue in or on coffee under US Federal Food, Drug and Cosmetic Act 0.1 ppm (2).
EEC maximum residue level for citrus fruit, berries, root, pod and tuber vegetables, brassicas, tomatoes and salads 0.1 ppm (1).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
EPA Toxicity Class IV (4).
ADI 0.01 mg kg^{-1} body weight (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (6).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. US EPA *Fed. Regist.* 1 Mar 1989, **54**(39), 8450.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK

F40 flubenzimine



$C_{17}H_{10}F_6N_4S$ **Mol. Wt.** 416.35 **CAS Registry No.** 37893-02-0

Synonyms *N*-[3-phenyl-4,5-bis[(trifluoromethyl)imino]-2-thiazolidinylidene]benzenamine; N^2,3-diphenyl-N^4,N^5-bis(trifluoromethyl)thiazolidine-2,4,5-triylidenetriamine; Cropotex; SLJ-312

EINECS No. 253-703-1 **RTECS No.** CY 1202500

Uses Superseded acaricide.

Physical properties

M. Pt. 118-119°C **Volatility** v.p. 1.0×10^{-5} mmHg at 20°C
Solubility Water: 30 mg l^{-1} at 20°C. Organic solvents: dichloromethane, hexane, isopropanol, toluene

Occupational exposure

Supply classification irritant, dangerous for the environment
Risk phrases Irritating to the eyes – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R36, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S26, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, golden orfe 0.12-0.26 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} oral bee >0.1 mg bee^{-1} (1).

Environmental fate

Abiotic removal

Hydrolysis $t_{1/2}$ ≈30 hr at pH 4, 30 min at pH 7, 10 min at pH 9 (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♀ rabbit 360 mg kg^{-1} (1).

LD_{50} oral rat 3750 mg kg^{-1} (2).

LC_{50} (4 hr) inhalation rat >357 mg m^{-3} (1).

Genotoxicity

Salmonella typhimurium (strain and metabolic activation unspecified) negative (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).

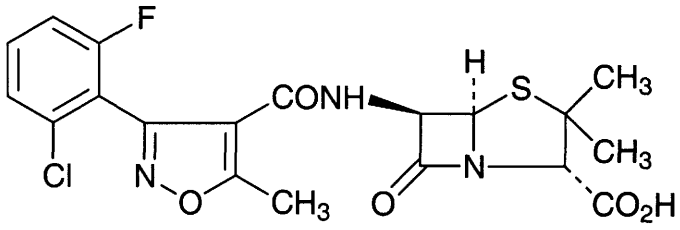
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

WHO Toxicity Class Table 5 (5).

References

1. *The Pesticide Manual* 8th ed., 1987, 406-407, British Crop Protection Council, Thornton Heath, UK.
2. Bluett, D. J. et al *Proc. Br. Crop Prot. Conf.-Pests Dis.* 1981, 75.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F41 flucloxacillin



$C_{19}H_{17}ClFN_3O_5S$ **Mol. Wt.** 453.88 **CAS Registry No.** 5250-39-5

Synonyms 6-[[[3-(2-chloro-6-fluorophenyl)-5-methyl-4-isoxazolyl]carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid; 3-(2-chloro-6-fluorophenyl)-5-methyl-4-isoxazolylpenicillin; Floxacillin; Abbaflox

EINECS No. 226-051-0

Uses Antibiotic.

Mammalian & avian toxicity

Metabolism and toxicokinetics

Rate of absorption from small intestine of anaesthetised rats decreased by increasing pH from 3 to 8, indicating better absorption of the un-ionised form, flucloxacillin being a weak acid (1).

Following intraperitoneal administration to human volunteers, $t_{1/2}$ was 2.1 hr in serum, 1.4 hr in lymph and 11.0 hr in blister fluid. Extravascular penetration was 20% to lymph and 30% to blister fluid. Considering the very high serum protein binding ability, flucloxacillin showed good tissue penetration. The high levels in lymph and blister fluid were explained in part by its affinity for extravascular albumin (2).

Metabolites identified in rat urine were unchanged flucloxacillin, (5*R*)-flucloxacillin penicilloic acid, 5'-hydroxymethylflucloxacillin, and (5*S*)-flucloxacillin penicilloic acid (3).

Other effects

Other adverse effects (human)

Hepatitis and cholestatic jaundice have been reported occasionally among patients. Phlebitis has also been reported following intravenous infusion (4).

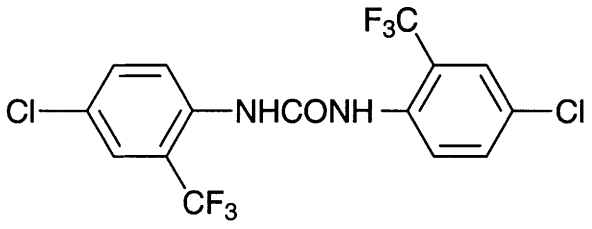
Other comments

Antibiotic active against penicillin-resistant staphylococci (5).

References

1. Nunez-Vergara, L. J. et al *Gen. Pharmacol.* 1988, **19**(3), 447-449.
2. Bergan, T. et al *Antimicrob. Agents Chemother.* 1986, **30**(5), 729-732.
3. Everett, J. R. et al *J. Pharm. Biomed. Anal.* 1989, **7**(3), 397-403.
4. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
5. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

F42 flucofuron



$C_{15}H_8Cl_2F_6N_2O$ **Mol. Wt.** 417.14 **CAS Registry No.** 370-50-3

Synonyms mitin N; *N,N'*-bis[4-chloro-3-(trifluoromethyl)phenyl]urea; 4,4'-dichloro-3.3'-bis(trifluoromethyl)carbanilide

EINECS No. 206-728-7

Uses Superseded insecticide used to control *Tineidae* sp. larvae, which attack cotton fabrics (moth-proofer).

Physical properties

M. Pt. 241-242°C

Ecotoxicity

Fish toxicity

LC_{50} (1 or 7 day) juvenile rainbow trout 150 and 96 μg l^{-1}, respectively (1).

Yearling rainbow trout (40 wk) at concentrations <10 μg l^{-1} survived for 40 wk. At concentrations >10 μg l^{-1} a dose-related decline in survival time was observed (1).

Bioaccumulation

Will accumulate in rainbow trout tissues. Fish exposed to lethal concentrations accumulated average concentrations of 10 mg kg^{-1} in muscle and 20 mg kg^{-1} in viscera. Fish exposed to sub-lethal concentrations accumulated average concentrations of 1 mg kg^{-1} in muscle and 3 mg kg^{-1} in viscera (1).

Mammalian & avian toxicity

Acute data

LD_{50} (unspecified route) rat 750 mg kg^{-1} (1).

Legislation

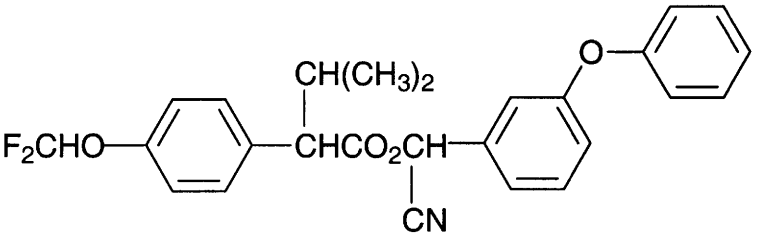
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Abram, F. S. H. et al *The Toxicities of Mitin N and Eulan WA New to Rainbow Trout* Report 156-M, June 1981, Water Research Centre Environmental Protection, Stevenage, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F43 flucythrinate



$C_{26}H_{23}F_2NO_4$ **Mol. Wt.** 451.47 **CAS Registry No.** 70124-77-5

Synonyms 4-(difluoromethoxy)-α-(1-methylethyl)benzeneacetic acid cyano(3-phenoxyphenyl)methyl ester; (±)-cyano-(3-phenoxyphenyl)methyl (+)-4-(difluoromethoxy)-α-(1-methylethyl)benzeneacetate; Cybolt; Guardian; Pay-Off; Stock Guard; Cythrin

EINECS No. 274-322-7 **RTECS No.** CY 1578620

Uses Insecticide. Acaricide.

Physical properties

B. Pt. 108°C at 0.35 mmHg **Specific gravity** 1.189 at 22°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.079 (1) **Volatility** v.p. 9×10^{-9} mmHg at 25 °C
Solubility Water: 0.5 mg l^{-1} at 21°C. Organic solvents: acetone, corn oil, cotton seed oil, hexane, *n*-propanol, soya bean oil, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, channel catfish, bluegill sunfish, sheepshead minnow 0.32-1.6 μg l^{-1} (1).

Invertebrate toxicity
LD_{50} topical bee 0.078 μg bee^{-1} (4).

Environmental fate

Degradation studies
Degradation in soil $t_{1/2}$ 9-12 days (2).

Abiotic removal
Hydrolysis at 27°C, $t_{1/2}$ 40 days at pH 3, 52 days at pH 6, 6.3 days at pH 9 (1).
Photolysis $t_{1/2}$ 3 days on leaf surface and 8 days on glass. The major metabolite is formed via decarboxylation (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♀, ♂ rat 67, 81 mg kg^{-1}, respectively (4).
LD_{50} oral ♀ mouse 76 mg kg^{-1} (4).
LC_{50} (4 hr) inhalation rat 4850 mg m^{-3} (1).
LD_{50} dermal rabbit >1000 mg kg^{-1} (5).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail, mallard duck 3440, 4890 mg kg^{-1} diet, respectively (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 60 mg kg^{-1} diet (1).

Teratogenicity and reproductive effects
Oral rat, three-generation study 30 mg kg^{-1} diet did not cause adverse effects on reproduction. No teratogenic, foetotoxic or mutagenic effects were reported (5).

Metabolism and toxicokinetics
Following oral administration to rats, 60-70% eliminated within 24 hr and >95% within 8 days, in the faeces and urine. In the faeces, excreted principally as the parent compound, but in the urine and tissues several metabolites were present. The major route of metabolism was via hydrolysis with subsequent hydroxylation of the hydrolysis products (1).
May be absorbed through the skin (1).

Sensitisation
Reported not to cause skin sensitisation (species unspecified) (1).

Other effects

Any other adverse effects
Symptoms of toxicity in acute studies in rats included increased agitation, loss of coordination, tremors, loss of appetite, convulsions, respiratory failure and finally death. Dermal application caused an increase in serum urea, transaminase and protein, and total bilirubin. Glycogen production in the liver was reduced and blood glucose levels increased (6).

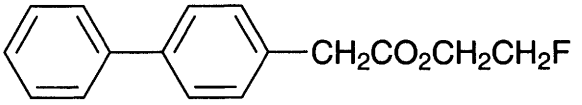
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).
WHO Toxicity Class 1b (9).
EPA Toxicity Class 1 (1).
Tolerable daily intake (TDI) humans 0.02 mg kg^{-1} (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Agnihotri, N. P. et al *Pesticides* 1987, **21**(6), 36-38.
3. Chattopadhyaya, S. et al *Pestic. Sci.* 1991, **31**(2), 163-173.
4. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
5. *The Pesticide Manual* 9th ed., 1991, 406-407, British Crop Protection Council, Farnham, UK.
6. Salek, M. A. A. et al *Egypt J. Food Sci.* 1986, **14**(1), 31-37.
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
9. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F44 fluenetil



$C_{16}H_{15}FO_2$ **Mol. Wt.** 258.29 **CAS Registry No.** 4301-50-2

Synonyms 2-fluoroethyl biphenyl-4-ylacetate; 2-fluoroethyl[1,1'-biphenyl]-4-acetate; 2-fluoroethyl 4-biphenylacetate; Fluenyl; Lambrol; Mytrol

RTECS No. DU 8335000

Uses Superseded insecticide.

Occupational exposure

Supply classification very toxic

Risk phrases Very toxic in contact with skin and if swallowed (R27/28)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S36/37, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6 mg kg^{-1} (1).

LD_{Lo} dermal rat 4 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 42 mg kg^{-1} (3).

Legislation

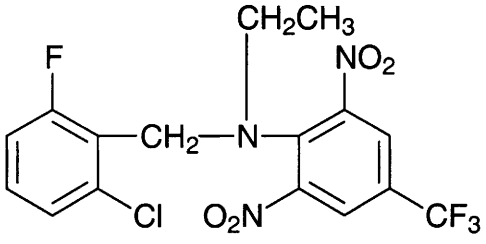
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. *Farm Chemicals Handbook* 1991, **C180**, Meister Publishing, Willoughby, OH, USA.
2. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, 593, Prague, Czechoslovakia.
3. *Environ. Health Perspect.* 1976, **14**, 93.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F45 flumetralin



$C_{16}H_{12}ClF_4N_3O_4$ **Mol. Wt.** 421.74 **CAS Registry No.** 62924-70-3

Synonyms *N*-(2-chloro-6-fluorophenyl)-*N*-ethyl-α,α,α-trifluoro-2,6-dinitro-*p*-toluidine; 2-chloro-*N*-[2,6-dinitro-4-(trifluoromethyl)phenyl]-*N*-ethyl-6-fluorobenzenemethanamine; Prime

RTECS No. DA 4391600

Uses Herbicide. Plant growth regulator.

Physical properties

M. Pt. 101-103°C **Specific gravity** 1.55 at 20°C **Partition coefficient** log P_{ow} 5.45 at 25°C (1)
Volatility v.p. 2.4×10^{-7} mmHg (25°C)
Solubility Water: 0.07 mg l^{-1} at 25°C. Organic solvents: acetone, ethanol, hexane, *n*-octanol, toluene

Environmental fate

Abiotic removal
Direct photolysis occurs in soils to depths of up to 0.4 mm (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >5000 mg kg^{-1} (1).
LD_{50} dermal rat >2000 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (5).
WHO Toxicity Class Table 5 (6).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Hebert, V. R. et al *J. Agric. Food Chem.* 1990, **38**(3), 913-918.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F46 fluoboric acid

$H[BF_4]$

BF_4H **Mol. Wt.** 87.81 **CAS Registry No.** 16872-11-0

Synonyms tetrafluoroboric acid; hydrogen tetrafluoroborate; fluoroboric acid; hydrofluoboric acid

EINECS No. 240-898-3 **RTECS No.** ED 2685000

Uses Catalyst. Electrolyte for electroplating and ion exchange.

Physical properties

B. Pt. 130°C (decomp.) **Specific gravity** 1.40 at 20°C **Volatility** v.p. <7.6 mmHg at 20°C ; v.den. 3.0
Solubility Water: miscible. Organic solvents: ethanol

Occupational exposure

UN No. 1775 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Causes burns (R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Take off immediately all contaminated clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S27, S45)

Ecotoxicity

Fish toxicity
LC_{50} (24, 48, 96 hr) rainbow trout 6950, 5000, 4200 mg l^{-1}, respectively, hard water tests (1).

Environmental fate

Abiotic removal
Undergoes limited hydrolysis in water to form hydroxyfluoborate ions (2).

Mammalian & avian toxicity

Irritancy
Extremely destructive to mucous membranes and the upper respiratory tract, eyes and skin (species unspecified) (3).

Other effects

Any other adverse effects
Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluoride: maximum admissible concentration 1500 μg l^{-1} for average water temperature of 8-12°C, 700 μg l^{-1} for average water temperature of 25-30°C. Boron guide level 1000 μg l^{-1} (4).
Limited under UK Water Quality Regulations. Boron: prescribed concentration 2000 μg l^{-1} (12-monthly average) (5).

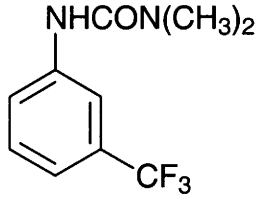
Other comments

Safety precautions and toxicity reviewed (6).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

References

1. Abram, F. S. H. et al *Water Research Centre Report* 1979, Report No. SL 462/00/00 1334c, Stevenage, UK.
2. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
3. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1686, Sigma-Aldrich, Milwaukee, WI, USA.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S.I. 1989 No. 1147, The Water Supply (Water Quality) Regulations* 1989, HMSO, London, UK.
6. *Chemical Safety Data Sheets* 1990, **3**, 103-105, The Royal Society of Chemistry, London, UK.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F47 fluometuron



$C_{10}H_{11}F_3N_2O$ **Mol. Wt.** 232.21 **CAS Registry No.** 2164-17-2

Synonyms *N,N*-dimethyl-*N'*-[3-(trifluoromethyl)phenyl]urea; 1,1-dimethyl-3-(α,α,α-trifluoro-*m*-tolyl)urea; 1,1-dimethyl-3-(3-trifluoromethylphenyl)urea; *N*-(3-trifluoromethylphenyl)-*N,N'*-dimethylurea; 3-(3-trifluoromethylphenyl)-1,1-dimethylurea; Cotoran; Meturon 4L; Coteran; Cotoguard; Coltonex; Dinagam

EINECS No. 218-500-4 **RTECS No.** YT 1575000

Uses Herbicide. Organic synthesis.

Physical properties

M. Pt. 163-164.5°C **Specific gravity** 1.39 at 20°C **Partition coefficient** log P_{ow} 1.7436 (1)
Volatility v.p. 5×10^{-7} mmHg at 20°C
Solubility Water: 80 ppm at 25°C. Organic solvents: acetone, dimethylformamide, dimethyl ether, ethanol, isopropanol, methanol, octan-1-ol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, catfish, bluegill sunfish, crucian carp 47-170 mg l^{-1} (2).

Environmental fate

Degradation studies
Undergoes microbial degradation in soils with the liberation of carbon dioxide. Photodecomposition and volatilisation are insignificant. $t_{1/2}$ in soils ≈30 days (2).

Abiotic removal
Decomposed by UV irradiation.

Adsorption and retention
Freundlich K values 0.37 for Uvrier sand, 1.07 for Callombey sand, 1.66 for Les Evouettes loam, 3.16 for Vetroz sandy clay loam and 1.36 for Illarsatz high organic soil, showing a general positive correlation with organic content of the soils (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, rat 2500, 6146 mg kg^{-1}, respectively (4,5).
LD_{50} dermal rabbit >10,000 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse, rat 550, 685 mg kg^{-1}, respectively (6).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral ring-necked pheasant, Japanese quail, mallard duck 3150, 4500, 4620 mg kg^{-1} diet, respectively (2).
Oral rat (90 day) 2000, 4000 mg kg^{-1} diet caused a dose-related increase in the incidence of red blood cells with polychromasia and anisocytosis. A two-fold increase in spleen weight occurred in ♂ rats fed 4000 mg kg^{-1} diet and in ♀ rats fed 2000 and 4000 mg kg^{-1} diet. Body weight gain was depressed by >10% in ♀ rats fed 4000 mg kg^{-1} diet (7).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (8).
Oral mouse (2 yr) 0, 500 or 1000 mg kg^{-1} diet. A dose-related incidence of tumours of the liver and haematopoietic system was observed in ♂ animals. A non-statistically significant increase in lymphoma or leukaemia was also observed in ♂ mice (7).
Oral rat (2 yr) 0, 125 or 250 mg kg^{-1} diet. No statistically significant difference in tumour incidence was observed between treated and control animals (7).

Teratogenicity and reproductive effects
Gavage rabbit 50, 500 or 1000 mg kg^{-1} day^{-1} on days 6-19 of gestation. Increased offspring liver weight and increased mean number of resorptions were reported at all doses. Reduced body weights and food consumption occurred in animals given 500 and 1000 mg kg^{-1} day^{-1}. Deaths, abortions and perforated stomachs were observed in animals given 1000 mg kg^{-1} day^{-1} (9).

Metabolism and toxicokinetics
Metabolised *in vitro* by human embryonic lung cell homogenate through oxidative pathways to: *N*-(3-trifluoromethylphenyl)-*N'*-formyl-*N'*-methylurea, *N*-(3-trifluoromethylphenyl)-*N'*-methylurea and *N*-[(3-trifluoromethyl)phenyl]urea (10).
Slowly absorbed from gastro-intestinal tract of rats. Absorption was incomplete after 72 hr. Following oral administration of radiolabelled fluometuron, radioactivity was detected in the liver, kidneys, adrenals, pituitary, red blood cells, blood plasma and spleen after 72 hr. The highest concentration was detected in red blood cells (11). Following an oral dose of 50 mg kg^{-1} to rats, up to 15% was excreted in the urine and 49% in the faeces (11).

Irritancy
Dermal rabbit (24 hr) application of powder (80%) caused severe irritation (12).

Sensitisation
Reported to be non-sensitising in a guinea pig study (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1537, TA1535 with and without metabolic activation negative (14,15).
Salmonella typhimurium TA1535 and *his*G46 weakly positive (16,17).
Saccharomyces cerevisiae D4 mitotic gene conversion without metabolic activation negative (18).
In vitro mouse lymphoma L5178Y tk^+/tk^- forward mutation assay negative (19).
In vitro Chinese hamster ovary cells, sister chromatid exhanges and chromosome aberrations positive (20).

In vivo mouse, oral doses up to 2000 mg kg^{-1} resulted in strong inhibition of testicular DNA synthesis. Equivocal results were obtained in the micronucleus test (17).
Treatment of cotton seeds with 0.01-1.0% formulation resulted in a dose- and time-dependent increase in chromosomal aberrations (21).

Other effects

Other adverse effects (human)
A frequency of 4.3-5.8% of aberrant metaphases in peripheral leucocytes was observed in exposed agricultural workers, compared with 2.5% prior to exposure (22).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (23).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (24).
WHO Toxicity Class Table 5 (25).
EPA Toxicity Class II (2).
Tolerable daily intake (TDI) humans 0.008 mg kg^{-1} (3).

Other comments

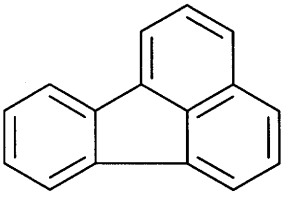
Physical properties, use, analysis, environmental fate, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (3,26).
Metabolic pathways reviewed (27).

References

1. McCoy, G. D. et al *Carcinogenesis (London)* 1990, **11**(7), 1111-1117.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *Drinking Water Health Advisory: Pesticides* 1989, 427-441, Lewis Publishers, Chelsea, MI, USA.
4. Ben-Dyke, R. et al *World Rev. Pest Control* 1970, **9**, 119-127.
5. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure* 1982, 116, CIP, Moscow, USSR.
6. *Proc. Eur. Soc. Toxicol.* 1976, **17**, 351.
7. *Bioassay of Fluometuron for Possible Carcinogenicity* 1980, National Cancer Institute, NCI-CG-TR-195, NTP-80-11, Bethesda, MD, USA.
8. *IARC Monograph* 1987, **Suppl. 7**, 63.
9. Arhur, A. et al *Teratology Study in Rabbits* 1984, Ciba-Geigy Corp., Report No. 217-84.
10. Liu, T. H. et al *J. Agric. Food. Chem.* 1976, **24**, 759-763.
11. Boyd, V. F. et al *Metabolism of Fluometurin in the Rat* 1967, Ciba Agrochemical Co. Research Report CF-1575.
12. Siglin, J. C. et al *Primary Skin Irritation in Rabbits* 1981, Study No. 6817A, Food and Drug Research Laboratories for Ciba-Geigy Corp, USA.
13. Galloway, D. *Guinea Pig Skin Sensitisation* 1984, Project No. 3397-84, Stillmeadow Inc. for Ciba Geigy Corp.
14. Dunkel, V. C. et al in *Molecular and Cellular Aspects of Carcinogen Screening Tests* 1980, 283-302, IARC Scientific Publications No. 27, Lyon, France.
15. Zeiger, E et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
16. Seiler, J. P. *Mutat. Res.* 1977, **48**, 225-236.
17. Seiler, J. P. *Mutat. Res.* 1978, **58**, 353-359.
18. Siebert, D. et al *Mutat. Res.* 1974, **22**, 111-120.
19. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **12**(1), 85-154.
20. Rosenkranz, H. S. et al *Mutagenesis* 1980, **5**(6), 559-571.
21. Sultanov, A. S. et al *Genetika (Moscow)* 1981, **17**, 2057-2060.
22. Kukanbaev, R. V. *Med. Zh. Uzb.* 1980, **10**, 65-67.
23. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
24. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
25. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.

26. *IARC Monograph* 1983, **30**, 245-253.
27. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

F48 fluoranthene



$C_{16}H_{10}$ **Mol. Wt.** 202.26 **CAS Registry No.** 206-44-0

Synonyms 1,2-benzacenaphthene; benzo[*jk*]fluorene; 1,2-(1,8-naphthylene)benzene

EINECS No. 205-912-4 **RTECS No.** LL 4025000

Physical properties

M. Pt. 111°C **B. Pt.** 384°C **Partition coefficient** log P_{ow} 5.20 **Volatility** v.p. 1.0×10^{-6} mmHg at 20°C
Solubility Water: 0.20-0.26 mg l^{-1}. Organic solvents: acetic acid, benzene, carbon disulfide, chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

Not overtly toxic to bluegill sunfish, perch or goldfish at 5 mg l^{-1} for 24 hr. Caused sickness in brown trout at 5 mg l^{-1} after 24 hr exposure (1).

The ultrastructural pathology of secondary gill lamellae of juvenile fathead minnows exposed for up to 96 hr to fluoranthene (6.1 or 12.5 μg l^{-1}) and for 12-24 hr UVA and UVB radiation was investigated. The observations demonstrated that the mode of action of photo-induced fluoranthene toxicity in fish is a disruption of mucosal cell membrane function and integrity (2).

Invertebrate toxicity

LC_{50} (10 day) *Chironomus tentans, Hyallela aztecca, Daphnia magna* 31.9-102.6 μg l^{-1} (3).

Concentrations of PAHs including fluoranthene in tail muscle and digestive glands of *Homarus americanus* exposed to effluent of two coking plants were detected before and after the plants closed. Levels of fluoranthene decreased after closure, but depuration of contaminated tissues occurred very slowly (4).

LC_{50} estuarine copepod *Schizopera knabeni* 2100 μg sediment-associated fluoranthene g^{-1} dry sediment (5).

The phototoxicity (as measured by LC_{50}s and EC_{50}s) of fluoranthene for the mysid *Mysidopsis bahia* and embryos and juveniles of the bivalve *Mulinia lateris* was greater under UV (UVA 397 ± 35.1, UVB 134 ± 22.8 μW cm^{-2}) than under fluorescent irradiation (UVA 9.70 ± 0.66, UVB 3.37 ± 0.22 μW cm^{-2}) by factors of 12.0, 54.1, and 1840, respectively (6).

Toxicity to other species

Bullfrog larvae were exposed to fluoranthene 10-60 μg l^{-1} and simulated solar UV radiation. Exposure to 60 μg l^{-1} for 48 hr caused a significant effect on locomotor activity; exposure to 40 μg l^{-1} for 96 hr caused hyperactivity. Sub-lethal concentrations (10 μg l^{-1}) caused signs of skin necrosis and structural alterations to the skin. The authors conclude that the photo-induced toxicity of fluoranthene, and hence other phototoxic PAHs, pose a potential hazard to ranid larvae well within the water solubility limits of the compound (7).

Bioaccumulation
Bioaccumulation factor for oysters 695 after 2 days exposure at 5.0 μg l^{-1} and 10,000 after 8 days exposure. $t_{1/2}$ for depuration 5 days (8).

Environmental fate

Degradation studies
Utilised as a sole carbon source by *Pseudomonas paucimobilis* EPA505 isolated from a creosote-contaminated soil (9).

Abiotic removal
Effectively removed from water together with other PAHs by adsorption onto activated carbon (10).
Resistant to photodegradation (11).
100% removed from river water containing 408 ng l^{-1} by a two-stage powdered/granular activated carbon process (12).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, rabbit 2000, 3200 mg kg^{-1}, respectively (13).
LD_{50} dermal rabbit 3180 mg kg^{-1} (13).
LD_{50} intravenous mouse 100 mg kg^{-1} (14).

Sub-acute and sub-chronic data
Intraperitoneal mouse 500 mg kg^{-1} day^{-1} for 7 days did not cause any fatalities (15).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, insufficient evidence for carcinogenicity to animals, IARC classification group 3 (16).
Dermal mouse (440 day), single dose of 40 μg did not induce any tumours (17).
Subcutaneous mouse (19 month), 5 injections of 10 mg (dosage schedule not specified) did not induce any tumours (18).

Metabolism and toxicokinetics
Metabolites identified in rat serum include the mutagenic agent 2,3-dihydrodiol. Other metabolites include 8-hydroxyfluoranthene, 3-hydroxyfluoranthene, 1-hydroxyfluoranthene and fluoranthene-2,3-quinone (19-21).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (21).
In vitro Chinese hamster ovary cell hypoxanthine-guanine phosphoribosyl transferase mutation assay with metabolic activation positive (22).
In vitro human lymphoblastoid HH-4 cell mutagenicity assay with metabolic activation positive (23).

Legislation

Limited under EC Directive on Drinking Water Quality. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1}, reference substances fluoranthene, benzo-3,4-fluoranthene, benzo-11,12-fluoranthene, benzo-3,4-pyrene, benzo-1,12-perylene, indeno(1,2,3-*cd*)pyrene (24).

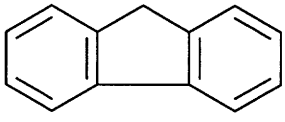
Other comments

Present with other PAHs in cigarette smoke, flue gases and engine exhaust and in tars from fossil fuels. Residues have been isolated from soils, water and sediments (25,26).
Physical properties, occurrence, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (25,27).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (28).

References

1. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, PB 87-200-275, Washington, DC, USA.
2. Weinstein, J. E. et al *Aquat. Toxicol.* 1997, **39**(1), 1-22.
3. Suedal, B. C. et al *J. Environ. Toxicol. Chem.* 1993, **12**, 155-165.
4. Uthe, J. F. et al *Bull. Environ. Contam. Toxicol.* 1986, **37**(5), 730-738.
5. Lotufo, G. R. *Mar. Environ. Res.* 1997, **44**(2), 149-166.
6. Pelletier, M. C. et al *Environ. Toxicol. Chem.* 1997, **16**(10), 2190-2199.
7. Walker, S. E. et al *Environ. Toxicol. Chem.* 1998, **17**(4), 734-739.
8. Lee, R. F. et al *Environ. Sci. Technol.* 1978, **12**(7), 832-838.
9. Mueller, J. G. et al *Report* 1989, EPA/600/D-89/254.
10. Lulek, J. et al *Bromatol. Chem. Toksykol.* 1987, **20**(2), 138-141 (Pol.) (*Chem. Abstr.* **108**, 100611s).
11. Korfmacher, W. A. et al *Environ. Sci. Technol.* 1980, **14**, 1094-1099.
12. Basu, D. K. et al *Environ. Sci. Technol.* 1978, **12**(7), 795-798.
13. Smyth, H. F. et al *Am. Ind. Hyg. J.* 1962, **23**, 95-107.
14. *Report* NX No.00205, US Army Armament Research and Development Command, Chemical Systems Laboratory, Aberdeen Proving Ground, MD, USA.
15. Gerarde, H. W. in *Elsevier Monographs on Toxic Agents* 1960, 249-321, Elsevier, Amsterdam, Netherlands.
16. *IARC Monograph* 1987, **Suppl. 7**, 63.
17. Van Duuren, B. L. et al *J. Natl. Cancer Inst.* 1976, **56**, 1237-1242.
18. Shear, M. J. *Am. J. Cancer* 1938, **33**, 499-537.
19. Polcaro, C. et al *J. Chromatogr.* 1988, **448**(1), 127-133.
20. Babson, J. R. et al *Toxicol. Appl. Pharmacol.* 1986, **85**(3), 355-366.
21. La Voie, E. et al *Carcinogenesis (London)* 1982, **3**, 841-846.
22. Li, A. P. *Environ. Mutagen.* 1984, **6**(4), 539-544.
23. Thilly, W. G. et al in *Chemical Mutagens. Principles and Methods for their Detection* 1980, **6**, 331-364, Plenum Press, New York, NY, USA.
24. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
25. *IARC Monograph* 1983, **32**, 355-364.
26. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, 671-674, Van Nostrand Reinhold, New York, NY, USA
27. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(2), 80-84.
28. *ECETOC Technical Report No. 71* 1996, European Chemical Industry Ecology and Toxicology Centre, B-1160 Brussels, Belgium

F49 fluorene



$C_{13}H_{10}$ **Mol. Wt.** 166.22 **CAS Registry No.** 86-73-7

Synonyms 9*H*-fluorene; *o*-biphenylenemethane; diphenylenemethane; 2,2'-methylenebiphenyl

EINECS No. 201-695-5 **RTECS No.** LL 5670000

Physical properties

M. Pt. 114-116°C **B. Pt.** 298°C **Flash point** >66°C **Specific gravity** 1.202 **Partition coefficient** log P_{ow} 4.18
Volatility v.p. 10 mmHg at 146°C
Solubility Water: 1.8 mg l^{-1}. Organic solvents: acetone, benzene, carbon disulfide, carbon tetrachloride, diethyl ether, ethanol, pyrimidine solution, toluene

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) fathead minnow >100 mg l^{-1} (1).
LC_{50} (24 hr) bluegill sunfish, goldfish ≈5 mg l^{-1} (2).
LC_{50} (unspecified exposure) himedaka killifish 3.3 mg l^{-1} (3).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 0.43 mg l^{-1} (1).
LC_{50} (96 hr) *Neanthes arenaceodentata* 1.0 mg l^{-1} (4).

Bioaccumulation

Bioconcentration factor for fish 4150 (5).

Environmental fate

Degradation studies

Completely degraded by *Pseudomonas fluorescens, Pseudomonas paucimobilis, Pseudomonas vesicularis* and *Alcaligenes denitrificans* when utilised as sole carbon source (6).

Adsorption and retention

Calculated log K_{oc} 3.76 (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >100 mg kg^{-1} (8).
LD_{50} intraperitoneal mouse 2000 mg kg^{-1} (9).

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, insufficient evidence for carcinogenicity to animals, IARC classification group 3 (10).
Oral ♀ rat (18 month) 0.05% diet. Tumours in 18 treated animals were 1 uterine carcinosarcoma, 1 uterine fibrosarcoma, 1 granulocytic leukaemia and 4 pituitary adenomas. Among 18 controls, 1 uterine adenocarcinoma, 2 uterine fibro-epithelial polyps, 5 adrenal cortical adenomas, 6 pituitary adenomas and 1 inguinal region fibroma were reported (11).
Dermal mouse (9 month) repeated application of fluorene in benzene, negative results were reported (12).
In a dermal study of fluorene on 3-methylcholanthrene-induced skin carcinogenesis, 20 mice received 6 μg fluorene 2 × wk^{-1} for 31 wk. No skin tumour was observed in this group. Another group of 20 mice received 3 μg fluorene plus 3 μg 3-methylcholanthrene 2 × wk^{-1} for 31 wk. 16/17 surviving mice developed skin tumours, with a mean latent period of 11.9 wk. In another group of 20 mice receiving 3 μg 3-methylcholanthrene 3 × wk^{-1} for 31 wk, all 19 survivors developed skin tumours with a latent period of 14.5 wk (13).
Subcutaneous mouse (18 month) 7 injections of 10 mg over a period of 16 month did not induce any cancers (14).

Metabolism and toxicokinetics

1-Hydroxyfluorene, 9-hydroxyfluorene and 9-ketrofluorene have been identified as metabolites of fluorene, following incubation with rat liver preparations (15).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (16).
In vitro primary rat hepatocytes, unscheduled DNA synthesis negative (17).
In vitro Chinese hamster lung cells, chromosomal aberrations with metabolic activation positive (18).
In vitro Chinese hamster bone marrow cells, sister chromatid exchanges negative (19).

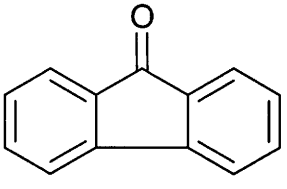
Other comments

Present with other PAHs in cigarette smoke, flue gases and engine exhausts, and in tars from fossil fuels. Residues have been isolated from soils, water and sediments (20).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (21).

References

1. Finger, S. E. et al *ASTM Spec. Tech. Publ. 865* 1985, 120-133.
2. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002; PB87-200-275, Washington, DC, USA.
3. Niiromi, J. et al *Mie-Ken Kankyo Kagaku Senta Hokoku* 1989, (9), 53-60 (Japan.) (*Chem. Abstr.* **111**, 189142x).
4. Rossi, S. S. et al *Mar. Pollut. Bull.* 1978, **9**, 220-223.
5. Schuurmann, G. et al *Chemosphere* 1988, **17**(8), 1551-1574.
6. Weissenfels, W. et al *DECHEMA Biotechnol. Conf.* 1989, **3**(B), 867-870.
7. Pussermier, L. et al *Chemosphere* 1990, **21**(10-11), 1199-1212.
8. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
9. *Russ. Pharmacol. Toxicol.* 1983, **48**, 143.
10. *IARC Monograph* 1987, **Suppl. 7**, 63.
11. Morris, H. P. et al *J. Natl. Cancer Inst.* 1960, **24**, 149-180.
12. Kennaway, E. L. *J. Ind. Hyg.* 1924, **5**, 462-490.
13. Riegal, B. et al *Cancer Res.* 1951, **11**, 301-306.
14. Shear, M. J. *Am. J. Cancer* 1938, **33**, 499-537.
15. LaVoie, E. J. et al *Polynuclear Aromatic Hydrocarbons: Chemical Analysis and Biological Fate, 5th Int. Symp.* 1981, 417-427, Battelle Press, Columbus, OH, USA.
16. Klopman. G. et al *Mutat. Res.* 1990, **228**, 1-50.
17. Probst, G. S. et al *Environ. Mutagen.* 1981, **3**, 11-32.
18. Matsuoka, A. et al *Mutat. Res.* 1991, **259**(1), 103-110.
19. Neal, S. B et al *Mutat. Res.* 1983, **113**(1), 33.
20. *IARC Monograph* 1983, **32**, 365-371.
21. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F50 9-fluorenone



$C_{13}H_8O$ **Mol. Wt.** 180.21 **CAS Registry No.** 486-25-9

Synonyms 9*H*-fluoren-9-one; fluoren-9-one

EINECS No. 207-630-7 **RTECS No.** LL 8925000

Uses Catalyst. Photolytic sensitiser. Solvent.

Occurrence Emitted into the atmosphere during fuel and waste combustion. Residues have been detected in water and sediments (1,2).

Physical properties

M. Pt. 82-85°C **B. Pt.** 342°C **Partition coefficient** log P_{ow} 3.58

Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 4.85 ppm Microtox test (3).

LC_{50} (96 hr) *Neanthes arenaceodentata* 1.0 mg l^{-1} static bioassay (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2000 mg kg^{-1} (5).

LD_{50} oral redwing blackbird 96 mg kg^{-1} (6).

Genotoxicity

Salmonella typhimurium TA98, TA1535, TA1538 with and without metabolic activation negative (7).

Escherichia coli PQ37, SOS chromotest negative (7).

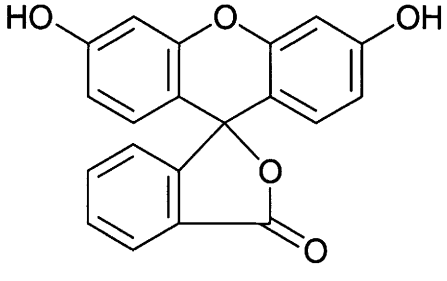
Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

References

1. Grifoll, M. et al *Arch. Environ. Contam. Toxicol.* 1990, **19**, 175-184.
2. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, 674-675, Van Nostrand Reinhold, NY, USA.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Rossi, S. S. et al *Mar. Pollut. Bull.* 1978, **9**, 220-223.
5. *Russ. Pharmacol. Toxicol. (Engl. Transl.)* 1985, **48**, 143.
6. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
7. Vasilieva, S. et al *Mutat. Res.* 1990, **244**(4), 321-329.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F51 fluorescein



$C_{20}H_{12}O_5$ **Mol. Wt.** 332.31 **CAS Registry No.** 2321-07-5

Synonyms 3′,6′-dihydroxy-*spiro*[isobenzofuran-1(3*H*), 9′-[9*H*]xanthen]-3-one; 9-(*o*-carboxyphenyl)-6-hydroxy-3*H*-xanthen-3-one; 3′,6′-dihydroxyfluoran; resorcinolphthalein; C.I. Solvent Yellow 94; C.I. 453501; Japan Yellow 201; C.I. Acid Yellow 73

EINECS No. 219-031-8 **RTECS No.** LM 5075000

Uses Fluorescent label used in immunoassays, diagnostic agent and tracer for water supplies. Used externally in some pharmaceuticals (1).

Physical properties

M. Pt. 314-316°C
Solubility Organic solvents: hot ethanol, glacial acetic acid

Environmental fate

Abiotic removal
A MODAR supercritical oxidation process can be used on wastewaters containing fluorescein to convert the compound into CO_2 and simple organic compounds (2).

Mammalian & avian toxicity

Acute data
LD_{Lo} intraperitoneal rat 600 mg kg^{-1} (3).
LD_{Lo} intravenous rabbit 300 mg kg^{-1} (3).

Metabolism and toxicokinetics
Injected intravenously into rabbits, fluorescein enters vitreous humour of eye as early as 1 hr after injection and persists for more than 6 hrs (4).
In humans, fluorescein is rapidly metabolised to fluorescein glucuronide (4).
In rats with transplanted carcinosarcomas, fluorescein tends to be concentrated in tumour tissue after administration (5).

Other effects

Any other adverse effects
Can cause photosensitisation. When given to rabbits as the sodium salt, there is increased sensitivity to blue light causing retinal damage, and reduced thresholds for light damage to the iris and cornea (6).

References

1. Bedzyk, W. D. *J. Biol. Chem.* 1990, **265**(1), 133-138.
2. Johnston, J. B. et al *Biol. Technol.* 1988, **6**(12), 1423-1427.
3. *Int. J. Lepr. Other Mycobact. Dis.* 1934, **2**, 257.
4. Piehwe, W. E. *Exp. Eye Res.* 1987, **44**(2), 209-215.
5. Barabash, R. D. *Farmakol. Toksikol. (Moscow)* 1990, **53**(3), 24-26 (Russ.) (*Chem. Abstr.* **113**, 52015e).
6. Hocheimer, B. et al *Appl. Ophthalmol.* 1987, **26**(8), 1473-1479

F52 fluorine

F_2

F_2 **Mol. Wt.** 38.00 **CAS Registry No.** 7782-41-4
Synonyms RCRA Waste No. P056
EINECS No. 231-954-8 **RTECS No.** LM 6475000
Occurrence Fluoride minerals include fluorite, cryolite and fluoropatite. Fluoride ions present in bones and teeth in trace quantities.

Physical properties

M. Pt. -219.6°C **B. Pt.** -188.1°C **Specific gravity** 1.513 at -188.1°C **Volatility** v.p. 1.0 mmHg at -223°C ; v.den. 1.695

Occupational exposure

DE-MAK 0.1 ppm (0.16 mg m^{-3})
FR-VLE 1 ppm (2 mg m^{-3})
SE-LEVL 0.1 ppm (0.2 mg m^{-3}) **SE-STEL** 0.3 ppm (0.5 mg m^{-3})
UK-STEL 1 ppm (1.6 mg m^{-3})
US-TWA 1 ppm (1.6 mg m^{-3}) **US-STEL** 2 ppm (3.1 mg m^{-3})

UN No. 1045 (compressed) **Conveyance classification** toxic gas, fire intensifying hazard, corrosive (compressed)
Supply classification very toxic
Supply classification corrosive
Risk phrases May cause fire – Very toxic by inhalation – Causes severe burns (R7, R26, R35)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S26, S36/37/39, S45)

Ecotoxicity

Fish toxicity
LC_{50} (21 day) rainbow trout 8.5 mg F^- l^{-1} (water hardness ≈12 mg l^{-1}); with hardness of 45 mg l^{-1} all fish survived 75 mg F^- l^{-1} but 100 mg F^- l^{-1} killed all fish in 21 days; with hardness of 320 mg l^{-1} all fish survived 100 mg F^- l^{-1} in 21 days (1).
LC_{50} (20 day) rainbow trout, carp 3.5-91 ppm in very soft water (2).

Mammalian & avian toxicity

Acute data
LC_{50} (1 hr) inhalation rat, mouse, guinea pig 150-185 ppm (2).

Carcinogenicity and chronic effects
Inadequate evidence of carcinogenicity to humans and animals for inorganic fluorides used in drinking water, IARC classification group 3 (3).

Teratogenicity and reproductive effects
Inhalation rat (3 hr) 25 mg m^{-3} caused testicular atrophy (4).

Irritancy
Whole body human exposure to 25 ppm for 5 min caused mild pulmonary irritation (5).
Dermal human (1 min) 100 ppm caused mild irritation (6).

Legislation

Halogens and their compounds are included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluoride: maximum admissible concentration 1500 μg l^{-1} at 8-12°C, 700 μg l^{-1} at 25-30°C (8).

Other comments

Safety precautions, carcinogenicity and toxicology of fluorine and fluorides reviewed (9-11).
Human ingestion 0.7-3.4 mg day^{-1} from food and water. Evidence that fluorine is an essential element obtained by maintaining rats on a fluoride-free diet, which resulted in decreased growth rate, decreased fertility and anaemia (12).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (13).

References

1. Herbert, D. W. M. et al *Water Waste Treat.* 1964.

2. Neuhold, J. M. et al *Trans. Am. Fish. Soc.* 1960, **89**, 358.
3. *IARC Monograph* 1987, **Suppl. 7**, 208-210.
4. Eagers, R. Y. *Toxic Properties of Inorganic Fluorine Compounds* 1969, 43, Elsevier, Amsterdam, Netherlands.
5. *Am. Ind. Hyg. Assoc. J.* 1968, **29**, 11.
6. Bellas, F. et al *Fluorine Handbook* 1965, NASA Lewis Research Centre, Cleveland, OH, USA.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
9. *IPCS Environmental Health Criteria No. 36: Fluorine and Fluorides* 1984, WHO, Geneva, Switzerland.
10. *IARC Monograph* 1982, **27**, 237-303.
11. *Chemical Safety Data Sheets* 1991, **4a**, 265-269, The Royal Society of Chemistry, London, UK.
12. *Kirk-Othmer Encyclopedia of Chemical Technology* 3rd ed., 1981, **15**, 593, Wiley & Sons, New York, NY, USA.
13. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F53 fluoroacetamide

$CH_2FC(O)NH_2$

C_2H_4FNO **Mol. Wt.** 77.06 **CAS Registry No.** 640-19-7

Synonyms 2-fluoroacetamide; FAA; Fluorakil 100; Fussol; Megatox; Navron; Rodex; Yanock

EINECS No. 211-363-1 **RTECS No.** AC 1225000

Uses Insecticide. Rodenticide.

Physical properties

M. Pt. 107-109°C **Partition coefficient** log P_{ow} −1.05 (1)

Solubility Water: very soluble. Organic solvents: acetone, chloroform, dimethyl sulfoxide, ethanol

Occupational exposure

UN No. 2811

Supply classification very toxic

Risk phrases Toxic in contact with skin – Very toxic if swallowed (R24, R28)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) harlequin fish 3500 mg l^{-1} (2).

Bioaccumulation

Calculated bioconcentration factor 0.1 indicates that environmental accumulation is unlikely (3).

Environmental fate

Abiotic removal

Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in the atmosphere 19 hr (4).

Adsorption and retention

Estimated K_{oc} 6.4 and solubility in water indicate the fluoroacetamide may leach from soil (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, redwing blackbird, quail 5.6-25 mg kg^{-1} (5-7).
LC_{50} (duration unspecified) inhalation mouse 550 mg m^{-3} (7).
LD_{50} dermal mouse, rat 34, 80 mg kg^{-1}, respectively (8,9).
LD_{50} intraperitoneal rat, mouse 12, 85 mg kg^{-1}, respectively (10,11).
LD_{50} intravenous rabbit 250 μg kg^{-1} (12).

Teratogenicity and reproductive effects

Oral rat (28 day) 3.4 mg kg^{-1} caused marked morphological changes in the nucleus of step-13 spermatids within 24 hr, and the entire cell became distorted within 5 days. 50% reduction in testes weight after 28 days (13).

Metabolism and toxicokinetics

Following intraperitoneal administration to rats and mice, undergoes defluorination to give fluoride ion which is evident in the kidney and urine. Other urinary metabolites include an *S*-(carboxymethyl) conjugate and sulfoxidation products. Biliary excretion includes *S*-(carboxymethyl) glutathione and an *O*-conjugate of fluoroacetate (14).

Genotoxicity

In vitro red muntjac cells, chromosomal aberrations and sister chromatid exchanges positive (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (16).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (17).
WHO Toxicity Class Ib (18).

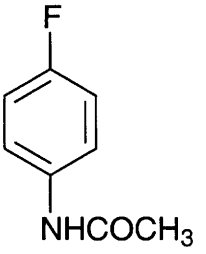
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (19).

References

1. Hansch, C. et al *Medchem. Project Issue No. 26.* 1985, Pomona College, Claremont, CA, USA.
2. Alabaster, J. S. *Int. Pest Control* 1969, 29-35.
3. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
4. Atkinson, R. *Environ. Toxicol. Chem.* 1988, **7**, 435-442.
5. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
6. *Pesticide Chemicals Official Compendium* 1966, 538, Assoc. American Pesticide Control Officials, Topeka, KS, USA.
7. *Agric. Biol. Chem.* 1967, **31**, 1294.
8. *World Rev. Pest Control* 1970, **9**, 119.
9. *Shokuhin Eiseigaku Zasshi* 1968, **9**, 1.
10. Matsumura, F. et al *Biochem. Pharmacol.* 1963, **12**, 1201.
11. *J. Sci. Food Agric.* 1957, **8**, 400.
12. *J. Chem. Soc.* 1949, 912.
13. Hayes, W. J. *Pesticide Studies in Man* 1982, 500, Williams and Wilkins, Baltimore, MD, USA.
14. Tecle, B. et al *Chem. Res. Toxicol.* 1989, **2**(6), 429-435.
15. He, W. et al *Huanjing Kexue Xuebao* 1983, **3**(2), 94.
16. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
17. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
18. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
19. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F54 4′-fluoroacetanilide



C_8H_8FNO **Mol. Wt.** 153.16 **CAS Registry No.** 351-83-7

Synonyms *N*-(4-fluorophenyl)acetamide

EINECS No. 206-515-9 **RTECS No.** AE 2977000

Physical properties

M. Pt. 153-155°C

Mammalian & avian toxicity

Acute data

LD_{Lo} oral cat 250 mg kg^{-1} (1).

References

1. *J. Am. Pharmaceut. Assoc.* 1939, **28**, 70

F55 fluoroacetic acid

FCH_2COOH

$C_2H_3FO_2$ **Mol. Wt.** 78.04 **CAS Registry No.** 144-49-0

Synonyms fluoroethanoic acid; monofluoroacetic acid; 2-fluoroacetic acid

EINECS No. 205-631-7 **RTECS No.** AH 5950000

Uses Chemical warfare agent. Catalyst for coatings.

Occurrence Occurs in *Dichapetalum cymosum* and *Palicourea maregiavii* leaves (1).

Physical properties

M. Pt. 33°C **B. Pt.** 165°C

Occupational exposure

UN No. 2642 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification very toxic

Risk phrases Very toxic if swallowed (R28)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – When using do not eat or drink – Do not breathe dust – In case of contact with eyes, rinse immediately with plenty of water and seek

medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S20, S22, S26, S45)

Ecotoxicity

Invertebrate toxicity

Cell multiplication inhibition test *Microcystis aeruginosa* 0.4 μg l^{-1}, *Entosiphon sulcatum* 31 mg l^{-1} (2,3).

Environmental fate

Carbonaceous inhibition

Pseudomonas cepacia is capable of growing in fluoroacetate-enriched solutions without any reduction in growth rate. Fluoroacetate was degraded to carbon dioxide at a rate of 23.5 ng per 10^9 cells hr^{-1} (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5 mg kg^{-1} (5).

LD_{50} intraperitoneal mouse 7 mg kg^{-1} (6).

LD_{50} intravenous mouse 13 mg kg^{-1} (7).

Sub-acute and sub-chronic data

In man, the symptoms of sub-acute fluoroacetate poisoning began between 30 min and several hr after exposure. Death occurred rapidly, preceded by convulsions and arrhythmia (8).

Metabolism and toxicokinetics

Fluoroacetate administered by intraperitoneal injection to rats and mice was defluorinated to yield the fluoride ion which was detected in urine and kidney. Urinary metabolites included an *S*-(carboxymethyl) conjugate complex in rats and mice and sulfoxidation products in rats. Bile metabolites included *S*-(carboxymethyl)-glutathione or a related conjugate and an *O*-conjugate of fluoroacetate. Metabolic defluorination of fluoroacetate was attributed to conjugation of fluoroacetate with reduced glutathione and conversion into (–)-*erythro*-fluorocitrate. Urine of rats and mice poisoned with fluoroacetate show elevated citrate and glucose levels and diminished urea, consistent with disruptions in the tricarboxylic acid (TCA) cycle and ammonia metabolism (9). After intraperitoneal administration to rats, fluoroacetic acid was detected in the liver, gastro-intestinal tract, lung, kidneys and brain (10).

Other effects

Other adverse effects (human)

Affects the human central nervous system causing convulsions and ventricular fibrillation (11).

Any other adverse effects

Neurotoxin (1,12).

In chicken liver gluconeogenesis, fluoroacetate intoxication blocked the TCA cycle in both fed and fasted birds. Inhibition of TCA cycle caused near maximum vasodilation in respiratory muscles and myocardium without affecting resting skeletal muscle (13,14).

Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (15).

References

1. Eckschmidt, M. et al *Braz. J. Med. Biol. Res.* 1989, **22**(8), 975-977.
2. Bringmann, G. et al *GWF-Wasser/Abwasser* 1976, **117**(9), 119.
3. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
4. Meyer, J. J. et al *Appl. Environ. Microbiol.* 1990, **56**(7), 2152-2155.
5. *Toxicol. Appl. Pharmacol.* 1968, **13**, 189.

6. Patterson, F. L. M. et al *J. Org. Chem.* 1956, **21**, 883.
7. *U.S. Army Arm. Res. and Ser. Command* NX 03014.
8. Peters, R. A. et al *J. Occup. Med.* 1981, **23**(2), 112-113.
9. Tecle, B. et al *Chem. Res. Toxicol.* 1989, **2**(6), 429-435.
10. *Foreign Compound Metabolism in Mammals* 1970, **1**, 93, The Chemical Society, London, UK.
11. Gribble, G. *J. Chem. Educ.* 1973, **50**(7), 460-462.
12. Hornfeldt, C. S. et al *Eur. J. Pharmacol.* **179**(3), 307-313.
13. Bobyleva-Guarrievo, V. et al *Fluoride* 1984, **17**(2), 94-104.
14. Johnson, R. L. *J. Appl. Physiol.* 1988, **64**(1), 174-180.
15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F56 fluoroacetyl chloride

$FCH_2C(O)Cl$

C_2H_2ClFO **Mol. Wt.** 96.49 **CAS Registry No.** 359-06-8

Synonyms 2-fluoroacetyl chloride

EINECS No. 206-623-6 **RTECS No.** AO 6825000

Uses Acylation agent.

Mammalian & avian toxicity

Acute data

LC_{Lo} (10 min) inhalation guinea pig, mouse 100, 200 mg m^{-3}, respectively (1).

Legislation

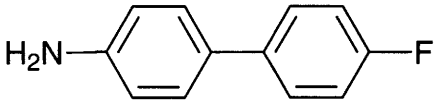
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluoride: maximum admissible concentration 1500 μg l^{-1} for average water temperatures of 8-12°C, 700 μg l^{-1} for average water temperatures of 25-30°C. Chloride: guide level 25 mg l^{-1} (2).

Limited under UK Water Quality Regulations. Chloride: Prescribed concentration 400 mg l^{-1} (12-monthly average) (3).

References

1. *Progress Report* 1943, No. 9-4-1-9, National Defense Research Committee, Office of Scientific Research and Development, USA.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S.I. 1989 No. 1147, The Water Supply (Water Quality) Regulations* 1989, HMSO, London, UK

F57 4′-fluoro-4-aminobiphenyl



$C_{12}H_{10}FN$ **Mol. Wt.** 187.22 **CAS Registry No.** 324-93-6

Synonyms 4-amino-4′-fluorodiphenyl; 4′-fluoro-(1,1-biphenyl)-4-amine; 4′-fluoroxenylamine

EINECS No. 206-306-2 **RTECS No.** DU 9625000

Physical properties

M. Pt. 121°C

Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 300 mg kg^{-1} (1).

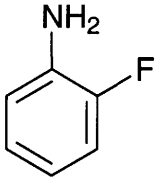
Genotoxicity

In vitro AKR leukaemia NIH Swiss mouse embryo system 0.1 μg ml^{-1} transforming activity positive. *In vivo* mouse transformation activity positive (2).

References

1. *Cancer Res.* 1966, **26**, 619.
2. Rhim, J. S. et al *J. Natl. Cancer Inst.* 1974, **52**(4), 1167-1173

F58 2-fluoroaniline



C_6H_6FN **Mol. Wt.** 111.12 **CAS Registry No.** 348-54-9

Synonyms *o*-fluoroaniline; 2-fluorobenzenamine

EINECS No. 206-478-9

Uses Organic synthesis.

Physical properties

M. Pt. –29°C **B. Pt.** 182-183°C **Flash point** 60°C **Specific gravity** 1.151 at 20°C

Partition coefficient log P_{ow} 1.26 (1)

Solubility Organic solvents: carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

UN No. 2941 (fluoroanilines) **HAZCHEM Code** 2W **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

IC_{50} (48 hr) *Tetrahymena pyriformis* 50 mg l^{-1} (1).

Mammalian & avian toxicity

Metabolism and toxicokinetics

Undergoes hydroxylation at the 4-position and defluorination by microsomal cytochrome P_{450} *in vitro* rat liver microsomes (2).

Irritancy

Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (3).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (4).
In vitro Chinese hamster lung fibroblast V79 cells DNA damage negative (4).

Other effects

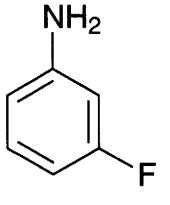
Other adverse effects (human)

Absorption into the body leads to the formation of methaemoglobin, which in sufficient concentration causes cyanosis (3).

References

1. Schultz, T. W. et al *Bull. Environ. Contam. Toxicol.* 1989, **43**(4), 564-569.
2. Rietjens, I. M. C. M. et al *Xenobiotica* 1989, **19**(11), 1297-1305.
3. Lenga, R. E. (Ed.) *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1693, Sigma-Aldrich, Milwaukee, WI, USA.
4. Zimmer, D. et al *Mutat. Res.* 1980, **77**(4), 317-326

F59 3-fluoroaniline



C_6H_6FN **Mol. Wt.** 111.12 **CAS Registry No.** 372-19-0

Synonyms *m*-fluoroaniline; 3-fluorobenzenamine

EINECS No. 206-747-0 **RTECS No.** BY 1400000

Uses Organic synthesis.

Physical properties

B. Pt. 186°C at 756 mmHg **Flash point** 77°C **Specific gravity** 1.156 at 20°C
Partition coefficient log P_{ow} 1.30 (1)
Solubility Organic solvents: carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

UN No. 2941 **HAZCHEM Code** 2W **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity
IC_{50} (48 hr) *Tetrahymena pyriformis* 67 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 56 mg kg^{-1} (2).
LD_{50} oral starling >100 mg kg^{-1} (2).

Metabolism and toxicokinetics
Undergoes hydroxylation at the 4-position and defluorination by microsomal cytochrome P_{450} *in vitro* rat liver microsomes (3).

Irritancy
Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (4).

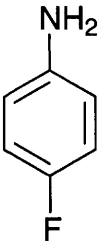
Other effects

Other adverse effects (human)
Absorption into the body leads to the formation of methaemoglobin, which in sufficient concentration causes cyanosis (4).

References

1. Schultz, T. W. et al *Bull. Environ. Contam. Toxicol.* 1989, **43**(4), 564-569.
2. Schafer, E. W. *Toxicol. Appl. Pharmacol.* 1972, **21**, 315-330.
3. Rietjens, I. M. C. M. et al *Xenobiotica* 1989, **19**(11), 1297-1305.
4. Lenga, R. E. (Ed.) *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1693, Sigma-Aldrich, Milwaukee, WI, USA

F60 4-fluoroaniline



C_6H_6FN **Mol. Wt.** 111.12 **CAS Registry No.** 371-40-4

Synonyms *p*-fluoroaniline; 4-fluorobenzenamine

EINECS No. 206-735-5 **RTECS No.** BY 1575000

Uses Intermediate in the manufacture of herbicides. Corrosion inhibitor for steel. Reagent for electrochemical analysis.

Physical properties

M. Pt. -1.9°C **B. Pt.** 187.4°C at 767 mmHg **Flash point** 73°C **Specific gravity** 1.1725 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.15 (1) **Volatility** v.p. 1 mmHg at 25°C
Solubility Water: very slightly soluble. Organic solvents: carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

UN No. 2941 **HAZCHEM Code** 2W **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity
LC_{50} (96 hr flow-through) fathead minnow 2.5 mg l^{-1} (2).

Invertebrate toxicity
IC_{50} (48 hr) *Tetrahymena pyriformis* 8 mg l^{-1} (1).
EC_{50} (30 min) *Photobacterium phosphoreum* 72 ppm Microtox test (3).

Bioaccumulation
Calculated bioconcentration factor of 4.4 indicates that environmental accumulation is unlikely (4).

Environmental fate

Degradation studies
Utilised as sole carbon and nitrogen source by the soil bacterium *Moraxella* (5).
Purified enzymes of the soil fungus *Geotrichum candidum* biotransformed 4-fluoroaniline to fluoroazobenzene (6).

Abiotic removal
Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in the atmosphere 6.5 hr (7).
Estimated $t_{1/2}$ for volatilisation in pond water 34.4 days, and in model river water 3.4 days (8).

Adsorption and retention
Estimated K_{oc} 10-100 indicates high mobility in soil, although some covalent bonding with humic material may be expected (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 100 mg kg^{-1} (9).
LD_{50} oral starling >100 mg kg^{-1} (9).
LD_{50} oral rat 420 mg kg^{-1} (10).

Metabolism and toxicokinetics

Undergoes 2- and 4-hydroxylation with resultant defluorination by microsomal cytochrome P_{450} *in vitro* rat liver microsomes (11).

Irritancy

Dermal rabbit (24 hr) 2 mg caused severe irritation and 250 µg instilled into rabbit eye for 24 hr caused severe irritation (12,13).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation weakly mutagenic (14).
In vitro Chinese hamster lung fibroblast V79 cells DNA damage negative (14).

Other effects

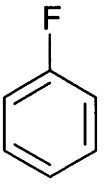
Any other adverse effects

Dermal administration to rats caused a significant increase in methaemoglobin (15).

References

1. Schultz, T. W. et al *Bull. Environ. Contam. Toxicol.* 1989, **43**(4), 564-569.
2. Hall, L. H. et al *Environ. Toxicol. Chem.* 1989, **8**(9), 783-788.
3. Kaiser, K. L. E. *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Behaviour of Organic Compounds* 1982, 5-4, McGraw-Hill, New York, NY, USA.
5. Zeyer, J. et al *Appl. Environ. Microbiol.* 1985, **50**, 447-453.
6. Bordeleau, L. M. et al *Can. J. Microbiol.* 1972, **18**, 1873-1882.
7. Eisenreich, S. J. et al *Environ. Sci. Technol.* 1981, **15**, 30-38.
8. Parris, G. E. *Environ. Sci. Technol.* 1980, **14**, 1099-1106.
9. Schafer, E. W. *Toxicol. Appl. Pharmacol.* 1972, **21**, 315-330.
10. *Cesk. Hyg.* 1978, **23**, 168.
11. Rietjens, I. M. C. M. et al *Xenobiotica* 1989, **19**(11), 1297-1305.
12. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, 611, Prague, Czechoslovakia.
13. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 95, Prague, Czechoslovakia.
14. Zimmer, D. et al *Mutat. Res.* 1980, **77**(4), 317-326.
15. Truhaut, R. et al *J. Eur. Toxicol.* 1972, **5**(3), 155

F61 fluorobenzene



C_6H_5F **Mol. Wt.** 96.10 **CAS Registry No.** 462-06-6

EINECS No. 207-321-7 **RTECS No.** DA 0800000

Uses Solvent.

Physical properties

M. Pt. –42°C **B. Pt.** 85°C **Flash point** –12°C **Specific gravity** 1.024 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.27 **Volatility** v.den. 3.31
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2387 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 183 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4400 mg kg^{-1} (2).
LC_{50} (2 hr) inhalation mouse 4500 mg m^{-3} (3).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation negative (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

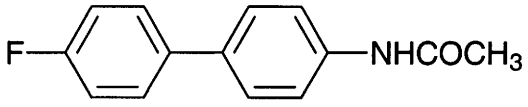
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk* 1965, **3**, 91.
3. Klopman, G. et al *Mol. Toxicol.* 1987, **1**, 61-81.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F62 *N*-(4′-fluorobiphen-4-yl)acetamide



$C_{14}H_{12}FNO$ **Mol. Wt.** 229.25 **CAS Registry No.** 398-32-3

Synonyms 4′-fluoro-4-acetylaminobiphenyl; *N*-(4′-fluoro-4-biphenyl)acetamide

EINECS No. 206-912-7 **RTECS No.** AE 3750000

Physical properties

M. Pt. 205-205.5°C

Mammalian & avian toxicity

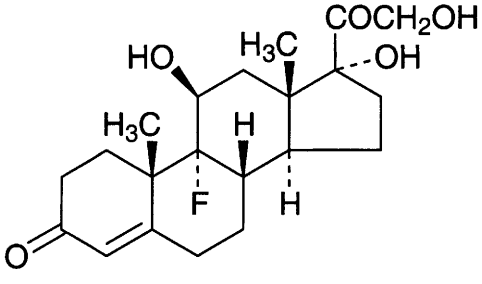
Carcinogenicity and chronic effects

Oral rat (52 wk) 0.04% diet induced bilateral renal cortical tumours in 75-90% of treated animals (1).

References

1. Histon, D. E. et al *Am. J. Pathol.* 1980, **100**(1), 317-320

F63 fluorocortisone



$C_{21}H_{29}FO_5$ **Mol. Wt.** 380.46 **CAS Registry No.** 127-31-1

Synonyms (11β)-9-fluoro-11,17,21-trihydroxypregn-4-ene-3,20-dione; 9-fluoro-11β,17,21-trihydroxypregn-4-ene-3,20-dione; Alflorone; Fludrone; Fludrocortisone; Fluohydrocortisone; 9α-fluorocortisol

EINECS No. 204-833-2 **RTECS No.** TU 5025000

Uses Glucocorticoid drug.

Physical properties

M. Pt. 260-262°C (decomp.)

Solubility Water: 0.14 mg l^{-1}. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 170 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Administration of 0.8 mg day^{-1} for 7 days to human volunteers (route not specified) caused an increase in blood pressure whereas plasma osmolality remained unaltered. Plasma vasopressin concentration increased, although this did not correlate with alterations in the blood pressure (2).

Teratogenicity and reproductive effects

TD_{Lo} oral rabbit 1 mg kg^{-1} day^{-1} on days 13-16 of gestation, teratogenic and foetotoxic effects (3).

Metabolism and toxicokinetics

Readily absorbed from gastro-intestinal tract (4).

Other comments

Fluorocortisone-induced hypertension reviewed (5).

References

1. MacDonald, J. R. *Compilation of LD_{50} Values of New Drugs* Dept. National Health and Welfare, Food and Drug Division, Ottawa, Canada.
2. Haller, H. et al *J. Hypertens.* 1987, 5(Suppl. 5), 111-113.
3. Foye, W. O. (Ed.) *Principles of Medicinal Chemistry* 1974, 85, Lea & Febiger, Philadelphia, PA, USA.
4. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
5. Whitworth, J. A. et al *J. Hypertens.* 1986, **4**(2), 133-139

F64 fluoroethane

$$CH_3CH_2F$$

C_2H_5F **Mol. Wt.** 48.06 **CAS Registry No.** 353-36-6

Synonyms ethyl fluoride; monofluoroethane; R161

EINECS No. 206-531-6 **RTECS No.** KI 3650000

Uses Blowing agent.

Physical properties

M. Pt. –143.2°C **B. Pt.** –38°C **Specific gravity** 0.8158 at –38°C **Volatility** v.den. 1.7

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2453 **HAZCHEM Code** 2WE **Conveyance classification** flammable gas

Environmental fate

Degradation studies

Nitrosomonas europaea metabolises fluoroethane by defluorination to ethane (1).

Mammalian & avian toxicity

Acute data

LC_{Lo} (4 hr) inhalation cat 26% (26 pph) (2).

References

1. Rasche, M. E. et al *J. Bacteriol.* 1990, **172**(9), 5368-5373.
2. *J. Ind. Hyg. Toxicol.* 1949, **31**, 343

F65 2-fluoroethanol

$$FCH_2CH_2OH$$

C_2H_5FO **Mol. Wt.** 64.06 **CAS Registry No.** 371-62-0

Synonyms ethylene fluorohydrin; β-fluoroethanol

EINECS No. 206-740-2 **RTECS No.** KL 1575000

Uses Intermediate in organic synthesis. Insecticide. Rodenticide.

Physical properties

M. Pt. –26.45°C **B. Pt.** 103.4°C at 757 mmHg **Flash point** 31°C **Specific gravity** 1.1040 at 20°C with respect to water at 4°C **Volatility** v.p. 16 mmHg at 20°C

Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LC_{50} (10 min) inhalation dog, rabbit, cat 7, 25, 35 mg m^{-3}, respectively (1).

LC_{50} (10 min) inhalation guinea pig, rat 35, 200 mg m^{-3}, respectively (1).

LC_{50} (10 min) inhalation mouse, monkey 1100, 1500 mg m^{-3}, respectively (1,2).

LD_{50} subcutaneous mouse 15 mg kg^{-1} (3).

LD_{50} intraperitoneal rat 1.75 mg kg^{-1} (4).

Metabolism and toxicokinetics

Following intraperitoneal administration to rats and mice, fluoracetate and fluoride were eliminated in the urine. Metabolism to fluoracetaldehyde by liver microsomes was also identified (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).

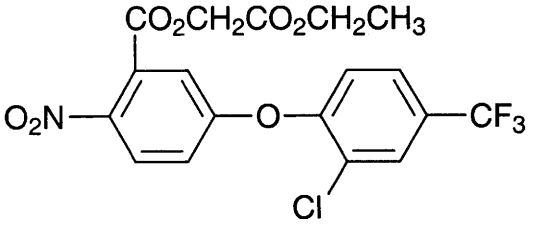
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

References

1. *NTIS Report* PB158-5087, Natl. Tech. Inf. Serv., Springfield, VA, USA.
2. *J. Chem. Soc.* 1949, 773.
3. *Nature (London)* 1953, **172**, 1139.
4. *J. Pharm. Pharmacol.* 1968, **20**, 465.
5. Teale, B. et al *Chem. Res. Toxicol.* 1989, **2**(6), 429-435.

6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F66 fluoroglycofen-ethyl



$C_{18}H_{13}ClF_3NO_7$ **Mol. Wt.** 447.75 **CAS Registry No.** 77501-90-7

Synonyms *O*-[5-(2-chloro-α,α,α-trifluorotolyloxy)-2-nitrobenzoyl]glycolic acid, ethyl ester; Compete

RTECS No. DG 5643100

Uses Herbicide.

Physical properties

M. Pt. 65°C **Specific gravity** 1.01 at 25°C **Partition coefficient** log P_{ow} 3.65 (1)
Solubility Water: 0.6 mg l^{-1} at 25°C. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 1.6 mg l^{-1}, trout 23 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* 30 mg l^{-1} (1).
LD_{50} contact bee >100 μg bee^{-1} (1).

Environmental fate

Degradation studies
In aqueous environment readily undergoes hydrolysis to the corresponding acid, which then undergoes microbial degradation (1).

Abiotic removal
Undergoes photodegradation in aqueous suspensions with $t_{1/2}$ of 230 days at pH 5, 15 days at pH 7 and 0.15 days at pH 9 (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1500 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >7.5 mg emulsifiable concentrate l^{-1} (2).
LD_{50} dermal rabbit >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LC_{50} (8 day) oral mallard duck, bobwhite quail >5000 mg kg^{-1} diet (1).

LC_{50} (1 yr) oral dog, no adverse effect level 320 mg kg^{-1} diet (1).

Irritancy

Slight skin and eye irritant in rabbit (2).

Genotoxicity

Salmonella typhimurium (strains and metabolic activation unspecified) mutagenicity assay negative (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Partition coefficient exceeds European Union limit of 3.0.

Other comments

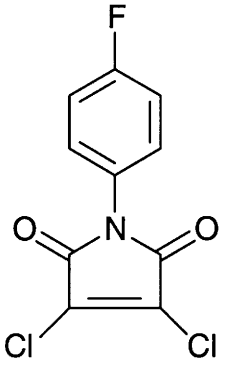
Mode of action – inhibits photosynthesis (1).

Metabolic pathways reviewed (5).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed, 1997, The British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

F67 fluoromide



$C_{10}H_4Cl_2FNO_2$ **Mol. Wt.** 260.05 **CAS Registry No.** 41205-21-4

Synonyms 3,4-dichloro-1-(4-fluorophenyl)-1*H*-pyrrole-2,5-dione; 2,3-dichloro-*N*-(4-fluorophenyl)maleimide; Spartcide; MK-23

RTECS No. UX 9560000

Uses Antifouling agent. Fungicide.

Physical properties

M. Pt. 240.5-241.8°C **Partition coefficient** log P_{ow} 2.301 (1)
Solubility Water: 5.9 mg l^{-1} at 20°C. Organic solvents: methanol

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 5-6 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse >15,000 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation ♂, ♀ rat 570, 720 mg m^{-3}, respectively (1).
LD_{50} dermal mouse >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (5 day) oral pheasant >27,000 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 600-2000 mg kg^{-1} diet (1).

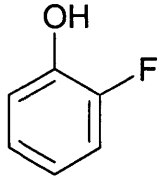
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
WHO Toxicity Class Table 5 (4).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemsistry, London, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F68 2-fluorophenol



C_6H_5FO **Mol. Wt.** 112.10 **CAS Registry No.** 367-12-4
Synonyms *o*-fluorophenol
EINECS No. 206-681-2 **RTECS No.** SL 4530000
Uses Organic synthesis.

Physical properties

M. Pt. 16.1°C **B. Pt.** 171-172°C at 741 mmHg **Flash point** 46°C **Specific gravity** 1.256 at 20°C
Partition coefficient log P_{ow} 1.65 (1)

Ecotoxicity

Invertebrate toxicity
IC_{50} (48 hr) *Tetrahymena pyriformis* 58 mg l^{-1} (2).

Environmental fate

Degradation studies
Metabolised to give 3-fluorobenzoate by anaerobic bacteria isolated from sediment (3).

Mammalian & avian toxicity

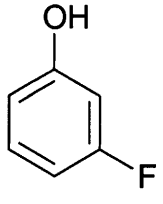
Acute data
LD_{50} intraperitoneal mouse 340 mg kg^{-1} (4).

Irritancy
Irritating to the skin, eyes, mucous membranes and upper respiratory tract (5).

References

1. Jaworska, J. S. et al *Bull. Environ. Contam. Toxicol.* 1991, **47**(1), 57-62.
2. Schultz, T. W. et al *Toxicol. Lett.* 1987, **37**(2), 121-130.
3. Chapman, P. J. *USEPA Res. Dev. Rep.* 1990, EPA-600/9-90/041, 30-32.
4. *J. Med. Chem.* 1975, **18**, 868.
5. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1718, Sigma-Aldrich, Milwaukee, WI, USA

F69 3-fluorophenol



C_6H_5FO **Mol. Wt.** 112.10 **CAS Registry No.** 372-20-3

Synonyms *m*-fluorophenol

EINECS No. 206-748-6

Uses Organic synthesis.

Physical properties

M. Pt. 14°C **B. Pt.** 178°C **Flash point** 71°C **Specific gravity** 1.238 at 20°C
Partition coefficient log P_{ow} 1.91 (1)

Ecotoxicity

Invertebrate toxicity
IC_{50} (48 hr) *Tetrahymena pyriformis* 38 mg l^{-1} (2).

Environmental fate

Degradation studies

Metabolised to give 2-fluorobenzoate by anaerobic bacteria isolated from sediment (3).

Mammalian & avian toxicity

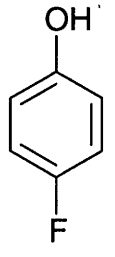
Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (4).

References

1. Jaworska, J. S. et al *Bull. Environ. Contam. Toxicol.* 1991, **47**(1), 57-62.
2. Schultz, T. W. et al *Toxicol. Lett.* 1987, **37**(2), 121-130.
3. Chapman, P. J. *US EPA Res. Dev. Rep.* 1990, EPA-600/9-90/041, 30-32.
4. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1718, Sigma-Aldrich, Milwaukee, WI, USA

F70 4-fluorophenol



C_6H_5FO **Mol. Wt.** 112.10 **CAS Registry No.** 371-41-5

Synonyms *p*-fluorophenol

EINECS No. 206-736-0 **RTECS No.** SL 4550000

Uses Chemical intermediate.

Physical properties

M. Pt. 46-48°C **B. Pt.** 185°C **Flash point** 68°C

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 19.5 ppm Microtox test (1).

Environmental fate

Anaerobic effects

The compound is not transformed to 4-fluorobenzoate by anaerobic phenol-degrading bacteria found in freshwater sediment (2).

Degradation studies

Peroxidases and lactases may be of possible use in removal from polluted soil and groundwater (3).

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Chernoff/Kavlock assay performed in Sprague-Dawley rats exposed on day-11 of gestation 0, 100, 333, 667 or 1000 mg kg^{-1}. High doses caused 81% mortality in dams; categorised as active in developmental potency (4).

Metabolism and toxicokinetics

Compound causes changes in potassium permeability of rat liver mitochondria, stimulates latent ATPase and causes cellular respiratory changes (5).

Other comments

Physico-chemical parameters that affect biodegradation of the compound have been reviewed (6).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361.
2. Genthner, B. R. S. *U.S. Environ. Prot. Agency Rev. Dev. Rep.* EPA 1990 EPA-600/9-90/041, 30-32.
3. Claus, H. et al *Water Sci. Technol.* 1990, **22**(6), 69-77.
4. Kavlock, R. J. *Teratology* 1990, **41**(1), 43-59.
5. Izushi, F. *Acta Med. Okayama* 1988, **42**(1), 7-14.
6. Urushigawa, Y. *Water Sci. Technol.* 1988, **20**(11-12) 459-461

F71 fluorophosphoric acid

H_2FPO_3

FH_2O_3P **Mol. Wt.** 99.99 **CAS Registry No.** 13537-32-1

Synonyms phosphofluoridic acid

RTECS No. TE 5000000

Uses Catalyst. Manufacture of wood preservatives.

Physical properties

Specific gravity 1.818 at 25°C with respect to water at 4°C **Volatility** v.den. 3.45

Occupational exposure

UN No. 1776

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 240-300 mg kg^{-1} (1,2).

Metabolism and toxicokinetics

Undergoes hydrolysis in humans with the release of fluoride ion. Apatite-catalysed breakdown, mediated by dental enamel, is believed to contribute significantly to the process (3,4).

Legislation

Phosphorus and its compounds are included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Limited under EC Directive on Drinking Water Quality 80/770/EEC. Phophorus: guide level 400 μg l^{-1} as P_2O_5, maximum admissible level 5000 μg l^{-1} as P_2O_5. Fluoride: maximum admissible concentration 1500 μg l^{-1} for average water temperatures of 8-12°C, 700 μg l^{-1} for average water temperatures of 25-30°C (6).

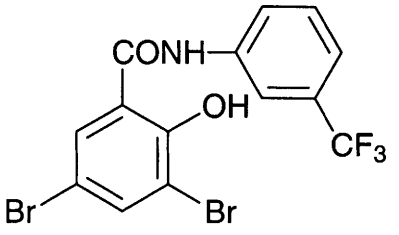
Other comments

Toxicity is related to the release of fluoride ion on hydrolysis (4).

References

1. Lim, J. K. et al *Caries Res.* 1978, **12**, 177-179.
2. Shourie K. L. et al *J. Dent. Res.* 1950, **29**, 529-533.
3. Bruun, C. et al *Scand. J. Dent. Res.* 1987, **95**(3), 202-204.
4. Smith, F. A. et al *Caries Res.* 1983, **17**(1), 36-45.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

F72 fluorosalan



$C_{14}H_8Br_2F_3NO_2$ **Mol. Wt.** 439.03 **CAS Registry No.** 4776-06-1

Synonyms 3,5-dibromo-2-hydroxy-*N*-[3-(trifluoromethyl)phenyl]benzamide; 3,5-dibromo-α,α,α-trifluoro-*m*-salicyl-*o*-toluidide; Fluorophene

EINECS No. 225-322-0 **RTECS No.** VO 6880000

Uses Disinfectant.

Physical properties

M. Pt. 161-163°C **Partition coefficient** log P_{ow} 6.11 (calc.) (1)

Mammalian & avian toxicity

Sensitisation

Reported to be a photosensitiser (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (4).

Other comments

Withdrawn from use in soaps and cosmetics when found to be a photosensitiser (3).

References

1. *Kirk-Othmer Encyclopedia of Chemical Technology* 3rd ed., 1979, **7**, 812, John Wiley & Sons, New York, NY, USA.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK

F73 fluorosilicate

$$[SiF_6]^{2-}$$

F_6Si **Mol. Wt.** 142.08 **CAS Registry No.** 17084-08-1

Synonyms hexafluorosilicate(2–); silicofluoride; silicon hexafluoride ion

RTECS No. VV 7790000

Uses Fluoridation of water. Electroplating. Wood preservative. Disinfectant.

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed (R22)

Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Avoid contact with skin and eyes (S2, S13, S24/25)

Environmental fate

Abiotic removal

Removed from wastewater by electrolysis, generating F^- which is then combined with added Ca^{2+} ($Ca(OH)_2$ (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral human 50 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Inadequate evidence of carcinogenicity to humans and animals for inorganic fluorides used in drinking water, IARC classification group 3 (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluoride: maximum admissible level 1500 μg l^{-1} for average water temperatures of 8-12°C, 700 μg l^{-1} for average water temperatures of 25-30°C (4).

Other comments

Toxicity of fluorosilicates used in drinking water and dental preparations reviewed (5).

Typical dosages for water fluoridation are up to 1.0 mg F^- l^{-1}; hydrofluorosilicic acid is often used in conjunction with a chelating agent, which may affect the solution chemistry (6).

References

1. Midorikawa, Y. et al (JGC Corp.) Jpn Kokai Tokkyo Koho JP 62,210,099 [87,210,099] (Il. C02F1/60) 16 Sep. 1987 (*Chem. Abstr.* **108**, 100654h).
2. *Br. Med. J.* 1936, **1**, 886.
3. *IARC Monograph* 1987, **Suppl. 7**, 208-210.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *IARC Monograph* 1982, **27**, 237-303.
6. Mantle, M. D. *J. Inst. Water Eng. Sci.* 1981, **35**(4), 365-370

F74 fluorosilicic acid

$$H_2SiF_6$$

F_6H_2Si **Mol. Wt.** 144.09 **CAS Registry No.** 16961-83-4

Synonyms hydrogen hexafluorosilicate; hexafluorosilicic acid; hydrosilicofluoric acid; silicofluoric acid

EINECS No. 241-034-8 **RTECS No.** VV 8225000

Uses In tanning, timber preservation, electroplating, cement hardening and electrolytic refining of lead. As a steriliser in brewing industry and in fluoridation of municipal water supplies.

Physical properties

B. Pt. decomposes **Specific gravity** 1.4634 (60.97% solution) at 25°C

Occupational exposure

UN No. 1778 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Causes burns (R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Take off immediately all contaminated clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S27, S45)

Ecotoxicity

Toxicity to other species
Lowest reported lethal dose (route unspecified) frog 140 mg kg^{-1} (1).

Mammalian & avian toxicity

Acute data
Effects of ingestion of toxic doses by humans include dose-related vomiting, abdominal pain and diarrhoea, and at fatal doses respiratory paralysis. Lethal dose 50-225 mg fluoride kg^{-1} (2).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, no adequate evidence for carcinogenicity to animals, IARC classification group 3 (3).

The long term and possible carcinogenic effects of inorganic fluorides have been extensively studied (2).

Teratogenicity and reproductive effects
Epidemiological tests have shown no association between the presence of fluorides in drinking water and the incidence of Downs Syndrome (4).

Metabolism and toxicokinetics
Fluoride ion is rapidly and extensively absorbed from the gut, and is transported in the blood in the free form (5). It is not accumulated in soft tissues, but accumulates in bones and teeth (6,7). Excretion occurs mainly via the kidneys (8) and sweat (9).

Irritancy
Corrosive to eyes and skin as concentrated solution (10).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 and *Escherichia coli* WP2*uvrA* with and without metabolic activation negative (11-12).
Drosophila melanogaster negative (12).
Mouse micronucleus test negative (12).

Other effects

Other adverse effects (human)
Long-term exposure to excessively high concentrations of soluble inorganic fluorides can have a variety of effects on teeth, bones, kidneys, reproduction system and blood. Levels in food or water that have been implicated in long-term exposure changes include: ≥2 ppm, mottled enamel ≥20-80 mg day^{-1}, crippling fluorosis; 100 ppm, growth retardation; and >125 ppm, kidney changes (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC for fluorides, maximum admissible concentration 1500 μg l^{-1} at 8-12°C, 700 μg l^{-1} at 25-30°C (13).

Other comments

In wastes from manufacturing processes including that of superphosphate production (14).
The toxicology of inorganic fluorides has been extensively reviewed (2).
Reviews on experimental toxicology, human health effects and physico-chemical properties listed (15).
When anhydrous, dissociates almost immediately to hydrogen fluoride. A 60-70% solution solidifies around 19°C to form a crystalline dihydrate.

References

1. *Compte Rendus* 1937, **124**, 133.
2. *IARC Monograph* 1982, **27**, 237-303.
3. *IARC Monograph* 1987, **Suppl. 7**, 208.
4. *IARC Monograph* 1987, **Suppl. 6**, 312-315.
5. Cremer, H. D. et al *Fluorides and Human Health* 1970, WHO, Geneva, Switzerland.
6. Hodge, H. C. et al *J. Am. Med. Assoc.* 1961, **177**, 313-316.
7. Taylor, B. M. et al *Toxicol. Appl. Pharmacol.* 1961, **3**, 290-314.
8. Smith, F. A. et al *Arch. Ind. Health.* 1955, **11**, 2-10.
9. Crosby, N. D. et al *Med. J. Aust.* 1956, **2**, 341-346.
10. *BDH Hazard Data Sheets* BDH, Dorset, UK.
11. Shimizu, H. et al *Sangyo Igaku* 1985, **27**(6), 400-419.
12. Gocke, E. M-T. et al *Mutat. Res.* 1981, **90**, 91.

13. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985, Luxembourg.
14. Chuturkova, R. et al *Khig. Zdraveopaz.* 1987, **30**(1), 28-32 (Bulg.) (*Chem. Abstr.* **107**, 120357w).
15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F75 fluorosulfonic acid

FSO_3H

FHO_3S **Mol. Wt.** 100.07 **CAS Registry No.** 7789-21-1

Synonyms fluorosulfuric acid; monofluorosulfuric acid

EINECS No. 232-149-4 **RTECS No.** LP 0715000

Uses Fluorinating agent, in alkylations, acylations and other chemical reactions.
Occurrence Occurs naturally in volcanic gases.

Physical properties

M. Pt. –89°C **B. Pt.** 163°C **Specific gravity** 1.726 at 25°C with respect to water at 4°C
Solubility Organic solvents: acetone

Occupational exposure

UN No. 1777 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance

Ecotoxicity

Invertebrate toxicity
Inhibitor of ATP sulfurylase thought to be derived from sulfide-oxidising bacteria living in volcanic vents (1).

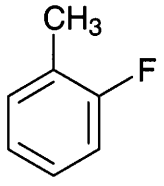
Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (2).
Reacts violently with water.

References

1. Renosto, F. *Arch. Biochem. Biophys.* 1991, **290**(1), 66-78.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F76 2-fluorotoluene



C_7H_7F **Mol. Wt.** 110.13 **CAS Registry No.** 95-52-3

Synonyms *o*-fluorotoluene; 1-fluoro-2-methylbenzene

EINECS No. 202-428-5 **RTECS No.** XT 2579000

Uses Chemical intermediate.

Physical properties

M. Pt. –62°C **B. Pt.** 114°C **Flash point** 12°C (closed cup) **Specific gravity** 1.001

Occupational exposure

UN No. 2388 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 100 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No evidence of carcinogenicity (2).

Teratogenicity and reproductive effects

No evidence of teratogenicity (2).

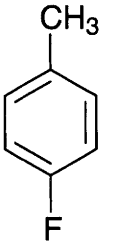
Genotoxicity

No evidence of mutagenicity (2).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *BDH Hazard Data Sheets* 1990, Merck Ltd., Dorset, UK

F77 4-fluorotoluene



C_7H_7F **Mol. Wt.** 110.13 **CAS Registry No.** 352-32-9

Synonyms 1-fluoro-4-methylbenzene; *p*-fluorotoluene

EINECS No. 206-520-6 **RTECS No.** XT 2580000

Uses Chemical intermediate.

Physical properties

M. Pt. –56°C **B. Pt.** 116°C **Flash point** 40°C **Specific gravity** 1.001 at 16°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2388 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 38.2 ppm Microtox test (1).
The toxicological significance of this result has been discussed (2).

Environmental fate

Degradation studies
Compound can be hydroxylated by *Mortierella isabellina* (3).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Kaiser, K. L. E. *ASTM Spec. Tech. Publ.* 1988, **1007**, 421-441.
3. Holland, H. L. *J. Chem. Soc., Perkin Trans.* 2 1990, (10), 1651-1655

F78 fluorotrichloromethane

CCl_3F

CCl_3F **Mol. Wt.** 137.37 **CAS Registry No.** 75-69-4

Synonyms trichlorofluoromethane; fluorochloroform; Freon MF; Halon 11; monofluorotrichloromethane; Isotron 11

EINECS No. 200-892-3 **RTECS No.** PB 6125000

Uses Aerosol propellant. In refrigeration machinery requiring a refrigerant effective at negative pressures. Blowing agent for polyurethane foams; fire extinguisher; solvent.

Physical properties

M. Pt. –111°C **B. Pt.** 23.7°C **Specific gravity** 1.494 at 17.2°C with respect to water at 4°C
Volatility v.p. 687.05 mmHg at 20°C ; v.den. 5.04
Solubility Water: 1100 mg l^{-1} at 25°C. Organic solvents: ethanol, diethyl ether

Occupational exposure

DE-MAK 1000 ppm (5700 mg m^{-3})
FR-VLE 1000 ppm (5600 mg m^{-3})
JP-OEL ceiling limit 1000 ppm (5600 mg m^{-3})
SE-LEVL 500 ppm (3000 mg m^{-3}) **SE-STEL** 750 ppm (4500 mg m^{-3})
UK-LTEL 1000 ppm (5710 mg m^{-3}) **UK-STEL** 1250 ppm (7140 mg m^{-3})
US-STEL ceiling limit 1000 ppm (5620 mg m^{-3})

Mammalian & avian toxicity

Acute data

LC_{50} (30 min) inhalation mouse, guinea pig, rabbit 10-25 pph (1,2).
LD_{Lo} (20 min) inhalation rat 10 pph (3).
LD_{50} intraperitoneal mouse 1743 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Gavage (78 wk) B6C3F1 mice 1962 or 3925 mg kg^{-1} day^{-1} in corn oil for 78 wk followed by observation for 13 wk. Neither group of ♂ or ♀ mice had an increased incidence of tumours compared to the controls (5).
Gavage (78 wk) Osborne-Mendel rats ♂ 488 or 977 mg kg^{-1} day^{-1}, ♀ 538 or 1077 mg kg^{-1} day^{-1} for 78 wk followed by 33 wk observation. There was a high number of early deaths in both ♂ and ♀ rats in this study. There were insufficient numbers of animals surviving long enough to assess the risk of late-developing tumours (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6).

Other comments

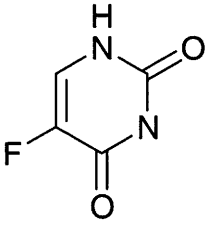
The standard *Escherichia coli* SOS chromotest was not valid for testing volatile compounds (7).
Human health effects, experimental toxicology, physico-chemical properties reviewed (8).

References

1. *Eur. J. Toxicol. Environ. Hyg.* 1976, **9**, 385.
2. *J. Eur. Toxicol.* 1976, **9**, 385.
3. *Arch. Ind. Hyg. Occup. Med.* 1950, **2**, 335.
4. *Toho Igukkai Zasshi* 1971, **18**, 363.

5. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-106, NIEHS, Research Triangle Park, NC, USA.
6. Zeiger, E. et al *Environ. Mol. Mutagen.* 1987, **9**(Suppl.9), 1-109.
7. Mersch-Sundermann, V. et al *Zentralbl. Hyg. Umweltmed.* 1989, **189**(3), 266-271 (Ger.) (*Chem. Abstr.* **112**, 193568d).
8. *ECETOC Technical Report No. 30(5)* 1994, European Chemical Industry Ecology and Toxicology Centre, B-1160 Brussels, Belgium

F79 5-fluorouracil



$C_4H_3FN_2O_2$ **Mol. Wt.** 130.08 **CAS Registry No.** 51-21-8

Synonyms 5-fluoro-2,4(1*H*,3*H*)pyrimidonedione; 2,4-dioxo-5-fluoropyrimidine; Fluracil; Uracil; Fluroblastin; Adrucil; Efudex

EINECS No. 200-085-6 **RTECS No.** YR 0350000

Uses Antineoplastic agent used in human and veterinary medicine. Of particular use in treatment of breast and gastro-intestinal tract cancers.

Physical properties

M. Pt. 282-283°C (decomp.)
Solubility Water: 12 mg ml^{-1} at 25°C. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 260 mg kg^{-1} (1).
LD_{50} intravenous rat 320 mg kg^{-1} (2).
Effects following acute administration included weight loss, diarrhoea, rectal bleeding, lethargy and ataxia. Bone marrow damage, lymphoid atrophy and cellular and humoral immunity depression have been reported in mice, while in rats, kidney, liver, spleen, lymph and adrenal damage has been seen (1-4).
Central nervous system effects have been reported in cats (5).

Sub-acute and sub-chronic data

Mortality curves for effects of repeated injections to mice showed that the treatment regime as well as the dose affected mortality (4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, no adequate evidence for carcinogenicity to animals, IARC classification group 3 (6).
Epidemiological studies involving use of 5-fluorouracil in association with other treatments have shown no evidence of carcinogenicity (7).
Oral administration to rats 5 × wk^{-1} for 1 yr 1-3 mg $animal^{-1}$ day^{-1} revealed no evidence of carcinogenicity (8).
Intravenous administration to mice wkly for 16 wk, 1 mg showed no induction of lung adenomas (9), while intravenous injection into rats 33 mg kg^{-1} wkly for 1 yr also gave a negative result (10).

Teratogenicity and reproductive effects

Syrian hamsters given intramuscular injections on days 8-11 of pregnancy exhibited teratogenic effects (11).
Single injections of 20-30 mg kg^{-1} to mice on day-11 of pregnancy have been reported to produce foetuses with limb abnormalities (12).
Some embryotoxicity (resorptions) has been seen in rhesus monkeys treated with 20-40 mg kg^{-1} (13).
Binding of fluorouracil to RNA and DNA of embryos from mice injected with the compound, has been detected (14).
Cultured 10.5-day-old rat embryos exposed to 2-8 μg ml^{-1} showed the compound to be embryopathic. *In vivo* concentrations of 2-17 μg ml^{-1} in plasma were also reported to be embryopathic (15).
Glutathione confers some protection against teratogenic effects in rats and mice (16).

Metabolism and toxicokinetics

Absorption through skin is minimal (17).
After administration by oral dose, or injection into animals, the compound rapidly enters all body compartments. Up to 80% of the dose is eliminated through metabolic degradation, but the parent compound is distributed to all tissue including bone marrow (7).
The compound requires metabolic activation, anabolic metabolism produces the cytotoxic nucleotides 5-fluoro-2′-deoxyuridine-5′-monophosphate and 5-fluorouridine-5′-triphosphate (18).
Catabolic metabolism is highly dependent on dose and blood flow, but follows the same pathways as endogenous uracil and thymine. In humans the compound is rapidly metabolised catabolically to dihydroxyfluorouracil which is then hydrolysed to α-fluoro-β-ureidopropionic acid and then α-fluoro-β-alanine, carbon dioxide and ammonia, or hydrolysed via α-fluoro-β-guanidopropionic acid. The liver is the major site, but a considerable amount of metabolism occurs at extra-hepatic sites (18-24).

Irritancy

Topical administration of 0.5 mg for 14 days to cheek pouch of hamsters caused erythema, necrosis and ulceration of mucosa with subsequent re-epithelisation (25).

Genotoxicity

Salmonella typhimurium TA92, TA98, TA100 without metabolic activation positive, with activation negative (26,27).
In vitro Chinese hamster lung fibroblast cells with metabolic activation induced chromosome aberrations (28).
In vivo mouse micronucleus test positive (29).
Did not induce sister chromatid exhanges without metabolic activation in cultured human lymphocytes (30).

Other effects

Other adverse effects (human)

Cardiotoxicity and neurotoxicity have been reported in patients treated with 5-fluorouracil. Clinical signs usually abate 1-6 wk after discontinuing therapy (31).
Adverse effects are those commonly seen with antineoplastic and immunosuppressive agents. The main such effects with fluoracil are on bone marrow and gastro-intesinal tract. Leucopenia, thrombocytopenia, stomatitis, gastro-intestinal ulceration, and bleeding, together with severe diarrhoea are signs which prompt the treatment to be suspended (17).

Any other adverse effects

Lethargy and ataxia observed in rodents, however neurotoxicity, including hyperexcitability, nervousness, muscle tremors and seizures have been reported in dogs and cats (32,33).

Other comments

Oral administration can be unpredictable and injection is frequently preferred for therapy (17).

References

1. Houghton, J. A. et al *Cancer Res.* 1979, **39**, 2406-2413.

2. Danhauser, L. L. et al *J. Lab. Clin. Med.* 1979, **93**, 1047-1053.
3. Harrison, S. D. et al *Cancer Treat. Rep.* 1978, **62**, 533-545.
4. Johnson, R. K. et al *Cancer Treat. Rep.* 1976, **60**, 1335-1345.
5. Harvey. H. J. et al *J. Am. Vet. Med. Assoc.* 1977, **17**, 277-278.
6. *IARC Monograph* 1987, **Suppl. 7**, 210.
7. *IARC Monograph* 1981, **26**, 217-235.
8. Hadidian, Z. et al *J. Natl. Cancer Inst.* 1968, **41**, 985-1036.
9. Homburger, J. A. et al *Oncology* 1971, **25**, 1-10.
10. Schmuhl, D. et al *Arzneim.-Forsch.* 1970, **20**, 1461-1467.
11. Shah, R. M. et al *J. Embryol. Exp. Morphol.* 1978, **43**, 47-54.
12. Imagawa, S. et al *Teratology* 1979, **20**, 155.
13. Wilson, J. G. *Fed. Proc.* 1971, **30**, 104-109.
14. Forsthoetel, P. F. et al *Teratology* 1978, **18**, 269-276.
15. Grafton, T. F. *Teratology* 1987, **36**(3), 371-377.
16. Naya, M. et al *Congenital Anomalies* 1987, **27**(3), 259-266.
17. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
18. Warren, B. S. *Cancer Res.* 1987, **47**(20), 5261-5265.
19. Myers, C. E. *Pharmacol. Rev.* 1981, **33**, 1-15.
20. Collins, J. M. et al *Clin. Pharmacol. Ther.* 1980, **28**, 235-246.
21. Au, J. L.-S. et al *J. Pharmacol. Exp. Ther.* 1983, **227**, 174-180.
22. Williams, W. M. et al *Proc. Soc. Exp. Biol. Med.* 1987, **184**, 326-336.
23. Lin, F. H. et al *Proc. Soc. Exp. Biol. Med.* 1988, **189**(3), 353-361.
24. Glaholm, J. et al *Br. J. Radiol.* 1990, **63**(751), 547-553.
25. Cherrick, U. M. et al *J. Invest. Dermatol.* 1974, **63**, 284-286.
26. Seino, Y. et al *Cancer Res.* 1978, **38**, 2148-2156.
27. Minnich, V. et al *Cancer* 1976, **38**, 1253-1258.
28. Ishidate, M. et al *Gann Monogr. Cancer Res.* 1980, **27**, 95-108.
29. Maier, P. et al *Mutat. Res.* 1976, **40**, 325-338.
30. Clare, M. G. et al *Eur. J. Cancer Clin. Oncol.* 1982, **18**, 979-989.
31. Weiss, U. D. et al *New Engl. J. Med.* 1974, **291**, 75-81.
32. Harvey, H. J. et al *J . Am. Vet. Med. Assoc.* 1977, **171**, 277-278.
33. Henness, A. M. et al *J. Am. Vet. Med. Assoc.* 1977, **171**, 692

F80 fluorspar

CaF_2

CaF_2 **Mol. Wt.** 78.07 **CAS Registry No.** 14542-23-5

Synonyms fluorite; acid-spar; calcium difluoride; liparite; Irtiran 3

EINECS No. 238-575-7

Uses Primary source of fluorine and its compounds. In production of hydrofluoric acid, in steelmaking and in paint pigments. Also in oral hygiene products.

Occurrence Naturally occurring mineral, obtained by mining or synthesis.

Physical properties

M. Pt. 1403°C **B. Pt.** 2500°C **Specific gravity** 3.18

Occupational exposure

SE-LEVL 2 mg m^{-3} (as F)

UK-LTEL 2.5 mg m^{-3} (as F)

Environmental fate

Abiotic removal

Fluorspar dust can be removed from waste gases generated during fluorspar processing using modified cyclones and centrifugal scrubbers (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, no adequate evidence for carcinogenicity to animals, IARC classification group 3 (2).

Sustained ingestion of excessive amounts of insoluble fluoride produces changes in teeth and skeleton of all species studied (3).

Mixed dust from a fluorspar mine induced a foreign body reaction only in rabbit lung. Fluorspar did not stimulate pulmonary or alveolar macrophages (4).

Other effects

Other adverse effects (human)

Emphysematous lesions seen in workers at fluorspar mines may result from the inhalation of a combination of fluorspar and silica (4).

Any other adverse effects

Field mice, voles and common shrews living on land contaminated by fluorspar accumulated it in the liver, kidney and bone (5).

Cytotoxic to rat alveolar macrophages (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC for fluoride, maximum admissible concentration 1500 $\mu g\ l^{-1}$ at 8-12°C and 700 $\mu g\ l^{-1}$ at 25-30°C (7).

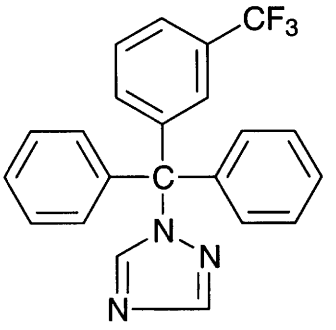
Other comments

The toxicity of inorganic fluorides has been reviewed extensively (2,8,9).

References

1. Zhulin, N. V. et al *Tsvetn. Met. (Moscow)* 1991, (2), 68-69 (Russ.) (*Chem. Abstr.* **115**, 98299v).
2. *IARC Monograph* 1987, **Suppl. 7**, 208.
3. Shupe, J. L. *Clin. Toxicol.* 1972, **5**, 195-213.
4. Xu, Y. *Environ. Res.* 1987, **3**(2), 350-358.
5. Cooke, J. A. et al *Water, Air, Soil Pollut.* 1990, **51**(1-2) 43-54.
6. Yang, S. et al. *Zhejiang Yike Daxue Xuebao* 1990, **70**(3), 435-444.
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *IARC Monograph* 1982, **27**, 237-303.
9. *IARC Monograph* 1987, **Suppl. 6**, 312

F81 fluotrimazole



$C_{22}H_{16}F_3N_3$ **Mol. Wt.** 379.38 **CAS Registry No.** 31251-03-3

Synonyms 1-(3-trifluoromethyltrityl)-1*H*-1,2,4-triazole; 1-[diphenyl[(3-trifluoromethyl)phenyl]methyl]-1*H*-1,2,4-triazole; Persulon

EINECS No. 250-534-5 **RTECS No.** XZ 4803020

Uses Superseded fungicide.

Physical properties

M. Pt. 132°C

Solubility Water: 1.5 μg l^{-1} at 20°C. Organic solvents: cyclohexanone, isopropanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) golden orfe >100 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >5 g kg^{-1} (1).
LD_{50} oral canary >1 g kg^{-1} (1).
LD_{50} dermal rat >1 g kg^{-1} (1).

Sub-acute and sub-chronic data

A 90-day feeding trial in dogs and rats established a no-effect level of 75 and 800 mg kg^{-1} diet, respectively (1).

Carcinogenicity and chronic effects

A 2-yr feeding trial in rats established a no-effect level of 50 mg kg^{-1} diet (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC for pesticides, maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

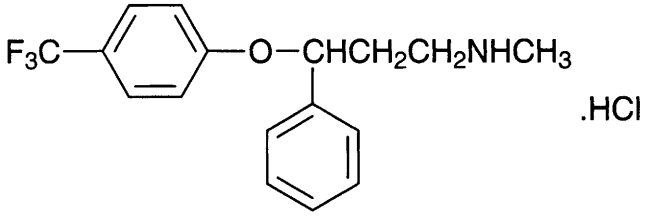
Other comments

Exerts synergistic action with dithianon (4).
Not harmful to honey bees (1).

References

1. *The Pesticide Manual* 8th ed., 1987, British Crop Protection Council, Farnham, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. Albert, G. et al *Ger. Offen.* DE 3,602,317 App. 27 Jan. 1986

F82 fluoxetine hydrochloride



$C_{17}H_{19}ClF_3NO$ **Mol. Wt.** 345.79 **CAS Registry No.** 59333-67-4

Synonyms (±)-*N*-methyl-3-phenyl-3-[(α,α,α-trifluoro-*p*-tolyloxy)]propylamine hydrochloride; benzenepropanamine, *N*-methyl-γ-[4-(trifluoromethyl)phenoxy]-, hydrochloride, (±)-; Prozac

Uses Antidepressant.

Physical properties

M. Pt. 179-182°C

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Oral Fischer 344 rat (days 6-15 of gestation) 0, 2, 5 or 12.5 mg kg^{-1} and oral Dutch belted rabbit (days 6-18 of gestation) 0, 2.5, 7.5 or 15 mg kg^{-1}. Maternal toxicity was indicated in rats at 12.5 mg kg^{-1} by a depression of weight gain and food consumption. Maternal and developmental no-observable-adverse-effect levels (NOAEL) were 5 and 12.5 mg kg^{-1}, respectively. Weight loss occurred in all treated rabbits, with depressed food consumption at the two higher doses. Abortions and maternal mortality occurred secondary to anorexia and cachexia at 15 mg kg^{-1}. The NOAEL for developmental effects in rabbits was 15 mg kg^{-1}. Foetal viability, weight and morphology were not affected at any dose level in either species (1).

Metabolism and toxicokinetics

Readily absorbed from the human gastro-intestinal tract, with peak plasma concentrations occurring 6-8 hr after administration. Extensively metabolised in the liver to its primary active metabolite norfluoxetine; the primary route of elimination involves further hepatic metabolism to inactive metabolites which are excreted in urine. The compound is extensively bound to plasma proteins and is widely distributed throughout the body. Its elimination $t_{1/2}$ is 2-3 days and that of its metabolite norfluoxetine is 7-9 days. Both fluoxetine and its metabolites are excreted in breast milk (2).

The washout period required after discontinuation is ≥5 weeks (3).

Other effects

Other adverse effects (human)

Adverse effects reported include gastro-intestinal disturbances (nausea, vomiting, diarrhoea), anorexia and weight loss. Neurological side-effects include anxiety, nervousness, insomnia and fatigue; headache, tremor,

dizziness, convulsions and decreased libido have also been reported. Excessive sweating, and pruritus and skin rashes have been seen in patients receiving the drug, with systemic events involving the lungs, kidneys or liver developing in those with skin rashes (2).

Angioedema, urticaria and anaphylaxis have been reported, and the presence of a skin rash requires the drug to be discontinued (4).

Nausea, vomiting and excitation of the central nervous system follow overdoses; deaths have also been reported (2).

The combination of the drug with other antidepressants, including monoamine oxidase inhibitors, lithium or tryptophan, may result in enhanced serotonergic effects. Although this enhancement may be beneficial in some cases, it can produce a life-threatening serotonin syndrome comprising hyperthermia, tremor and convulsions (2).

Of 67 adult subjects who overdosed on Prozac alone, 15 developed tachycardia, 14 were drowsy, 5 suffered tremors, 4 were nauseous and 4 suffered vomiting (5).

Of 37 subjects who overdosed on the drug alone, 7 remained asymptomatic, 7 were sleepy, 9 had a sinus tachycardia (≥100 beats min^{-1}) and 3 had diastolic pressure of >100 mmHg (6).

A 6-wk-old infant referred for colic whose mother was using the drug and breast-feeding the child showed symptoms of increased crying and vomiting, decreased sleep and watery stools. These symptoms were reduced when the infant was formula-fed, suggesting a possible relationship between colic and associated symptoms and the drug in breast milk (7).

Case reports suggest the drug may produce suicidal tendencies in some patients (8).

Suicide was the most common cause of death found in a review of all deaths in Maryland where either fluoxetine or tricyclic antidepressant (TCA) use was detected. Violent methods were more often associated with fluoxetine suicides than with TCA suicides. Possible explanations include the inherent lower lethality of fluoxetine compared to TCA, necessitating the use of additional means to complete the act of suicide, or that the drug may be associated with the induction of violence and/or suicidal ideation (9).

Three or more minor anomalies occurred in more than twice as many babies born to women taking Prozac (fluoxetine): 15.5% compared to control women 6.5%, in one study. The rate of spontaneous abortion and major structural anomalies was the same in both groups. The results came from analysing pregnancy outcomes in 228 women taking Prozac; problems were most common in infants exposed to fluoxetine during the third trimester. These women were five times more likely to be delivered prematurely, and had nine times the incidence of poor neonatal adaption, respiratory difficulty, cyanosis on feeding and jitteriness. A similar study by the European Teratology Information Service evaluating data on 689 pregnancies with exposure to antidepressants including fluoxetine found that 97% of live births were morphologically normal (10).

Other comments

Has been used for the treatment of obsessive compulsive disorders, pain syndromes including diabetic neuropathy and fibrositis, panic disorders, sleep disorders and bulimia nervosa (2).

Potent inhibitor of cytochrome P_{450} (CYP2D6) isozyme in human liver microsomes with the potential for many metabolically based drug interactions (11).

Fluoxetine is a potent inhibitor of 5-HT neuronal uptake, and can bind directly to 5-HT2 receptors (12).

References

1. Byrd, R. A. *Fundam. Appl. Toxicol.* 1994, **22**(4), 511-518.
2. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
3. Marino, M. R. et al *Clin. Pharmac. Therap.* 1996, **59**, 180.
4. *British National Formulary* 1997, **34**, The British Medical Association and The Royal Pharmaceutical Society of Great Britain, London, UK.
5. Borys, D. J. et al *Am. J. Emerg. Med.* 1992, **10**(2), 115-120.
6. Borys, D. J. et al *J. Toxicol. Clin. Toxicol.* 1990, **28**(3), 331-340.
7. Lester, B. M. et al *J. Am. Acad. Child Adolescent Psychiatry* 1993, **32**(6), 1253-1255.
8. Bost, R. O. et al *J. Anal. Toxicol.* 1992, **16**(2), 142-145.
9. Frankenfield, D. L. et al *Forensic Sci. Int.* 1994, **64**(2-3), 107-117.
10. Major, S. *Br. Med. J.* 1996, **313**(7062), 902.
11. Otton, S. V. et al *Clin. Pharmacol. Ther.* 1993, **53**(4), 401-409.
12. Wong, D. T. et al *Neuropsychopharmacol.* 1991, **5**, 43-47

F83 flupropanate-sodium

$F_2CHCF_2CO_2Na$

$C_3HF_4NaO_2$ **Mol. Wt.** 168.02 **CAS Registry No.** 22898-01-7

Synonyms sodium 2,2,3,3-tetrafluoropropionate; sodium 2,2,3,3-tetrafluoropropanoate; Frenock

EINECS No. 245-311-4 **RTECS No.** UF 7770000

Uses Herbicide used to control annual and perennial grasses in pastures and in uncultivated land.

Physical properties

M. Pt. 165-167°C (decomp.) **Specific gravity** 1.45 **Partition coefficient** log P_{ow} <–1.9 (1)
Volatility v.p. <40 mPa at 138°C
Solubility Water: 3.9 kg l^{-1}

Ecotoxicity

Fish toxicity
Median tolerance limit (48 hr) carp and rainbow trout >10,000 mg l^{-1} (1).

Environmental fate

Adsorption and retention
Field tests indicate that flupropanate-sodium is immobile and persistent in the soil (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂, ♀ quail 6750, 11,000 mg kg^{-1}, respectively (1).
LD_{50} oral rat 11,900 mg kg^{-1} (1).
LD_{50} oral mouse 9600 mg kg^{-1} (1).
LD_{50} percutaneous rat 5500 mg kg^{-1} (1).
LD_{50} percutaneous rabbit 4000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (14 day) inhalation rat >1740 mg m^{-3} (1).
Oral rat (3 month) 5 mg kg^{-1} showed no observable effect (1).

Carcinogenicity and chronic effects
Oral mouse (1 yr) 6.6 mg kg^{-1} showed no observable effect (1).

Metabolism and toxicokinetics
Flupropanate-sodium administered to rats was not detected in internal organs after 14 days (1).

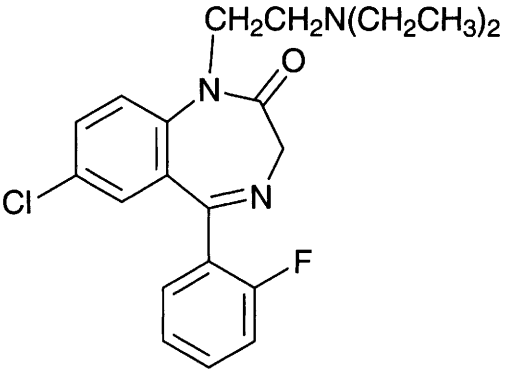
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F84 flurazepam



$C_{21}H_{23}ClFN_3O$ **Mol. Wt.** 387.88 **CAS Registry No.** 17617-23-1

Synonyms 7-chloro-1-[2-(diethylamino)ethyl]-5-(2-fluorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one; Felmane; Noctosom; Stauroderm

EINECS No. 241-591-7 **RTECS No.** DF 2368050

Uses Sedative and hypnotic for use in both human and animal medicine. Usually administered as monohydrochloride in the UK and dihydrochloride in the USA.

Physical properties

M. Pt. 77-82°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 500, 796 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal rat 152 mg kg^{-1} (3).
LD_{50} subcutaneous rat 600 mg kg^{-1} (4).
LD_{50} intravenous rat 39 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 186 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Rats treated with flurazepam for 1 wk developed tolerance to effects of benzodiazepines seen at a cellular level (5).

Metabolism and toxicokinetics

Readily absorbed from gastro-intestinal tract when used as monohydrochloride. It undergoes extensive first-pass metabolism and is excreted in urine chiefly as conjugates. Major active metabolite is *N*-desalkylflurazepam, which reaches highest plasma concentration 10 hr after administration to humans and has a $t_{1/2}$ of 71 hr. It can still be detected 9 days later (3,6,7).
Minor metabolites include hydroxyethylflurazepam and flurazepam aldehyde (6).
Metabolism may occur in small bowel mucosa, but hepatic biotransformation is thought to be the main cause of the first-pass effect (8,9).

Other effects

Other adverse effects (human)

The compound may cause dependence (10-12).
It has been reported to have induced cholestatic jaundice and to have porphyria-inducing actions (13,14).

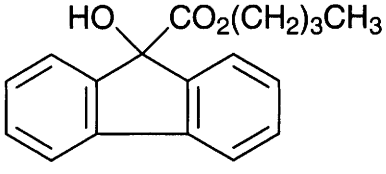
Other comments

Reduced dosage is necessary in the elderly (10).

References

1. *Yakkyoku* 1978, **29**, 29.
2. *Therapie* 1971, **26**, 439.
3. *Iyakuhin Kenkyu* 1975, **6**, 530.
4. *Drugs in Japan: Ethical Drugs* 6th ed., 1982, **6**, 706.
5. Ngur, D. O. *Eur. J. Pharmacol.* 1990, **176**(3), 351-356.
6. Miller, L. G. et al *Psychopharmacology* 1988, **94**(3), 386-391.
7. Kaplan, S. A. et al *J. Pharm. Sci.* 1973, **62**, 132-135.
8. Ochs, H. R. et al *J. Pharmacol. Exp. Ther.* 1987, **243**(3), 852-856.
9. Mahon, W. A. et al *Clin. Pharmacol. Ther.* 1977, **22**, 228-233.
10. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
11. Falk, J. L. *J. Pharmacol. Exp. Ther.* 1989, **249**(1), 143-148.
12. Bixter, E. et al *Pharmacology* 1987, **35**(5), 286-300.
13. Fang, M. H. et al *Ann. Intern. Med.* 1978, **89**, 363-364.
14. Reynolds, R. et al *Can. Med. Assoc. J.* 1981, **124**, 893-894

F85 flurenol-butyl



$C_{18}H_{18}O_3$ **Mol. Wt.** 282.34 **CAS Registry No.** 2314-09-2

Synonyms 9-hydroxyfluorene-9-carboxylic acid, butyl ester; 9-hydroxy-9*H*-fluorene-9-carboxylic acid, butyl ester; IT3233; Anten

EINECS No. 219-011-9 **RTECS No.** LL 6490000

Uses Plant growth inhibitor and herbicide potentiator.

Physical properties

M. Pt. 71°C **Specific gravity** 1.15 at 20°C **Partition coefficient** log P_{ow} 3.7 **Volatility** v.p. 2.3×10^{-7} mmHg at 25°C

Solubility Water: 36.5 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, carbon tetrachloride, cyclohexane, isopropanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 12.5 mg l^{-1} (1).

LC_{50} (96 hr) carp 18.2 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} contact honey bee ≈0.1 mg bee^{-1} (1).

Environmental fate

Degradation studies

Microbial degradation in soil and water is rapid, $t_{1/2}$ 1.5 days in soil and $t_{1/2}$ 1-4 days in water (2). Compound is reported to have no residue problems (3).

Abiotic removal

Decomposes in simulated daylight (2).

Adsorption and retention

In soils with 0.5-2.6% organic carbon, pH 6.0-7.6, adsorption of 1.6-5 mg kg^{-1} has been reported (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >10 g kg^{-1} (1).
LD_{50} oral mouse >5 g kg^{-1} (1).
LD_{50} dermal rat >10 g kg^{-1} (1).

Sub-acute and sub-chronic data

In a 78-day feeding trial in rats, a no-effect level of 1 g kg^{-1} was established (1).
In an 81-day feeding trial in dogs, a no-effect level of 1 g kg^{-1} was established (1).

Metabolism and toxicokinetics

In rats following oral administration, 70-90% was eliminated within 24 hr, principally in urine (2).

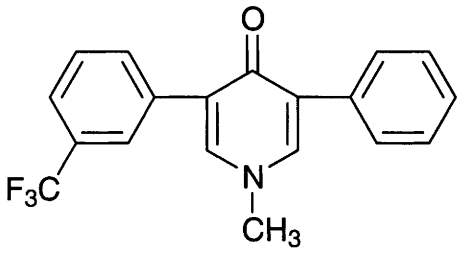
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Sheikh, A. S. et al *Egypt. J. Bot.* 1989, **29-30**(1-3), 245-272.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F86 fluridone



$C_{19}H_{14}F_3NO$ **Mol. Wt.** 329.32 **CAS Registry No.** 59756-60-4

Synonyms 1-methyl-3-phenyl-5-(α,α,α-trifluoro-*m*-tolyl)-4-pyridone; 1-methyl-3-phenyl-5-(3-trifluoromethylphenyl)-4(1*H*)-pyridinone; Sonar; Pride; Brake

EINECS No. 261-916-6 **RTECS No.** UU 7786500

Uses Pre-emergence and aquatic herbicide.

Physical properties

M. Pt. 151-154°C **Partition coefficient** log P_{ow} 1.86 at 25°C, pH 7 (1) **Volatility** v.p. 9.7×10^{-8} mmHg at 25°C
Solubility Water: 12 mg l^{-1} at pH 7, 25°C. Organic solvents: chloroform, methanol, hexane

Ecotoxicity

Fish toxicity
LC_{50} rainbow trout 11.5 mg l^{-1} (2).
LC_{50} bluegill sunfish 6.3 mg l^{-1} (2).

Environmental fate

Degradation studies
Microbial degradation is principal cause of dissipation in soil (1).
Decay is dependent on temperature, moisture and pH, with persistence being greater over winter months (3-5).
$t_{1/2}$ 21 days in water, and $t_{1/2}$ 147 days in sandy loam soil (1,4).

Abiotic removal
Decomposed by UV radiation, $t_{1/2}$ in deionised water 23 hr (1).

Adsorption and retention
Less adsorption is seen at higher pHs (5).
Coefficients have been calculated for a variety of conditions (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail >2 g kg^{-1} (2).
LD_{50} oral rat, mouse >10 g kg^{-1} (2).
LD_{50} oral dog >500 mg kg^{-1} (2).
LD_{50} oral cat >250 mg kg^{-1} (2).
LD_{50} dermal rabbit >5000 mg kg^{-1} (2).

Sub-acute and sub-chronic data
LC_{50} (5 day) bobwhite quail, mallard duck 5000 mg kg $diet^{-1}$ (1).

Carcinogenicity and chronic effects
2-yr feeding study in rats, no adverse effects at 200 mg kg^{-1} diet day^{-1} (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).
WHO Toxicity Class Table 5 (9).

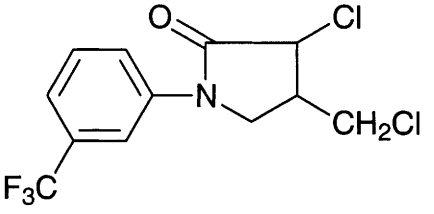
Other comments

Pollutant of water, contaminant of food and animal feed.
Metabolic pathways reviewed (10).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Zandvoort, R. *Neth. J. Agric. Sci.* 1989, **37**(3), 257-262.
4. Malik, N. et al *J. Environ. Sci. Health, Part B* 1990, **B25**(4), 447-472.
5. Malik, N. et al *Can. J. Soil Sci.* 1989, **69**(3), 567-577.
6. Malik, N. et al *Can. J. Soil Sci.* 1990, **70**(3), 435-444.
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
9. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
10. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

F87 flurochloridone



$C_{12}H_{10}Cl_2F_3NO$ **Mol. Wt.** 312.12 **CAS Registry No.** 61213-25-0

Synonyms 3-chloro-4-(chloromethyl)-1-[3-(trifluoromethyl)phenyl]-2-pyrrolidinone; (3*RS*,4*RS*:3*RS*,4*SR*)-3-chloro-4-chloromethyl-1-(α,α,α-trifluoro-*m*- tolyl)-2-pyrrolidinone (in ratio 3:1); fluorochloridone; Racer; R-40244

EINECS No. 262-661-3 **RTECS No.** UY 5746500

Uses Pre-emergence herbicide.

Physical properties

M. Pt. 61-73°C (technical) **Partition coefficient** log P_{ow} 3.362 at 20°C **Volatility** v.p. 6.02×10^{-3} mmHg at 25°C
Solubility Water: 28 mg l^{-1} at 20°C. Organic solvents: acetone, chloroform, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 5 mg l^{-1} (1).
LC_{50} (96 hr) rainbow trout 3 mg l^{-1} (1).

Invertebrate toxicity

Not dangerous to bees (1).
LD_{50} oral and contact bee >100 μg bee^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil has been reported as 9-70 days (1).
Stable to light (2).
Persistence is increased and movement decreased by covering treated soil with clear, perforated polyethylene sheeting (3).
Movement and persistence in sandy loam soil has been assessed by a computer model (4).
Flurochloridone was applied pre-emergence in potato crops at the rate of 500 g active ingredient ha^{-1}. During the 10 weeks following herbicide application, half-lives in the soil were 41, 48, 67 and 74 days for, respectively, plots untreated with organic fertilizer and plots treated with green manure, pig slurry, or cow manure. The same regime the following year resulted in the following $t_{1/2}$ values: 50, 58, 80, and 70 days, respectively. In both years, after the first 10 week period following flurochloridone application the rates of flurochloridone biodegradation increased and its soil residues became very low in all plots. After potato harvest and tilling, flurochloridone was no longer detectable in the soil (limit of sensitivity 0.01 mg flurochloridone kg^{-1} dry soil) (5).

Abiotic removal

In acidic media and at elevated temperatures decomposition occurs (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral Japanese quail >2.15 g kg^{-1} (1).
LD_{50} oral rat 4 g kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >0.121 mg l^{-1} air (1).
LD_{50} dermal rabbit >5 g kg^{-1} (1).

Carcinogenicity and chronic effects

A 2-yr feeding study in rats established no-effect levels of 100 mg kg^{-1} diet (♂) and 400 mg kg^{-1} diet (♀) (1).

Irritancy

In rabbits, mild irritant to skin and non-irritant to eyes (1).

Sensitisation

Not a skin sensitiser in guinea pigs (1).

Genotoxicity

Salmonella typhimurium (strains and metabolic activation unspecified) negative (2).
Mouse lymphoma test negative (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
WHO Toxicity Class Table 5 (8).

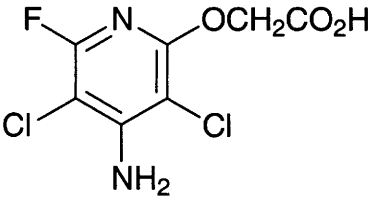
Other comments

Environmental pollutant. Food contaminant.

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Bond, W. et al *Am. Appl. Biol.* 1989, **114**(1), 133-140.
4. Walker, A. *Weed Res.* 1987, **27**(2), 143-152.
5. Rouchard, J. et al *Toxicol. Environ. Chem.* 1997, **61**(1-4), 251-257.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991, No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F88 fluroxypyr



$C_7H_5Cl_2FN_2O_3$ **Mol. Wt.** 255.03 **CAS Registry No.** 69377-81-7

Synonyms [(4-amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy]acetic acid; Starane; Barclay Hurler; Trastan

RTECS No. AF 2500000

Uses Selective herbicide for broad-leaved weeds.

Physical properties

M. Pt. 232-233°C **Partition coefficient** log P_{ow} –1.23 **Volatility** v.p. 9.42×10^{-7} mmHg at 25°C

Solubility Water: 91 mg l^{-1} at 20°C. Organic solvents: acetone, ethyl acetate, isopropanol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, golden orfe >100 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* >100 mg l^{-1} (1).

LD_{50} (48 hr) honey bee >100 mg bee^{-1} (2).

Environmental fate

Degradation studies

Rapidly degraded by aerobic microorganisms to 4-amino-3,5-dichloro-6-fluoropyridin-2-ol, 4-amino-3,5-dichloro-6-fluoro-3-methoxypyridine and CO_2 (2).

$t_{1/2}$ in soil 50 days. No evidence of leaching below level of top soil (2,3).

Abiotic removal

$t_{1/2}$ 185 days in water at 20°C (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck, bobwhite quail >2 g kg^{-1} (2).
LD_{50} oral rat 2.4 g kg^{-1} (4).
LC_{50} inhalation (4 hr) rat >0.296 mg l^{-1} (2).
LD_{50} dermal rabbit >5 g kg^{-1} (4).
LD_{50} intraperitoneal ♂ rat 458 mg kg^{-1} ♀ rat 519 mg kg^{-1} (4).

Carcinogenicity and chronic effects

No evidence of carcinogenicity (1).
2-yr feeding study in rats established a no-effect level of 80 mg kg^{-1} day^{-1} (1).
1.5-yr feeding study in mice established a no-effect level of 320 mg kg^{-1} day^{-1} (1).

Teratogenicity and reproductive effects

No reproductive effects in rats, no teratogenic effects in rats or rabbits (1).

Metabolism and toxicokinetics

After oral administration to rats, the compound is excreted unchanged, mostly in urine (2).

Genotoxicity

Salmonella typhimurium (strains and metabolic activation unspecified) negative (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
WHO Toxicity Class Table 5 (7).
ADI 0.8 mg kg^{-1} body weight (1).

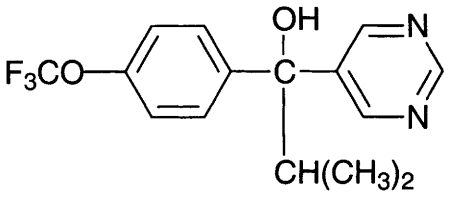
Other comments

Metabolic pathways reviewed (8).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. Bergstroem, L. F. *Pestic. Sci.* 1990, **29**(4), 405-417.
4. Paul, J. A. *Proc. Br. Crop. Prot. Conf.-Weeds* 1985, 939.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S.I. 1991, No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
8. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

F89 flurprimidol



$C_{15}H_{15}F_3N_2O_2$ **Mol. Wt.** 312.29 **CAS Registry No.** 56425-91-3

Synonyms α-(1-methylethyl)-α-[4-(trifluoromethoxy)phenyl]-5-pyrimidinemethanol; α-isopropyl-α-[*p*-(trifluoromethoxy)phenyl]-5-pyrimidinemethanol; Cutless; EL-5000; Topflor

RTECS No. UV 9283500

Uses Plant growth regulator.

Physical properties

M. Pt. 94-96°C **B. Pt.** 264°C **Specific gravity** 1.34 at 24°C **Partition coefficient** log P_{ow} 3.34 at pH 7 and 20°C **Volatility** v.p. 3.64×10^{-7} mmHg (25°C)
Solubility Water: 115 mg l^{-1} at 20°C, pH 7. Organic solvents: acetone, ethanol, methanol

Ecotoxicity

Invertebrate toxicity
LD_{50} (48 hr) contact bee >100 μg bee $^{-1}$ (1).

Environmental fate

Degradation studies
Degraded in soil to more than 30 breakdown products (1).
The compound translocates in plants, but little metabolism by plants occurs (2).

Abiotic removal
Photolytically decomposed in water with $t_{1/2}$ ~3 hr (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral quail >2 g kg^{-1} (1).
LD_{50} oral ♂ mouse 602 mg kg^{-1}, ♀ 702 mg kg^{-1} (1).
LD_{50} oral ♂ rat 914 mg kg^{-1}, ♀ 709 mg kg^{-1} (1).
Minimum toxic dose reported oral rat >500 mg kg^{-1} (3).
LD_{50} dermal rabbit >2 g kg^{-1} (3).
LD_{50} dermal rat >5 g kg^{-1} (1).

Sub-acute and sub-chronic data
A 5-day toxicity study in quail gave an LC_{50} of 500 mg kg^{-1} diet and in mallard duck an LC_{50} of 1.8 g kg^{-1} diet (1).
A 90-day feeding study in rats established a no-effect level of 1.8 mg kg^{-1} (1).

Carcinogenicity and chronic effects
A 2-yr study in rats established a no-effect level of 4 mg kg^{-1}, and in mice 1.2 mg kg^{-1} (1).
A 1-yr feeding study in dogs established a no-effect level of 7 mg kg^{-1} (1).

Metabolism and toxicokinetics

In mammals, after oral administration, the compound is eliminated in urine and faeces within 48 hr. No accumulation occurs and more than 30 metabolites have been identified (1).

Skin offers a significant barrier to penetration (1).

Irritancy

Irritant to skin and eyes (species, duration unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Log P_{ow} exceeds the European Union limit of 3.0.

WHO Toxicity Class III (6).

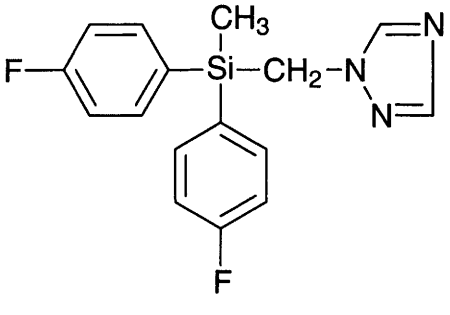
Other comments

Soil residual effects were examined. Succeeding crops of wheat, rape, turnip, Italian ryegrass and field bean were sown 200 days after flurprimidol application to the previous crop. It reduced stem length or plant height and dry matter production in all the species tested in a dose-dependent manner, indicating long-term persistence in soil (7).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Sternett, J. P. *J. Am. Soc. Hortic. Sci.* 1987, **112**(2), 341-345.
3. Thompson, L. G. *Proc. West. Soc. Weed Sci.* 1982, **35**, 113.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
7. Hampton, J. G. *N. Z. J. Exp. Agric.* 1988, **16**(2), 167-172

F90 flusilazol



$C_{16}H_{15}F_2N_3Si$ **Mol. Wt.** 315.40 **CAS Registry No.** 85509-19-9

Synonyms 1-[[bis(4-fluorophenyl)methylsilyl]methyl]-1*H*-1,2,4-triazole; bis(4-fluorophenyl)methyl (1*H*-1,2,4-triazol-1-ylmethyl)silane; flusilazole; Nustar; Punch

RTECS No. XZ 4105000

Uses Broad-spectrum agricultural fungicide with some action against plant mites.

Physical properties

M. Pt. 53°C **Partition coefficient** log P_{ow} 3.74 at pH 7 and 25°C **Volatility** v.p. 0.29×10^{-6} mmHg at 25°C **Solubility** Water: 54 mg l^{-1} (pH 7.2) and 900 mg l^{-1} (pH 1.1) at 20°C. Organic solvents: most organic solvents

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish 1.2-1.7 mg kg^{-1} (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia* sp. 3.4 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂ rat 1100 mg kg^{-1} (2).
LD_{50} oral ♀ rat 674 mg kg^{-1} (2).
LD_{50} dermal rabbit >2000 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral (90 day) rat no-effect level 10 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects

Oral (1 yr) dog no-effect level 5 mg kg^{-1} diet day^{-1} (1).
Oral (18 month) mouse no-effect level 25 mg kg^{-1} diet day^{-1} (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
Partition coefficient exceeds European Union limit of 3.0.
WHO Toxicity Class III (5).
ADI 0.001 mg kg^{-1} body weight (6).

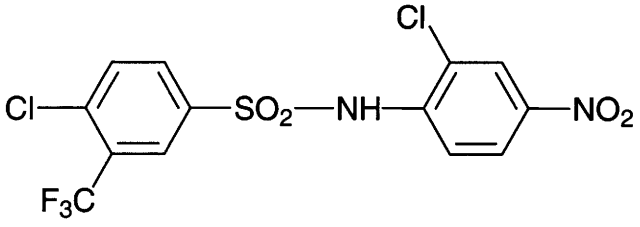
Other comments

Toxicology and field action reviewed (2).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Fort, T. M. et al *Proc. Br. Crop Plant. Conf. Pest. Dis.* 1984, 413.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991, No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
6. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

F91 flusulfamide



$C_{13}H_7Cl_2F_3N_2O_4S$ **Mol. Wt.** 415.18 **CAS Registry No.** 106917-52-6

Synonyms 2,4'-dichloro-α,α,α-trifluoro-4'-nitro-*m*-toluenesulfonanilide; 4-chloro-*N*-(2-chloro-4-nitrophenyl)-3-(trifluoromethyl)-benzenesulfonamide; Nebijn

RTECS No. DB 1420000

Uses Fungicide.

Physical properties

M. Pt. 167-168°C **Specific gravity** 1.739 **Partition coefficient** log P_{ow} 2.4 (1) **Volatility** v.p. 358 nPa at 20°C **Solubility** Water: 2.9 mg kg^{-1} at 25°C. Organic solvents: acetone, methanol, tetrahydrofuran, xylene

Ecotoxicity

Fish toxicity

TL_m (48 hr) carp 0.21 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* 0.29 mg l^{-1} (1).

LD_{50} bee >200 μg bee^{-1} (1).

Environmental fate

Degradation studies

Stable in the dark for 90 days between 35 and 80°C (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂, ♀ rat 180, 132 mg kg^{-1}, respectively (1).

LD_{50} oral mouse 245-254 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat 0.47 mg l^{-1} (1).

LD_{50} percutaneous rat >2000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No-observable-effect level (2 yr) ♂, ♀ rat 0.1037, 0.1323 mg kg^{-1} day^{-1}, respectively (route of administration not given) (1).

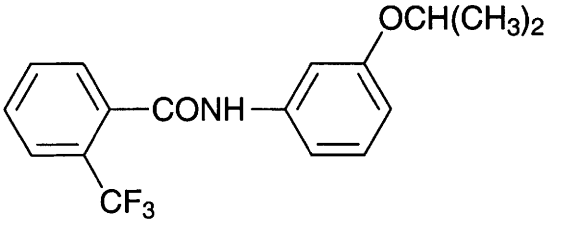
Legislation

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (2). Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (3).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations*, 1991, HMSO, London, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

F92 flutolanil



$C_{17}H_{16}F_3NO_2$ **Mol. Wt.** 323.31 **CAS Registry No.** 66332-96-5

Synonyms α,α,α-trifluoro-3'-isopropoxy-*o*-toluanilide; *N*-[3-(1-methylethoxy)phenyl]-2-(trifluoromethyl) benzamide; NNF-136; Moncut; Iota; Symphonie

RTECS No. CV 5581320

Uses Systemic fungicide.

Physical properties

M. Pt. 102-103°C **Specific gravity** 1.32 at 20°C **Partition coefficient** log P_{ow} 3.7 **Volatility** v.p. 1.33×10^{-5} mmHg at 20°C

Solubility Water: 6.53 mg l^{-1} at 20°C. Organic solvents: chloroform, methanol, toluene

Occupational exposure

JP-OEL 10 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 2.4 mg l^{-1} (1).

LC_{50} (96 hr) rainbow trout 5.4 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (3 hr) *Daphnia* sp. >50.6 mg l^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil 40-60 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >2 g kg^{-1} (1).

LD_{50} oral rat, mouse >10 g kg^{-1} (2).

LC_{50} inhalation rat >5.98 mg l^{-1} (1).
LD_{50} dermal rat >5 g kg^{-1} (1).

Irritancy
Non-irritant to skin and eyes of rabbits (1).

Genotoxicity

Salmonella typhimurium (strains and metabolic activation unspecified) negative (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class Table (5).
EPA Toxicity Class IV (2).

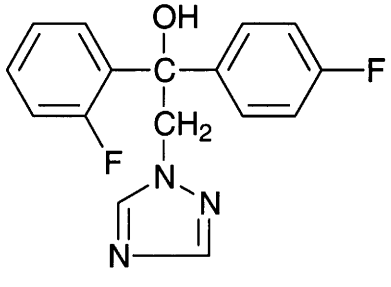
Other comments

Environmental pollutant in soil and water.

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991, No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F93 flutriafol



$C_{16}H_{13}F_2N_3O$ **Mol. Wt.** 301.30 **CAS Registry No.** 76674-21-0

Synonyms (±)-α-(2-fluorophenyl)-α-(4-fluorophenyl)-1*H*-1,2,4-triazole-1-ethanol; (*RS*)-2,4′-difluoro-α-(1*H*-1,2,4-triazol-1-ylmethyl)benzhydryl alcohol; Flutriafen; Impact; R-152450

RTECS No. XZ 4825000

Uses Systemic fungicide.

Physical properties

M. Pt. 130°C **Specific gravity** 1.41 g ml^{-1} at 20°C **Partition coefficient** log P_{ow} 2.3 at 20°C
Volatility v.p. 3.0×10^{-9} mmHg at 20°C

Solubility Water: 1.30 mg l^{-1} at 20°C and pH 7. Organic solvents: acetone, dichloromethane, hexane, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 61 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* sp. 78 mg l^{-1} (1).
No effect on microbial populations (2).
LD_{50} oral honey bee >5 μg bee^{-1} (1).

Environmental fate

Nitrification inhibition
No effect on nitrogen transformation in soil (2).

Carbonaceous inhibition
No effect on carbon transformation in soil (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂ rat 1.14 g kg^{-1}, ♀ 1.48 g kg^{-1} (3).
LD_{50} dermal rabbit, rat >2-10 g kg^{-1} (3).

Sub-acute and sub-chronic data
A 90-day feeding trial in rats established a no-effect level of 20 mg kg $diet^{-1}$ (1).
A 90-day feeding trial in dogs established a no-effect level of 5 mg kg^{-1} (1).

Teratogenicity and reproductive effects
Not teratogenic in rat and rabbit (1).

Irritancy
Mild irritant to rabbit eye, non-irritant to skin (dose, duration unspecified) (2).

Genotoxicity

Salmonella typhimurium (strains and metabolic activation unspecified) negative (1).
In vivo cytogenic tests negative (1).

Legislation

Limited Under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentrations 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No.472, 1991 (5).
WHO Toxicity Class III (6).
EPA Toxicity Class III (1).

Other comments

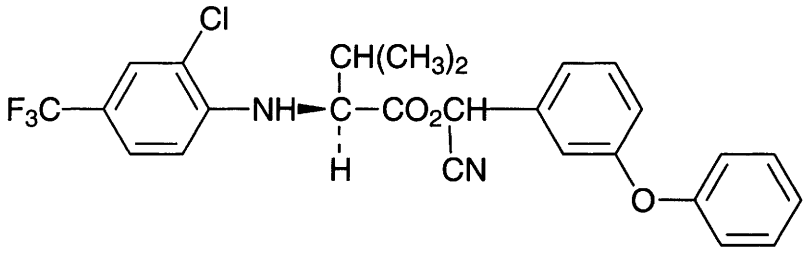
Contaminant of air, grain, vegetables and fruit (7).
Toxicology reviewed (3).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.

3. Skidmore, A.M. et al *Proc. 10th Int. Congr. Plant Prot.* 1983, **1**, 368.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
7. Girenko, D. B. *Gig. Sanit.* 1988, (9), 41-42 (Russ.) (*Chem. Abstr.* **109**, 209736h)

F94 τ-fluvalinate



$C_{26}H_{22}ClF_3N_2O_3$ **Mol. Wt.** 502.92 **CAS Registry No.** 102851-06-9

Synonyms (*RS*)-α-cyano-3-phenoxybenzyl-*N*-(2-chloro-α,α,α-trifluoro-*p*-tolyl) D-valinate; cyano(3-phenoxyphenyl)methyl-*N*-[2-chloro-4-(trifluoromethyl)phenyl] D-valinate; Apistan; fluvalinate; Klartan; Mavrik; Spur; Yardex

Uses Insecticide and acaricide with a contact and stomach action.

Physical properties

B. Pt. 164°C at 0.07 mmHg (tech.) **Flash point** 90°C (closed cup) **Specific gravity** 1.29 at 25°C

Partition coefficient log P_{ow} 4.26 at 25°C **Volatility** v.p. 6.8×10^{-13} mmHg

Solubility Water: 1.03 μg l^{-1} at pH 7 and 20°C. Organic solvents: aromatic hydrocarbons, benzene, diethyl ether, ethanol

Occupational exposure

Supply classification harmful, dangerous for the environment

Risk phrases Harmful if swallowed – Irritating to the skin – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R38, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – Refer to manufacturer/supplier for information on recovery/recycling – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S24, S59, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 6.2 μg l^{-1} (1).

LC_{50} (96 hr) rainbow trout, carp 2.9, 4.9 μg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* sp. 10 μg l^{-1} (1).

Environmental fate

Degradation studies

Compound is rapidly degraded in soil aerobically, $t_{1/2}$ 6-8 days. Primary metabolites are the corresponding aniline acids and the parent aniline (2).

Abiotic removal

Decomposes with sunlight. Hydrolyses at 25°C, pH 1 or 3, $t_{1/2}$ >30 days; at pH 9, $t_{1/2}$ <1 hr (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail >2.5 g kg^{-1} (1).
LD_{50} oral rat >3 g kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >5.1 mg l^{-1} (1).
LD_{50} dermal rat >2 g kg^{-1} (1).
LD_{50} dermal rabbit >2 g kg^{-1} (1).

Sub-acute and sub-chronic data

LC_{50} (8 days) bobwhite quail and mallard duck >5.6 g kg^{-1} diet (1).

Carcinogenicity and chronic effects

A no-effect level for a feeding study (duration unspecified) in rats of 1 mg kg^{-1} day^{-1} has been reported (1).

Metabolism and toxicokinetics

Rats given the compound orally excreted >95% in 4 days. Approximately half was via urine and half by faeces (2). Principal metabolites are 3-phenoxybenzoic acid (free and glycine conjugate) and 3-(4-hydroxyphenoxy)benzoic acid (free and sulfate conjugate) (3).

Irritancy

Moderate eye irritant and mild skin irritant in rabbit (dose and duration unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
WHO Toxicity Class II (6).
EPA Toxicity Class II (1).

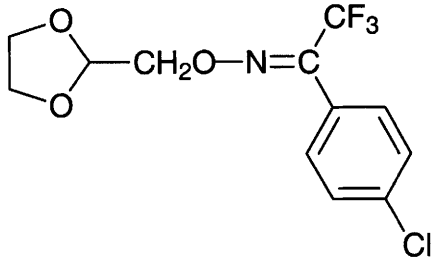
Other comments

Food contaminant.
Not dangerous to bees (1).
Material is a 1:1 mixture of (*R*)-α-cyano-, 2-(*R*)- and (*S*)-α-cyano-, 2-(*R*)- diastereoisomers (1).
Persistence on eggplant ranged from 0.01-0.40 μg g^{-1} (7).
Many literature references for this compound are indexed to RN 69409-94-5 (DL-isomers) in error.

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Staiger, L. E. et al *J. Agric. Food. Chem.* 1983, **31**, 399.
3. Staiger, L. E. et al *J. Agric. Food. Chem.* 1984, **32**, 1130.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991, No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
7. Mukherjee, I. et al *Pestic. Sci.* 1992, **36**(3), 175-179

F95 fluxofenim



$C_{12}H_{11}ClF_3NO_3$ **Mol. Wt.** 309.67 **CAS Registry No.** 88485-37-4

Synonyms 4'-chloro-2,2,2-trifluoroacetophenone *O*-1,3-dioxolan-2-ylmethyloxime; 1-(4-chlorophenyl)-2,2,2-trifluoro-1-ethanone *O*-(1,3-dioxolan-2-ylmethyl)oxime; Concep III

Uses Herbicide safener.

Physical properties

B. Pt. 94°C at 0.1 mmHg **Flash point** >93°C **Specific gravity** 1.36 at 20°C **Partition coefficient** log P_{ow} 2.9

Volatility v.p. 38 mPa at 20°C

Solubility Water: 30 mg l^{-1} at 20°C. Organic solvents: acetone, hexane, methanol, octanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} trout, bluegill sunfish 0.86, 2.5 mg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} *Daphnia magna* 0.22 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail >2000 mg kg^{-1} (1).

LD_{50} oral rat 670 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat >1.2 mg l^{-1} (1).

LD_{50} dermal rat 1540 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral rat (90 day) no-observed effect 1 mg kg^{-1} body weight daily (1).

Oral dog (90 day) no-observed effect 20 mg kg^{-1} body weight daily (1).

Metabolism and toxicokinetics

Rapidly absorbed in the rat and rapidly excreted in urine and faeces. Tissue residues were low. Metabolised via hydrolysis of the dioxolane ring and subsequent oxidation steps, then cleavage of the oxime ether (1).

Irritancy

Not a skin or eye irritant (species unspecified) (1).

Sensitisation

Not a skin sensitiser (species unspecified) (1).

Legislation

WHO Toxicity Class II (2).

Limited under EC Directive on Drinking Water Quality 80/788/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedules 5 and 6 (Release into Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

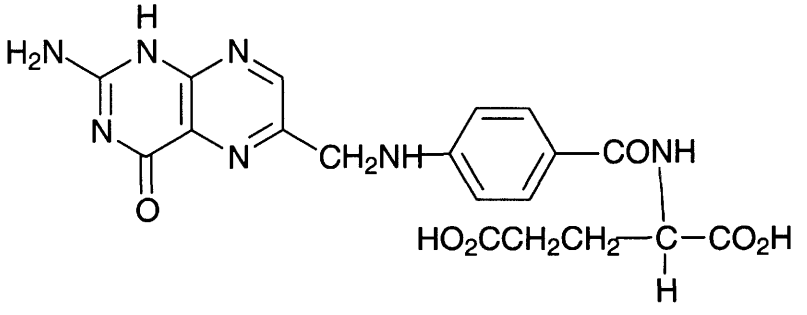
Other comments

Material comprises both *Z*- and *E*-isomers.

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F96 folic acid



$C_{19}H_{19}N_7O_6$ **Mol. Wt.** 441.40 **CAS Registry No.** 59-30-3

Synonyms pteroyl-L-glutamic acid; *N*-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-L-glutamic acid; *N*-(*p*-[(2-amino-4-hydroxypyrimido[4,5-*b*]pyrazin-6-yl)methylamino]benzoyl)-glutamic acid; vitamin B_c; vitamin M; Folicet; Folvite

EINECS No. 200-419-0 **RTECS No.** LP 5425000

Uses Haematopoietic vitamin; nutritional factor, especially as a dietary requirement in poultry.
Occurrence Haematopoietic vitamin, present in its free or combined form (with one or more additional molecules of L-glutamic acid) in liver, kidney, mushrooms, nuts, yeast, green leaves and grasses.

Physical properties

M. Pt. 250°C
Solubility Water: 1.6 mg l^{-1} at 25°C. Organic solvents: methanol, phenol, pyridine

Environmental fate

Degradation studies
The cellular slime moulds *Dictyostelium discoideum* strains NC4 and AX-2 and *Polysphondylium violaceum* contain enzymes in their extracellular, intracellular and particulate fractions which inactivate folic acid, converting it into 2-deaminofolic acid (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 10 g kg^{-1} (2).
LD_{50} intravenous mouse 282 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 85 mg kg^{-1} (3).
LD_{Lo} subcutaneous mouse 200 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Newborn rats were given a subcutaneous injection of 250 mg kg^{-1} folic acid on postnatal days 1, 8 or 15, and renal function tested by a basal clearance test and a hydropenia challenge 1, 2 or 5 days after treatment. No difference in renal toxicity with age was observed; kidney weights were increased and kidneys showed uremia with decreased creatinine clearance, increased fractional excretion of water and a lowered hydropenia response. Renal toxicity from folic acid appears to be a nonspecific response to injury to cells within the kidney tubules (5).

Metabolism and toxicokinetics

In humans, reduced to tetrahydrofolate after absorption from the small intestine. Distributed throughout body tissues, and appears in the portal circulation as 5-methyltetrahydrofolate, extensively bound to plasma proteins. Stored mainly in the liver, but is also concentrated in the cerebrospinal fluid. About 4 to 5 μg folic acid is excreted in the urine daily (6).

Genotoxicity

Intraperitoneal rat, mouse 150, 250 mg kg^{-1}, respectively, causes unscheduled DNA synthesis (7).
Tradescantia paludosa micronucleus test negative (8).
Folic acid significantly suppresses the mutagenic activity of aflatoxin B1 in the *Salmonella typhimurium* TA100 mutagenicity assay with metabolic activation (9).

Other effects

Any other adverse effects

Folic acid deficiency in Swiss mice resulted in increased incidence of micronuclei in peripheral blood erythrocytes, suggesting increased chromosomal damage in nucleated erythrocyte precursors (10).
Injection of folic acid into the amygdaloid complex of rats induced limbic seizure/brain damage syndrome, with myoclonic unilateral jerks of head and limbs (11).
In pregnant rats, a folic acid-deficient diet results in abnormal morphogenesis in the embryo, particularly of the neural tube (12).

Other comments

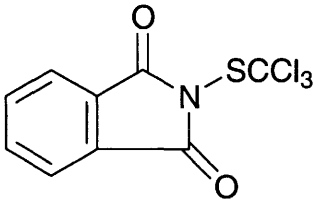
Deficiency can lead to megaloblastic anaemia (6).
Given to pregnant women in the prophylaxis of megaloblastic anaemia and in the prevention of foetal neural tube defects in women known to be at risk (6).
The effects of drugs on folic acid metabolism in humans and animals reviewed (13).
The effects of alcohol on folic acid metabolism reviewed (14).
Folic acid safety and toxicity reviewed (15).
Folic acid metabolism in malaria reviewed (16,17).
The biological role of folates reviewed (18).

References

1. Pan, P. et al *J. Bacteriol.* 1978, **136**(3), 955-959.
2. *Toxicol. Appl. Pharmacol.* 1972, **23**, 537.
3. *Experientia* 1985, **41**, 72.
4. *Proc. Soc. Exp. Biol. Med.* 1949, **71**, 544.
5. Kavlock, R. J. et al *Toxicol. Appl. Pharmacol.* 1985, **81**(3, Pt.1), 407-415.
6. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.

7. *Cancer Res.* 1969, **29**, 136.
8. Ma, T. H. et al *Mutat. Res.* 1984, **138**(2-3), 157-167.
9. Bhattacharya, R. K. et al *Mutat. Res.* 1987, **188**(2), 121-128.
10. MacGregor, J. T. et al *Proc. Natl. Acad. Sci. U.S.A.* 1990, **87**(24), 9962-9965.
11. Tremblay, E. et al *Neuroscience (Oxford)* 1984, **12**(2), 569-589.
12. Bremert, J. C. et al *Nutr. Res. (N.Y.)* 1989, **9**(1), 105-112.
13. Lindenbaum, J. *Curr. Concepts Nutr.* 1983, **12**, 73-87.
14. Hillman, R. S. et al *Annu. Rev. Med.* 1982, **33**, 345-354.
15. Butterworth, C. E., Jr. et al *Am. J. Clin. Nutr.* 1989, **50**(2), 353-358.
16. Ferone, R. *Bull. WHO* 1977, **55**(2-3), 291-298.
17. Krungkrai, J. et al *Parasitol. Today* 1990, **6**(12), 388-391.
18. Ljungdhal, L. G. *Folates Pterins* 1984, **1**, 555-579

F97 folpet



$C_9H_4Cl_3NO_2S$ **Mol. Wt.** 296.56 **CAS Registry No.** 133-07-3

Synonyms 2-[(trichloromethyl)thio]-1*H*-isoindole-1,3(2*H*)-dione; *N*-(trichloromethylthio)phthalimide; *N*-(trichloromethylmercapto)phthalimide; Phaltan; Acritene; Buvicid; Dipet; Falben; Mildin; Myco

EINECS No. 205-088-6 **RTECS No.** TI 5685000

Uses Agricultural fungicide.

Physical properties

M. Pt. 177°C (decomp.) **Partition coefficient** log P_{ow} 3.11 **Volatility** v.p. 9.7×10^{-6} mmHg at 20°C
Solubility Water: 1 mg l^{-1}. Organic solvents: slightly soluble in organic solvents

Occupational exposure

Supply classification harmful
Risk phrases Irritating to the eyes – Possible risk of irreversible effects – May cause sensitisation by skin contact (R36, R40, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Environmental fate

Degradation studies
Complexation with β-cyclodextrin in activated sludge, decreases toxicity (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck 2 g kg^{-1} (2).

LD_{50} oral rat >5 g kg^{-1} (3).
LD_{50} dermal rabbit >23 g kg^{-1} (4).

Carcinogenicity and chronic effects
A 1.4-yr feeding study in rats and dogs produced no-effect levels of 10 and 1.5 g kg $diet^{-1}$, respectively (4).

Teratogenicity and reproductive effects
150 or 75 mg kg^{-1} injected into N2 white rabbits on days 6-16 of pregnancy produced no teratogenic effects (5,6).
Injection into Dutch belted rabbits during the same period also produced negative results (6).
Injection into chick embryos, after 4 days of incubation, of 12 mg kg^{-1} produced teratogenic effects (7).
A three-generation study in which rats were fed 1 g kg $diet^{-1}$ showed no teratogenic or reproductive effects (4).

Irritancy
Irritant to eyes, skin and mouth (2).

Sensitisation
Allergic reactions are frequent in agricultural workers (8,9).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive (10,11).
Salmonella typhimurium TA104 with metabolic activation positive, TA102 with metabolic activation negative (12).
Chromosome aberrations in *Saccharomyces cerevisiae* without metabolic activation positive (11).
Escherichia coli SOS chromotest positive (13).

Other effects

Any other adverse effects
Thought to bind to a reactive site on cytochrome P_{450} and thereby decrease activity of a variety of mixed function oxidase enzymes such as aminopyrene *N*-demethylase and aniline hydrogenase (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (15).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).
Partition coefficient exceeds European Union limit of 3.0.
WHO Toxicity Class Table 5 (17).
EPA Toxicity Class IV (formulation) (4).
ADI 0.1 mg kg^{-1} body weight (4).

Other comments

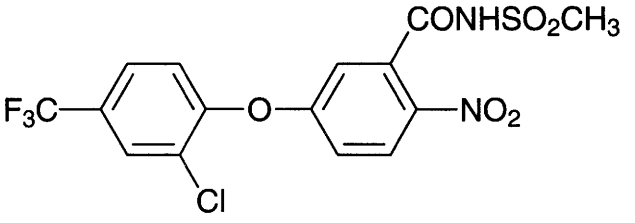
Reviews on human health effects, experimental toxicology and physico-chemical properties listed (18).
Clinical toxicology reviewed (19).
Non-toxic to bees (2).

References

1. Olah, J. *Water Res.* 1988, **22**(11), 1345-1351.
2. *The Agrochemicals Handbook* 3rd ed., The Royal Society of Chemistry, London, UK.
3. Gaines, T. B. et al *Fundam. Appl. Toxicol.* 1986, **7**, 299.
4. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
5. McLaughlin, J. et al *Toxicol. Appl. Pharmacol.* 1969, **12**, 641.
6. Kennedy, G. et al *Toxicol. Appl. Pharmacol.* 1968, **13**, 420.
7. Martin, D. H. et al *Bull. Environ. Contam. Toxicol.* 1978, **20**, 155-158.
8. Lisi, P. et al *Contact Dermatitis* 1987, **17**(4), 212-218.
9. Lisi, P. et al *Contact Dermatitis* 1986, **15**(5), 266-269.
10. McCann, J. et al *Proc. Natl. Acad. Sci. U. S. A.* 1975, **72**(12), 5135-5139.

11. Choi, E. J. *Environ. Mutagen. Carcinog.* 1985, **5**(1), 11-18.
12. Burrueco, C. et al *Mutagenesis* 1988, **3**(6), 467-480.
13. Xu, H. *Toxic. Assess.* 1990, **5**(1), 1-14.
14. Dalvi, R. R. *Pharmacol. Toxicol. (Copenhagen)* 1990, **66**(3), 231-233.
15. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
16. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
17. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
18. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
19. Gosselin, R. E. et al (Eds.) *Clinical Toxicology of Commercial Products* 5th ed., 1984, Williams & Wilkins, Baltimore, MD, USA

F98 fomesafen



$C_{15}H_{10}ClF_3N_2O_6S$ **Mol. Wt.** 438.77 **CAS Registry No.** 72178-02-0

Synonyms 5-[2-chloro-4-(trifluoromethyl)phenoxy]-*N*-(methylsulfonyl)-2-nitrobenzamide; 5-(2-chloro-α,α,α-trifluoro-*p*-tolyloxy)-*N*-mesyl-2-nitrobenzamide; Flex; Reflex

EINECS No. 276-439-9 **RTECS No.** CV 2475000

Uses Herbicide

Physical properties

M. Pt. 220-221°C **Specific gravity** 1.28 at 20°C **Partition coefficient** log P_{ow} 2.90 at pH 1 (1)
Volatility v.p. $<7.5 \times 10^{-7}$ mmHg at 50°C
Solubility Water: ~50 mg l^{-1} at 20°C (but <1 mg l^{-1} at pH 1-2). Organic solvents: acetone, cyclohexanone, dichloromethane, *n*-hexane, xylene

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 680 mg l^{-1} (sodium salt 170 mg l^{-1}) (1,2).
LC_{50} (96 hr) bluegill sunfish 6030 mg l^{-1} (1).

Invertebrate toxicity
LD_{50} oral bee ≥50 μg bee^{-1} (1).
LD_{50} contact bee ≥100 μg bee^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ for degradation in soil under aerobic conditions >6 months, and for anaerobic conditions <1 month (1).

Abiotic removal

Undergoes photodegradation on the soil surface (1).
Decomposed by light (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >5000 mg kg^{-1} (1).
LD_{50} oral rat 1250-2000 mg kg^{-1} (1).
LD_{50} dermal rabbit >1000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LD_{50} mallard duck, bobwhite quail (5 day) >20 g kg^{-1} diet (1).
Oral dog (6 month) no-adverse-effect level 30-40 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects

Oral rat (2 yr) no-adverse-effect level 100 mg kg^{-1} diet (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class III (5).
EPA Toxicity Class III (2).

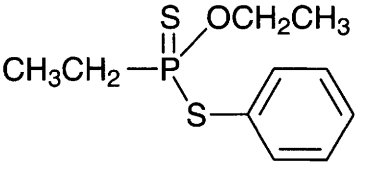
Other comments

Metabolic pathways reviewed (6).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
6. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

F99 fonofos



$C_{10}H_{15}OPS_2$ **Mol. Wt.** 246.33 **CAS Registry No.** 944-22-9

Synonyms ethylphosphonodithioic acid, *O*-ethyl *S*-phenyl ester; *O*-ethyl *S*-phenyl ethyl phosphonothiolothionate; N-2790; Dyfonate; Capfos; Cudgel; Tycap

EINECS No. 213-408-0 **RTECS No.** TA 5950000

Uses Insecticide.

Physical properties

B. Pt. 130°C at 0.1 mmHg **Specific gravity** 1.154 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} 3.90 at 20°C **Volatility** v.p. 2.1×10^{-3} mmHg at 25°C
Solubility Water: 13 mg l^{-1}. Organic solvents: miscible with acetone, ethanol

Occupational exposure

FR-VME 0.1 mg m^{-3}
US-TWA 0.1 mg m^{-3}
Supply classification very toxic, dangerous for the environment
Risk phrases Very toxic in contact with skin and if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R27/28, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 0.05 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish 0.028 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (5 min) *Photobacterium phosphoreum* 5.15 ppm Microtox test (2).
EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) 9.2 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) 8.8 mg l^{-1} (3).
LD_{50} 0.0087 mg bee^{-1} (1).

Environmental fate

Degradation studies
10 ppm applied to soils ranging from loamy sand to clay loams to peat, under aerobic conditions, resulted in $t_{1/2}$ 3-16 wk (1).
Breakdown products include *O*-ethylethane phosphonothioic acid (major degradate), fonofos oxon, *O*-ethylethane phosphonic acid, *O*-ethyl-*O*-methylethyl phosphonate, diphenyl sulfide, methylphenyl sulfoxide and methylphenyl sulfone (1).
Metabolised by the soil fungus *Rhizopus japonicus* to yield dyfoxon, thiophenol, ethylethoxy phosphonic acid and methylphenyl sulfoxide (4).

Abiotic removal
Hydrolysed in acidic and alkaline media; $t_{1/2}$ 101 days at pH 4, 74-127 days at pH 7, depending on buffer (1).

Adsorption and retention
K_{oc} for soil 6.8×10^{-2} (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 10 mg kg^{-1} (6).
LD_{50} oral starling 42.2 mg kg^{-1} (6).
LD_{50} oral quail 31.6 mg kg^{-1} (6).
LD_{50} oral rat 3 mg kg^{-1} (7).
LD_{50} oral ♂ rat 11.5 mg kg^{-1}, ♀ 5.5 mg kg^{-1} (1).
LD_{50} dermal guinea pig 278 mg kg^{-1} (8).
LD_{50} dermal rabbit 25 mg kg^{-1} (8).
LC_{50} (4 hr) inhalation ♂ rat 51 µg l^{-1}, ♀ rat 17 µg l^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (5 day) oral bobwhite quail, Japanese quail, ring-necked pheasant 133-295 mg kg^{-1} diet (9).
LC_{50} (5 day) oral mallard duck 1225 mg kg^{-1} diet (9).
Oral rat (13 wk) 0, 0.5, 1.6 or 5 mg kg^{-1} day^{-1} caused inhibition of cholinesterase activity in the serum and red blood cells in ♀ rats and in the brain of both sexes (10).

Carcinogenicity and chronic effects
Oral (2 yr) rat, dog no-effect level 0.5, 0.2 mg kg^{-1} day^{-1}, respectively (1).
Oral rat (2 yr) 0, 0.5, 1.6 or 5 mg kg^{-1} day^{-1}, no carcinogenic effects were observed (11).

Teratogenicity and reproductive effects
Oral rat (three-generation study) 0, 0.5 or 1.6 mg kg^{-1} day^{-1}. No maternal toxicity, foetotoxicity or teratogenicity was observed (12).
Gavage mouse 0, 2, 4, 6 or 8 mg kg^{-1} day^{-1} on days 6-15 of gestation. Maternal toxicity was observed for the two highest doses. In the offspring, increased incidences of variant ossifications of the sternebrae were reported for the 8 mg kg^{-1} group and a slight dilation of the 4th ventricle of the brain in the 4 and 8 mg kg^{-1} groups (13).

Metabolism and toxicokinetics
In animals, metabolism involves oxidation to the phosphonothioate and hydrolytic cleavage of the thiophenol residue (1).
Following oral administration of radiolabelled compound to rats, 80-90% was absorbed by the gut. Highest concentrations of radioactive label were found in the kidneys, blood, liver and intestine. 99.3% of the administered radioactivity was eliminated during, 2-16 days after dosing (14).
Following oral administration, 2.6-7.1% was recovered as unchanged fonofos in the urine. The remainder was metabolised to *O*-ethylethane phosphonothioic acid, *O*-ethylethane phosphonic acid, and *O*-conjugates of 3- and 4-(hydroxyphenyl)methyl sulfone (15).

Irritancy
Dermal rabbit (24 hr) 115 mg and 23 mg kg^{-1} instilled into rabbit eye caused negligible irritation, but these doses were lethal to all treated animals (16).

Genotoxicity

Salmonella typhimurium TA92, TA98, TA100, TA1535, TA1537, TA2637 with and without metabolic activation negative (17).
Saccharomyces cerevisiae D3 mitotic recombination negative (18).
In vitro human fibroblasts unscheduled DNA synthesis negative (18).

Other effects

Other adverse effects (human)

Following accidental ingestion by a 19-yr-old woman, the individual developed nausea, vomiting, salivation, sweating and suffered cardio-respiratory arrest. The patient developed a pancreatic pseudocyst. A second person who also ate the contaminated food died (19).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (20).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (21).
WHO Class Ia (22).
EPA Toxicity Class I or II (1).

Other comments

Pollutant of soil and groundwater, contaminant of food.
Chiral forms of the compound have been isolated. (*R*) is more toxic to insects and mice and is a more potent inhibitor of cholinesterase than the (*S*) isomer (1).
Toxicology reviewed (23,24).
Physical properties, environmental fate and toxicity reviewed (23).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Guzzella, L. et al *Bull. Environ. Contam. Toxicol.* 1997, **59**, 313-320.
4. Lichtenstein, E. P. et al *J. Agric. Food Chem.* 1977, **25**(4), 845-848.
5. Jury, W. A. *J. Environ. Qual.* 1987, **16**(4), 422-428.
6. *Farm Chemicals Handbook* 1980, D121, Meister Publishing Co., Willoughby, OH, USA.
7. *World Rev. Pest Control* 1970, **9**, 119.
8. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
9. Hill, E. F. et al *Lethal Dietary Toxicities of Environmental Pollutants to Birds* 1975, US Fish and Wildlife Service, Report Wildlife No. 191, Washington, DC, USA.
10. Cockrell, K. O. et al *N-2790 Safety Evaluation by Repeated Oral Administration to Dogs for 14 Wk and to Rats for 13 Wk* 1966, Woodard Res. Gp, MRID 0090818.
11. Banergee, B. M. et al *Dyfonate (N-2790) Safety Evaluation by Dietary Administration to Rats for 105 Wk* 1968, Woodard Res. Corp., MRID 00082232.
12. Woodard, M. W. et al *Dyfonate (N-2790) Three-generation Reproduction Study in Rats* 1968, Woodard Res. Corp., MRID 00082234.
13. Minor, J. et al *A Teratology Study in CD-1 Mice with Dyfonate Technical T-10192* 1982, Stauffer Chemical Corp., MRID 00118423.
14. Hoffman, L. J. et al *Pestic. Biochem. Physiol.* 1971, **1**, 349-355.
15. McBain, J. B. et al *Pestic. Biochem. Physiol.* 1971, **1**, 356-365.
16. Dean, W. P. *Acute Oral and Dermal Toxicity in Male and Female Rats* 1977, Int. Res. Dev. Corp., MRID 0059860, 00059856, 00059857.
17. Remondelli, P. et al *Med. Biol. Environ.* 1986, **14**(1), 377-386.
18. Simmon, V. F. *In vitro Microbiological Mutagenicity and Unscheduled DNA Synthesis Studies of Eighteen Pesticides* 1979, EPA-600/1-79-041, NTIS, Springfield, VA, USA.
19. Hayes, W. J. *Pesticide Studies in Man* 1982, 413, Williams & Wilkins, Baltimore, MD, USA.
20. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
21. *S. I. 1991 No. 472, The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
22. *The WHO Recommenced Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21
23. *Dangerous Prop. Ind. Mater. Rep.* 1990, **10**(6), 44-54.
24. *Toxic Substances List* 1974, Christensen, H. E. (Ed.) 24. *Drinking Water Health Advisory: Pesticides* 1989, 443-457, Lewis Publishers, Chelsea, MI, USA

F100 formaldehyde

HCHO

CH_2O **Mol. Wt.** 30.03 **CAS Registry No.** 50-00-0

Synonyms methanal; oxomethane; oxymethylene; methylene oxide; methylaldehyde

EINECS No. 200-001-8 **RTECS No.** LP 8925000

Uses Bactericide and fungicide for many purposes including agricultural, cosmetic, sterilising and embalming uses. Also as a chemical intermediate and in textile production.

Occurrence Naturally occurring substance, detected in a variety of sources particularly air, tobacco smoke, effluent waters and fabrics including clothing, chipboard and plastics (1).

Natural sources include production as a metabolite of blue green algae and as an intermediate of mammalian metabolism (2,3).

Physical properties

M. Pt. –92°C **B. Pt.** –19.5°C **Flash point** (15% methanol free) 50°C (closed cup) **Specific gravity** 1.081-1.085 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 0.35 **Volatility** v.p. 10 mmHg at –88°C ; v.den. 1.08

Solubility Water: 550 g l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 0.5 ppm (0.62 mg m^{-3})

FR-VME 0.5 ppm **FR-VLE** 1 ppm

JP-OEL 0.5 ppm (0.61 mg m^{-3})

SE-LEVL 0.5 ppm (0.6 mg m^{-3}) **SE-CEIL** 1 ppm (1.2 mg m^{-3})

UK-LTEL MEL 2 ppm (2.5 mg m^{-3}) **UK-STEL** MEL 2 ppm (2.5 mg m^{-3})

US-STEL ceiling limit 0.3 ppm (0.37 mg m^{-3})

UN No. 1198 (solution, flammable)

UN No. 2209 (solutions with ≥25% formaldehyde) **HAZCHEM Code** 2YE (solution) **HAZCHEM Code** 2Z (solutions with ≥25% formaldehyde) **Conveyance classification** flammable liquid, corrosive (solution) **Conveyance classification** corrosive substance (solutions with ≥25% formaldehyde)

Supply classification toxic

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Causes burns – Possible risk of irreversible effects – May cause sensitisation by skin contact (R23/24/25, R34, R40, R43)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Use only in well ventilated areas (S1/2, S26, S36/37/39, S45, S51)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 440-618 mg l^{-1} (4).

LC_{50} (96 hr) bullhead 62.1 µl l^{-1} (4).

LC_{50} (96 hr) bluegill sunfish 100 µl l^{-1} (4).

The toxicity to fish has been examined extensively (4).

Invertebrate toxicity

LC_{50} (30 min) *Photobacterium phosphoreum* 3-10.2 ppm, preferred value 8.46 ppm (5).

Bioaccumulation
Bioaccumulation does not occur (1,6).

Environmental fate

Degradation studies
Can be degraded by certain bacteria in soil to carbon dioxide and water (1,6).

Mammalian & avian toxicity

Acute data
LC_{50} (30 min) inhalation rat 0.82 mg l^{-1} (7).
LC_{50} (4 hr) inhalation mouse 0.48 mg l^{-1} (7).
Concentrations in the range of 5-15 ppm for up to 10 hr killed approximately half test groups of mice, guinea pigs and rabbits (8).
Typically inhalation causes increased airway resistance, decreased sensitivity of the nasopalatine nerve, irritation of eyes and respiratory system. High doses cause vomiting (in appropriate species), cramps and death (1,9).

Carcinogenicity and chronic effects
Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (10).
A number of epidemiological studies have been conducted and are judged to have given inconclusive results (11).
Retrospective cohort studies in the garment industry have shown increased incidence of mortality from cancers of the buccal cavity, connective tissue, trachea, bronchus, lung, pharynx and other tissues, but not all increases were significant (12).
Humans may be less susceptible to carcinogenic effects of formaldehyde than rats (13).
Mice exposed to ≤0.2 mg l^{-1} for 1 hr day^{-1} for 35 wk did not develop pulmonary tumours (9), while ♂ mice exposed to 14.3 ppm for 6 hr day^{-1} for ≤2 yr showed lesions and some squamous cell carcinomas of the nasal cavity (14).
Rats similarly exposed for 2 yr to 14.3 ppm developed significant increases in squamous cell carcinomas of the nasal cavities (14).
Exposure of rats for 8 wk at 14.7 ppm along with hydrochloric acid gas (10.6 ppm). Rats developed squamous metaplasia of the nasal mucosa on exposure to formaldehyde alone as well as with the mixture (15).
Hamsters demonstrated a tumour potentiating role for formaldehyde (16).
Sarcomas have been produced following subcutaneous injections (17) and rabbits whose oral mucosa was repeatedly exposed to formaldelhyde have developed carcinomas (18).
Rats receiving the compound in drinking water at 0.02-0.05% for 2 yr showed toxicity, with total mortality at the highest dose. Hyperplasia and ulcers of the forestomach were seen at this dose and at 0.1%. A no-effect level of 0.02% was established (19).
Physical damage of the nasal mucosa by electrocoagulation increased the incidence of nasal tumours in rats exposed to formaldehyde vapour ≤10 ppm for ≤28 months (20).

Teratogenicity and reproductive effects
Mice receiving up to 185 mg kg^{-1} on days 6-15 of gestation showed no embryotoxic or teratogenic effect (21).
Mice receiving the compound intravenously (100 µl of 37% formaldehyde solution) on day-16 of pregnancy developed foetuses that 24 days later demonstrated chromosome aberrations in cultured liver cells (22).

Metabolism and toxicokinetics
Formaldehyde vapour is absorbed primarily in the upper respiratory tract and is distributed to many tissues where it is metabolised and incorporated in the C1-metabolic pool (23).
Route of administration does not influence metabolism (23).
Converted to formate and is a normal metabolite in mammalian systems. Numerous enzymes can catalyse conversion to formate, which is further metabolised to CO_2 (24).
Formaldehyde can react with histones, proteins and amino acids (24).

Irritancy

Severely irritating to eyes, skin and mucous membranes. It can cause hypersensitivity with a variety of manifestations (25).

Sensitisation

In humans a type IV immune reaction (probably mediated by formaldehyde reaction with epidermal Langerhan's cell protein) is held to be responsible for allergenic contact dermatitis (26).

In humans acute and chronic skin sensitisation are observed. The acute manifestations seem to be related to airborne formaldehyde and affect mainly the face (periorbital oedema). The chronic manifestation, an eczema of the hands and arms, is associated with handling of formaldehyde-based resins (27).

In humans the estimated threshold for induction of allergic dermatitis is ≤5% formaldehyde in a water solution. The threshold for elicitation of allergic contact dermatitis in sensitised humans was 30 ppm (w/w) for patch-testing and 60 ppm for products containing formaldehyde (28).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive, with metabolic activation negative; TA1535, TA1537, TA1538 negative with or without metabolic activation (29).

Drosophila melanogaster positive (30).

Mouse micronucleus test negative (29).

Mixed human lymphocytes chromosome aberration negative and positive results reported (31,32).

Sister chromatid exchange, in human lymphocytes negative (32).

Other effects

Other adverse effects (human)

A cohort study of workers exposed to formaldehyde in the UK chemical industry in any one of six factories has been extended to 1989 after the earlier published report in 1984. Update finds 1 death from nasal cancer (1.7 expected), which does not support original finding of possible human nasal carcinogenicity. No definitive indication of excess in lung cancer (33).

Any other adverse effects

After inhalation, the functional state of lymphocytes in peripheral blood is sensitised (34).

Other comments

Toxicity and environmental effects reviewed (10,11,35-38).

DNA damage to the nasal cavity caused by formaldehyde is reviewed (39).

References

1. *IARC Monograph* 1982, **29**, 345.
2. Yamada, H. et al *Int. J. Environ. Stud.* 1991, **38**(1), 55-64.
3. Hutson, D. H. *Foreign Compound Metabolism in Mammals* 1970.
4. Bills, T. D. et al *Investigations in Fish Control* No. 73, US Dep. Int. Fish and Wildlife Science, 1977, Washington, DC, USA.
5. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
6. Kitchens, J. F. et al *EPA-560/2-76-009* 1976.
7. ACS Symp. Ser. *Anal. Chem. Toxicol.* 1985, (210), 217-277.
8. Iwanoff, N. *Arch. Hyg.* 1911, **73**, 307.
9. Horton, A. W. *J. Natl. Cancer Inst.* 1963, **30**, 31-43.
10. *IARC Monograph* 1987, **Suppl. 7**, 211.
11. *IARC Monograph* **Suppl. 6**, 19, 321.
12. Stayner, L. T. et al *Am. J. Ind. Med.* 1988, **13**(6), 667-682.
13. Purchase, I. F. H. et al *Cancer Lett. (Shannon, Irel.)* 1989, **46**, 79-85.
14. Kerns, W. D. et al. *Cancer Res.* 1983, **40**, 4382-4392.
15. Albert, R. E. *J. Natl. Cancer Inst.* 1982.
16. Dalby, W. L. *Toxicology* 1981, **1**, 138.

17. Wantabe, F. *Gann* 1954, **45**, 451-452.
18. Muller, P. *Exp. Pathol.* 1978, **16**, 36-42.
19. Marks, T. A. et al. *Teratology* 1980, **22**(1), 51-58.
20. Feron, V. J. *Proc. 2nd Int. Conf. Role Formaldehyde Biol. Syst.* 1987, 73-77.
21. Tobe, M. et al *Toxicology* 1989, **56**(1), 79-86.
22. Okui, T. et al *Hokkaidoritsu Eisei Kenkyushoho* 1989, (39), 110-112 (Japan.) (*Chem. Abstr.* **110**, 210416b).
23. Heck, H. d'A. et al *Proc. Third Annual CIIT Conf.: Formaldehyde Toxicity* 1982, Hemisphere Publishing Corp., New York, NY, USA.
24. *Formaldelyde. An Assessment of its Health Effects. Natl. Acad. Sci.* 1980, National Research Council, Washington, DC, USA.
25. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
26. Maurice, F. et al *J. Allergy Clin. Immunol.* 1986, **77**, 594-597.
27. Harris, D. K. *Br. J. Ind. Med.* 1953, **10**, 255-268.
28. *NIOSH: Criteria for a Recommended Standard – Occupational Exposure to Formaldehyde* 1976, Pub. No. 77-126, NTIS Pub. No. PB-273-805, Springfield, VA, USA.
29. Gocke, E. et al *Mutat. Res.* 1981, **90**, 91-109.
30. Alderson, T. et al *Nature (London)* 1967, **215**, 1281-1283.
31. Fleig, I. et al *J. Occup. Med.* 1985, **24**, 1009-1012.
32. Bauchinger, M. et al *Mutat. Res.* 1985, **155**, 195-199.
33. Gardner, M. J. et al *Br. J. Ind. Med.* 1993, **50**(9), 827-834.
34. Dueva, L. A. *Gig. Tr. Prof. Zabol.* 1988, (5), 7-10 (Russ.) (*Chem. Abstr.* **109**, 333066b).
35. Berry, C. L. et al *Teratology*, Springer, New York, NY, USA.
36. Festy, B. *Hommage Professeur Rene Truhaut* 1984, 368-371 (Fr.) (*Chem. Abstr.* **106**, 79675n).
37. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
38. *Appl. Occup. Environ. Hyg.* 1992, **7**(12), 852-874.
39. Mathison, B. H. et al *Mutat. Res.* 1997, **380**(1,2), 77-96

F101 formamide

$HC(O)NH_2$

CH_3NO **Mol. Wt.** 45.04 **CAS Registry No.** 75-12-7

Synonyms carbamaldehyde; methanamide

EINECS No. 200-842-0 **RTECS No.** LQ 0525000

Uses Solvent. Organic synthesis.

Physical properties

M. Pt. 2-3°C (99+% purity) **B. Pt.** 210°C (decomp.) **Flash point** 154°C (open cup) **Specific gravity** 1.134 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –1.51 **Volatility** v.p. 29.7 mmHg at 129.4°C ; v.den. 1.0

Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

FR-VME 20 ppm (30 mg m^{-3})
SE-LEVL 10 ppm (20 mg m^{-3}) **SE-STEL** 15 ppm (30 mg m^{-3})
UK-LTEL 20 ppm (37 mg m^{-3}) **UK-STEL** 30 ppm (56 mg m^{-3})
US-TWA 10 ppm (18 mg m^{-3})

F100 for

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor of 0.042 indicates that environmental accumulation is unlikely (1).

Environmental fate

Degradation studies
Removal from wastewater by activated sludge: 1.6% of ThOD after 6 hr, 4.7% of ThOD after 12 hr, 11.8% of ThOD after 24 hr (2).

Abiotic removal
Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in the atmosphere ≈2.1 hr (3).

Adsorption and retention
Estimated K_{oc} of 3.6 indicates that adsorption to soil and sediments would not be significant (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 2150, 5700 mg kg^{-1}, respectively (4).
LD_{50} intraperitoneal mouse, rat 2450, 5700 mg kg^{-1}, respectively (5,6).

Sub-acute and sub-chronic data
Inhalation (2 wk) rat 0, 100, 500 or 1500 ppm, 6 hr day^{-1} 5 days wk^{-1}. ♂ Rats exposed to 1500 ppm had significantly reduced body weights. Platelet and/or lymphocyte counts were reduced in rats exposed to 500 or 1500 ppm. Minimal to severe renal necrosis and regeneration of renal tubular epithelial cells were observed in rats exposed to 1500 ppm (7).

Teratogenicity and reproductive effects
Oral rat, lowest toxic dose, foetal deaths 1200 mg kg^{-1} day^{-1} on days 11-12 of gestation (8).
Oral rabbit, lowest toxic dose, 910 mg kg^{-1} day^{-1} on days 6-18 of gestation (post-implantation mortality, foetotoxicity, musculoskeletal teratogenic effects) (9).

Metabolism and toxicokinetics
Formamide is absorbed directly through guinea pig skin (10).

Irritancy
100 mg instilled into rabbit eye caused severe irritation (exposure unspecified) (11).

Sensitisation
No allergic skin sensitisation was reported in guinea pigs (12).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (13).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).

Other comments

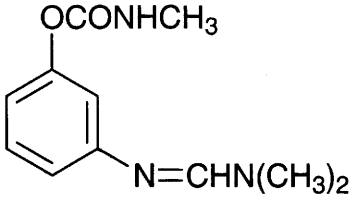
Environmental fate reviewed (15).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).
Autoignition temperature >500°C.

References

1. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods*, 1982, McGraw-Hill, New York, NY, USA.
2. Maloney, G. W. et al *J. Water Pollut. Control Fed.* 1969, **41**(2), Part 2, R18-R33.

3. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
4. Saratikov, A. S. et al *Gig. Sanit.* 1987, (3), 72-73 (Russ.) (*Chem Abstr.* **107**, 34485e).
5. Pham-Huu-Chanh, et al *Toxicol. Appl. Pharmacol.* 1973, **26**, 596.
6. *Naunyn-Schmiedeberg's Arch. Exp. Pathol. Pharmacol.* 1957, **230**, 559.
7. Warheit, D. B. et al *Fundam. Appl. Toxicol.* 1989, **13**(4), 702-713.
8. *Toxicol. Appl. Pharmacol.* 1977, **41**, 35.
9. *Arzneim.-Forsch.* 1980, **30**, 1557.
10. Clayton G. D. et al (Eds.) *Patty's Industrial Hygiene and Toxicology* 2nd ed., 1983, **2**, 1829, Interscience Publishers, New York, NY, USA.
11. *Am. J. Ophthalmol.* 1946, **29**, 1363.
12. *Documentation of Threshold Exposure Limits Values and Biological Exposure Indices* 5th ed., 1986, 274, American Conference of Governmental Industrial Hygienists, Cincinnati, OH, USA.
13. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
14. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
15. Howard, P. H. (Ed.) *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1993, **4**, 305-310, Lewis Publishers, Chelsea, MI, USA.
16. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F102 formetanate



$C_{11}H_{15}N_3O_2$ **Mol. Wt.** 221.26 **CAS Registry No.** 22259-30-9

Synonyms 3-dimethylaminomethyleneaminophenylmethylcarbamate; *N,N*-dimethyl-*N'*-[3-[[(methylamino)carbonyl]oxy]phenyl]methanimidamide; *N'*-(*m*-hydroxyphenyl)-*N,N*-dimethylformamidinmethylcarbamate ester; Dicarzol; Formetanat; Carzal; 3-dimethylaminomethylene iminophenyl-*N*-methylcarbamate

EINECS No. 244-879-0 **RTECS No.** FC 2513000

Uses Insecticide. Acaricide. Cholinesterase inhibitor.

Physical properties

M. Pt. 102-103°C **Partition coefficient** log P_{ow} –2.7 (hydrochloride) (1) **Volatility** v.p. 1.2×10^{-5} mmHg at 25°C (hydrochloride)
Solubility Water: miscible. Organic solvents: acetone, chloroform

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Very toxic by inhalation and if swallowed – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R26/28, R43, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous

waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S24, S28, S37/39, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish, black bullhead 3-75 mg l^{-1} (hydrochloride) (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* sp. 93 μg l^{-1} (hydrochloride) (1).

LD_{50} contact bee 14 μg bee^{-1} (hydrochloride) (1).

Environmental fate

Abiotic removal

Hydrolysis (hydrochloride) at 22°C, $t_{1/2}$ ~62 days at pH 5, 23 hr at pH 7, and 2 hr at pH 9; hydrolysis product 3-aminophenol (1).

Photolysis of aqueous solution at wavelengths >290 nm, $t_{1/2}$ ~55 days at pH 5, 17 hr at pH 7, ~3 hr at pH 9 (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken, mallard duck, bobwhite quail 12-42 mg kg^{-1} (hydrochloride) (1,3).

LD_{50} oral rat, mouse 18-20 mg kg^{-1} (1,4).

LC_{50} (4 hr) inhalation rat 2.8 mg l^{-1} (air aerosol); 0.29 mg l^{-1} (air dust) (hydrochloride) (1).

LD_{50} dermal rat >5600 mg kg^{-1}, rabbit >10,200 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Oral mouse, dog (2 yr); no-adverse-effect level for mice 50 mg kg^{-1} diet, for dogs 10 mg kg^{-1} diet (1).

Metabolism and toxicokinetics

In plants and animals metabolism involves hydrolysis and oxidative demethylation (1).

Metabolites include *m*-formaminophenyl-*N*-methyl carbamate, *m*-formaminophenol, *m*-aminophenol, *m*-acetamidophenol, and glucuronide and sulfate of *m*-acetamidophenol (1,5).

Following oral administration of radiolabel to rats, rapid absorption and excretion occurred, 85% of the label was excreted in the urine and 8% in faeces after 72 hr. 2% of label was retained (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 with and without metabolic activation negative (6).

Drosophila melanogaster sex-linked recessive lethal assay negative (6).

In vitro Chinese hamster ovary cells sister chromatid exchanges negative (6).

In vitro mouse lymphoma L5178Y tk^+/tk^- cells, with and without metabolic activation negative (6).

Other effects

Any other adverse effects

Injection of a single dose of 0.5 mg kg^{-1} produced a pronounced suppression of behavioural response in trained rats. It was concluded that formetanate acts as an indirect antagonist on central and peripheral muscarinic receptors, by inhibiting acetylcholinesterase activity, to produce changes in schedule-controlled response (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (8).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

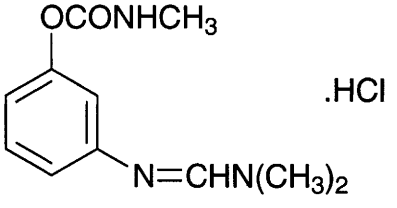
WHO Toxicity Class Ib (10).

EPA Toxicity Class I (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *Defence des Vegetaux* 1974, **28**, 43.
3. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
4. *World Rev. Pest Control* 1970, **9**, 119.
5. *Foreign Compound Metabolism in Mammals* 1972, **2**, 145-295, The Chemical Society, London, UK.
6. Garnett, N. E. et al *Mutat. Res.* 1986, **168**(3), 301-325.
7. Moser, V. C. et al *Pharmacol. Biochem. Behav.* 1987, **26**(1), 119-121.
8. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
10. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F103 formetanate hydrochloride



$C_{11}H_{16}ClN_3O_2$ **Mol. Wt.** 257.72 **CAS Registry No.** 23422-53-9

Synonyms *N,N*-dimethyl-*N'*-[3-[[(methylamino)carbonyl]oxy]phenyl]methanimidamide monohydrochloride; 3-dimethylaminomethyleneiminophenyl-*N*-methylcarbamate hydrochloride; ENT 27566; Dicarzol

EINECS No. 245-656-0 **RTECS No.** FC 2514000

Uses Acaricide. Insecticide.

Physical properties

M. Pt. 200-202°C (decomp.) **Partition coefficient** log P_{ow} -3.30 (1) **Volatility** v.p. 1.2×10^{-5} mmHg at 25°C
Solubility Water: >822 g l^{-1} at 25°C. Organic solvents: acetone, chloroform, dichloromethane, ethyl acetate, hexane, methanol

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Very toxic by inhalation and if swallowed – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R26/28, R43, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S24, S28, S37/39, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 2.8-4.4 mg kg^{-1} (1).
LC_{50} (96 hr) bluegill sunfish 2.8-20 mg l^{-1} (1).
LC_{50} (96 hr) black bullhead 75 mg l^{-1} (1).

F102 for

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* sp. 93 μg l^{-1} (1).

LD_{50} contact bee 14 μg bee^{-1} (1).

Environmental fate

Degradation studies

River bottom samples were incubated with ^{14}C-labelled formetanate hydrochloride for 16 days. Metabolites formed included *m*-formaminophenol (59%), *m*-formaminophenyl-*N*-methylcarbamate (7.8%), demethylformetanate (1.2%), *m*-aminophenol (19%) and *m*-[(dimethylaminomethylene)imino]phenol (1.9%) (2).

Abiotic removal

$t_{1/2}$ for hydrolysis at 22°C, 62.5 days at pH 5, 23 hr at pH 7, 2 hr at pH 9 (1).

Undergoes photolytic degradation in aqueous solution, with $t_{1/2}$ 55.5 days at pH 5, 17 hr at pH 7, 2.9 hr at pH 9. Principal degradation products included: 3'-hydroxyformanilide with 3-formamidophenyl methylcarbamate and *m*-[(dimethylaminomethylene)amino]phenol (2,3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, dog, chicken, mallard duck, bobwhite quail 12-42 mg kg^{-1} (1,4).

LC_{50} (4 hr) inhalation rat 2800 mg m^{-3} (1).

LD_{50} dermal rat, rabbit 5600, 10,200 mg kg^{-1}, respectively (4).

Carcinogenicity and chronic effects

Oral mouse and dog (2 yr) no-adverse-effect level for mice 50 mg kg^{-1} diet, and for dogs 10 mg kg^{-1} diet. No carcinogenic effects were reported (1,2).

Genotoxicity

Formetanate hydrochloride was one of a group of pesticides which gave negative results in all genotoxicity bioassays in which they were evaluated (no specific details reported) (5).

Other effects

Any other adverse effects

Inhibits cholinesterase activity (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

EPA Toxicity Class I (3).

ADI 0.037 mg kg^{-1} (taking safety factor of 10 for cholinesterase inhibition) (3).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Mergic, C. M. *Metabolism of Pesticides: Update II* 1978, U.S. Department of the Interior, Fish, Wildlife Service, Special Scientific Report – Wildlife No. 212, Washington, DC, USA.
3. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
4. *Pesticide Index* 1976, **5**, 118.
5. Garrett, N. E. et al *Mutat. Res.* 1986, **168**(3), 301-325.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F104 formic acid

HCO_2H

CH_2O_2 **Mol. Wt.** 46.03 **CAS Registry No.** 64-18-6

Synonyms aminic acid; formylic acid; hydrogen carboxylic acid; methanoic acid; E236; Amasil; Sintas 90

EINECS No. 200-579-1 **RTECS No.** LQ 4900000

Uses Disinfectant. Preservative. Descaler. Organic synthesis.
Occurrence Occurs in ants, some plants and dairy products.

Physical properties

M. Pt. 8.2-8.4°C **B. Pt.** 100-101°C **Flash point** 68°C **Specific gravity** 1.220 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.54 **Volatility** v.p. 35 mmHg at 20°C ; v.den. 1.6
Solubility Water: miscible. Organic solvents: benzene, diethyl ether, ethanol, glycerol, toluene

Occupational exposure

DE-MAK 5 ppm (9.5 mg m^{-3})
FR-VLE 5 ppm (9 mg m^{-3})
JP-OEL 5 ppm (9.4 mg m^{-3})
SE-LEVL 3 ppm (5 mg m^{-3}) **SE-STEL** 5 ppm (9 mg m^{-3})
UK-LTEL 5 ppm (9.6 mg m^{-3})
US-TWA 5 ppm (9.4 mg m^{-3}) **US-STEL** 10 ppm (19 mg m^{-3})

UN No. 1779 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Causes severe burns (R35)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S26, S45)

Ecotoxicity

Fish toxicity
Not toxic to brown trout, bluegill sunfish, yellow perch or goldfish at 5 mg l^{-1} for 24 hr (1).

Invertebrate toxicity
IC_{Lo} (4 days) *Scenedesmus quadricauda* 100 mg l^{-1} at 20°C (2).

Bioaccumulation
Calculated bioconcentration factor of 0.22 indicates that environmental pollution is unlikely (3).

Environmental fate

Degradation studies
Catabolised by *Butyribacterium methylotropicum* to acetate and carbon dioxide (under aerobic conditions) when utilised as sole carbon source (4).
Readily oxidised by acclimated activated sludge microorganisms at 1600 mg l^{-1} under aerobic conditions, and at 760 mg l^{-1} under anaerobic conditions (5,6).
ThOD 0.35 mg l^{-1} O_2, BOD_{20} 0.250 mg l^{-1}, BOD_5 O_2 0.86 mg l^{-1} O_2 (7,8).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >110 mg kg^{-1} (9).
LD_{50} oral mouse, rat, dog 700, 1100, 4000 mg kg^{-1}, respectively (10-12).
LC_{50} (15 min) inhalation mouse, rat 6200, 15,000 mg m^{-3}, respectively (10).
Subcutaneous rabbit, single injection of 300 mg kg^{-1} was tolerated without any adverse effects (13).
LD_{50} intravenous mouse 145 mg kg^{-1} (12).
LD_{50} intraperitoneal mouse 940 mg kg^{-1} (14).

Sub-acute and sub-chronic data

Oral rat, (6 wk) 0.5 or 1% in diet or drinking caused a reduction in organ weight and body weight gain (12).

Teratogenicity and reproductive effects

No toxic or teratogenic effects occurred after injection of 20 mg into fertilised chicken eggs (12).

Metabolism and toxicokinetics

Following intragastric administration of 300 mg kg^{-1} to rabbits the bulk of the formate was excreted in urine within 15 hr, although urinary pH was reduced for up to 30 hr after administration (15).

Irritancy

Dermal rabbit 610 mg caused mild irritation, 122 mg instilled into rabbit eye caused severe irritation (exposure not specified) (16).

Sensitisation

Sensitisation is rare, but has been reported in workers previously sensitised to formaldehyde (17).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (18).
In vitro Chinese hamster ovary cells, chromosomal aberrations with and without metabolic activation positive (19).

Other effects

Other adverse effects (human)

In exposed workers, urinary excretion of calcium was linearly correlated with formic acid excretion, while urinary ammonia inversely correlated with formic acid excretion (15).
There has been a report of three patients who swallowed descaling agents containing 40 or 55% formic acid in which the major complications included local corrosive effects, metabolic acidosis, derangement of blood-clotting mechanisms and acute onset of respiratory and renal failure. All three patients died 3-14 days after admission to hospital (20).
A report of 53 cases of formic acid ingestion included 15 fatalities (21).

Legislation

Tolerable daily intake (human) for formic acid and ethyl formate 3 mg kg^{-1} (22).

Other comments

Physical properties, toxicity and health hazards reviewed (23,24).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (25).
Autoignition temperature 50°C.

References

1. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA560/6-87-002, PB-87-200-275, Washington, DC, USA.
2. Bringmann, G. et al *Gesund.-Ing.* 1959, **80**, 115-120.

3. Lyman, W. J. et al *Handbook of Chemical Properties Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
4. Kerby, R. et al *J. Bacteriol.* 1987, **169**(5), 2063-2068.
5. Dickenson, B. W. et al *Proc. 9th Ind. Waste Conf. Purdue Univ.* 1954, Engng. Extn. Ser. No. 87, 331-351.
6. McCarthy, P. L. et al *J. Water Pollut. Control Fed.* 1963, **35**, 1501-1506.
7. Meirck, F. et al *Les Eaux Residuaires Industrielles* 1970.
8. Zoeteman, B. C. J. et al H_2O 1971, **4**(16), 367-371.
9. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
10. *Gig. Tr. Prof. Zabol.* 1979, **23**(12), 49.
11. *AMA Arch. Ind. Health* 1959, **20**, 517.
12. Malorny, G. *Ernaehrungswiss.* 1969, **9**, 332-339 (*Chem. Abstr.* **72**(7), 30395m).
13. Lund, A. *Acta Pharmacol. Toxicol.* 1948, **4**, 99-107.
14. *Igiena* 1962, **11**, 507.
15. Liesivuori, J. et al *Klin. Wochenschr.* 1987, **65**(18), 860-863.
16. *Union Carbide Data Sheet* 8 May 1968.
17. Fassett, D. W. et al (Eds.) *Toxicology* 1963, **2**, Wiley Interscience, New York, NY, USA.
18. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141.
19. Morita, T. et al *Mutat. Res.* 1990, **240**(3), 195-202.
20. Naik, R. B. et al *Postgrad. Med. J.* 1980, **56**, 451-456.
21. Rajan, N. et al *Postgrad. Med. J.* 1981, **61**, 35-36.
22. *Evaluation of Certain Food Additives: 23rd Report of the Joint FAO/WHO Expert Committee on Food Additives* 1990, WHO Tech. Rep. Ser. 648, Geneva, Switzerland.
23. *Cah. Notes Doc.* 1987, **129**, 687-691 (Fr.) (*Chem. Abstr.* **109**, 175483f).
24. *Chemical Safety Data Sheets* 1990, **3**, 115-118, The Royal Society of Chemistry, Cambridge, UK.
25. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F105 formothion

$$(CH_3O)_2P(S)SCH_2C(O)N(CH_3)CHO$$

$C_6H_{12}NO_4PS_2$ **Mol. Wt.** 257.27 **CAS Registry No.** 2540-82-1

Synonyms *O,O*-dimethyl *S*-[2-(formylmethylamino)-2-oxoethyl] phosphorodithioate; *O,O*-dimethyl ester, *S*-ester with *N*-formyl-2-mercapto-*N*-methylacetamide; 2-dimethoxyphosphinothioylthio-*N*-formyl-*N*-methylacetamide; Aflix; Anthio; Toprose

EINECS No. 219-818-6 **RTECS No.** TE 1050000

Uses Insecticide and acaricide.

Physical properties

M. Pt. 25-26°C **B. Pt.** Decomp. on distillation **Specific gravity** 1.361 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.48 (1) **Volatility** v.p. 8.5×10^{-7} mmHg at 20°C
Solubility Water: 2.6 g l^{-1} at 24°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, toluene, xylene, ligroin, paraffin oil

Occupational exposure

Supply classification harmful
Risk phrases Harmful in contact with skin and if swallowed (R21/22)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) carp >50 mg l^{-1} (1).

Environmental fate

Degradation studies

Undergoes hydrolysis to dimethoate and (dimethoxyphosphinothioylthio)acetic acid. Hydrolysis is more rapid under alkaline conditions, $t_{1/2}$ in loamy soils <1 day (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral pigeon 630 mg kg^{-1} (1).
LD_{50} oral mouse, cat, rat, rabbit 190, 210, 250, 420 mg kg^{-1}, respectively (2-4).
LC_{50} (4 hr) inhalation rat 4500 mg m^{-3} (1).
LD_{50} dermal rat 353 mg kg^{-1} (5).
LD_{50} intravenous rat 35 mg kg^{-1} (6).

Sub-acute and sub-chronic data

Gavage rat (2 month) doses of 0.01-0.05 of LD_{50} caused a dose-dependent decrease in acetylcholinesterase activities of splenocytes. A decrease in thymocytes was not significant. Possible mechanisms of immunosuppressive effects are discussed (7).

Carcinogenicity and chronic effects

Oral rat and dog (2 yr) 80 mg kg^{-1} diet caused no adverse effects (1).

Metabolism and toxicokinetics

Following oral administration to mammals is metabolised to (dimethoxyphosphinothioylthio)acetic acid and polar metabolites. Elimination occurs within 24 hr (1).

Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation positive (8).
Onion and barley, chromosomal aberrations in meristem with and without metabolic activation positive (9).

Legislation

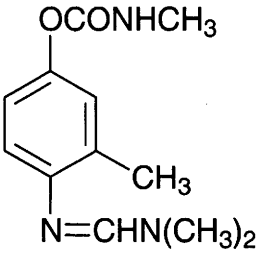
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
EEC maximum residue limits: citrus fruits 0.2 ppm; other fruit and vegetables 0.1 ppm (1).
WHO Toxicity Class II (12).
EPA Toxicity Class II (13).
ADI 0.02 mg kg^{-1} body weight (13).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Liesche, K. *Dtsch. Apoth. Ztg.* 1968, **108**, 604 (Ger.) (*Chem. Abstr.* **69**, 26287y).
3. *Int. Arch. Gewerbepathol. Gewerbehyg.* 1964, **21**, 92.
4. *Spec. Publ. – Entomol. Soc. Am.* 1978, **78-1**, 31.
5. *Br. J. Ind. Med.* 1969, **26**, 59.
6. *Int. Arch. Gewerbepathol. Gewerbehyg.* 1966, **22**, 246.
7. Gushchin, G. V. et al *Byull. Eksp. Biol. Med.* 1991, **111**(2), 144-146 (Russ.) (*Chem. Abstr.* **114**, 223169k).
8. Bergeneva, N. S. et al *Vestn. Akad. Nauk Kaz. SSR* 1986, (12), 65-67 (Russ.) (*Chem. Abstr.* **106**, 114702t).
9. Grover, I. S. et al *Prog. Clin. Biol. Res.* 1990, **340 E**, 91-106.

10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
13. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

F106 formparanate



$C_{12}H_{17}N_3O_2$ **Mol. Wt.** 235.29 **CAS Registry No.** 17702-57-7

Synonyms *N,N*-dimethyl-*N'*-[2-methyl-4-[[(methylamino)carbonyl]oxy]phenyl]methanimidamide; ENT 27305; Schering 36103; VC25074

RTECS No. FB 9880000

Uses Superseded insecticide.

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 7.2, 17 mg kg^{-1}, respectively (1,2).

Other effects

Any other adverse effects

Carbamate pesticides, including formparanate, are cholinesterase inhibitors (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. *USDA Information Memorandum* 1966, **20**(26), Agricultural Research Service, Beltsville, MD, USA.
2. *Eur. J. Toxicol. Environ. Hyg.* 1974, **7**, 152.
3. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F107 fosamine-ammonium

$$H_2N(O)CP(O)(OCH_2CH_3)O^- NH_4^+$$

$C_3H_{11}N_2O_4P$ **Mol. Wt.** 170.11 **CAS Registry No.** 25954-13-6

Synonyms ammonium ethyl carbamoylphosphonate; ammonium ethyl (aminocarbonyl)phosphonate; ethyl ammonium (aminocarbonyl)phosphonate; Krenite

EINECS No. 247-363-3 **RTECS No.** BQ 4112000

Uses Herbicide.

Physical properties

M. Pt. 175°C **Specific gravity** 1.33 at 20°C **Volatility** v.p. 4.0×10^{-6} mmHg at 25°C
Solubility Water: 2.5 kg l^{-1} at 25°C. Organic solvents: acetone, benzene, chloroform, dimethylformamide, ethanol, hexane, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 280-670 mg l^{-1} (1,2).
LC_{50} (96 hr) fathead minnow, rainbow trout >1000 mg l^{-1} (2).

Bioaccumulation
Bioaccumulation factor in channel catfish exposed to 1.1 mg l^{-1} for 4 wk <1. No adverse effects were observed during this study (3).

Environmental fate

Degradation studies
$t_{1/2}$ for microbial degradation in soils 7-10 days (1).

Abiotic removal
Decomposes in dilute solutions of acids (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail >10,000 mg kg^{-1} (4).
LD_{50} oral rat, guinea pig 7.4-24 g kg^{-1} (1,2,5,6).
LC_{50} (1 hr) inhalation rat >56 g m^{-3} (1).
LD_{50} dermal rabbit >1700 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral rat (90 days) 1000 mg kg^{-1} diet caused no adverse effects (1).

Teratogenicity and reproductive effects
Mallard and bobwhite quail eggs were immersed in 1.5, 6.5 or 30% fosamine-ammonium solution at 96 hr development. 6.5% solution reduced hatching success to 33 and 85% in mallards and bobwhite quail, respectively. 30% solution caused 95-100% mortality in both species by the time of hatching. Most abnormal embryos had severe oedema and some stunting. Mallard hatchlings from the 1.5 and 6.5% groups had reduced body weight and lower plasma alanine aminotransferase and aspartate aminotransferase activities, with elevated plasma glucose and cholesterol concentrations. Brain acetylcholinesterase activity was unaffected in embryos and hatchlings (7).

Metabolism and toxicokinetics
Following oral administration to rats 87% was eliminated in the faeces and 13% in urine after 72 hr. Intact fosamine (87%) and carbamoylphosphonic acid (13%) were excreted (8).

Other effects

Other adverse effects (human)

No excess mortality was found in a cohort study among forestry workers (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

WHO Toxicity Class Table 5 (12).

EPA Toxicity Class IV (4).

Other comments

Approved under UK Agricultural Chemicals Approval Scheme for use on barks beside water (2).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *Guidelines for the Use of Herbicides on Weeds In or Near Watercourses and Lakes* 1985, MAFF, Alnwick, Northumberland, UK.
3. Han, J. C. et al *J. Toxicol. Environ. Health* 1979, 5(5), 957-963.
4. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
5. Perkow, W. *Wirksubstanzen der Pflanzenschutz und Schlaedlings-bekaempfurngsmittel* 1971/76, Verlag Paul Parey, Berlin, Germany.
6. *Agricultural Chemicals* 1977, **2**, 209, Thomas Publications, Fresno, CA, USA.
7. Hoffran, D. J. *Environ. Toxicol. Chem.* 1988, **7**(1), 69-75.
8. Chrzanowski, R. L. et al *J. Agric. Food Chem.* 1979, **27**(3), 550-554.
9. Green, L. M. *Br. J. Ind. Med.* 1991, **48**(4), 234-238.
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F108 fosetyl-aluminium

$$[CH_3CH_2OP(O)(H)O^-]_3\ Al^{3+}$$

$C_6H_{18}AlO_9P_3$ **Mol. Wt.** 354.11 **CAS Registry No.** 39148-24-8

Synonyms aluminium tris(ethyl phosphite); aluminium tris(*O*-ethyl phosphorate); monoethyl phosphonate, aluminium salt; Aliette; Efosite Al; Phosethyl Al

EINECS No. 254-320-2 **RTECS No.** SZ 9640000

Uses Fungicide.

Physical properties

M. Pt. >200°C **Partition coefficient** log P_{ow} -2.7 (pH 4) (1) **Volatility** v.p. $<9.75 \times 10^{-8}$ mmHg (25°C)
Solubility Water: 120 g l^{-1} at 20°C. Organic solvents: methanol, propylene glycol, acetone, ethyl acetate, acetonitrile, hexane

Occupational exposure

SE-LEVL 1 mg m^{-3}
UK-LTEL 2 mg m^{-3}
US-TWA 2 mg m^{-3}

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 430 mg l^{-1} (1).

Invertebrate toxicity
Not lethal by contact to honey bees at 0.2 mg bee^{-1} (2).

Environmental fate

Abiotic removal
Stable under normal storage conditions. Undergoes hydrolysis at 70°C, $t_{1/2}$ of 6 hr at pH 1.2, 12 hr at pH 12.8 (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 3700, 5800 mg kg^{-1}, respectively (1,3).
LD_{50} oral bobwhite quail >8000 mg kg^{-1} (1).
LD_{50} dermal rabbit >2000 mg kg^{-1}, rat >3200 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 550 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral rat and dog (90 days) no-adverse-effect level for rats 5000 mg kg^{-1} diet, and for dogs 50,000 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) 0, 100, 400, 2000 mg kg^{-1} day^{-1} (the high dose was reduced to 1500 mg kg^{-1} day^{-1} after 2 wk following observations of staining of abdominal fur and red coloration of the urine). No carcinogenic effects were observed in ♀ rats. Urinary bladder and adrenal medulla tumours occurred in ♂ rats (4).
Oral mouse (2 yr) 0, 360, 1500, 2900 mg kg^{-1} day^{-1} (the high dose was increased to 4300 mg kg^{-1} day^{-1} at wk-19 because of the absence of any effects). No evidence of carcinogenesis was observed (4).

Metabolism and toxicokinetics
Following oral administration the compound was rapidly metabolised to yield mainly carbon dioxide (60%) recovered from the exhaled air. 26% of the dose was eliminated in the urine, partly as unchanged substance plus a larger amount of phosphite. 3-4% of the administered dose was recovered in the faeces (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (5).
Saccharomyces cerevisiae D7, reverse mutation assay negative (5).
Escherichia coli pol-A, DNA damage and repair test negative (5).
In vitro mouse micronucleus test negative (5).

Legislation

EEC maximum residue levels: grapes, citrus fruit, strawberries 5 ppm; apples, pineapples, tomatoes, French chicory 1 ppm (1).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
Tolerence permitted on citrus fruits under Federal Food, Drug and Cosmetic Act 0.5 ppm (8).
WHO Toxicity Class Table 5 (9).

EPA Toxicity Class III (2).
ADI 3 mg kg^{-1} (2).

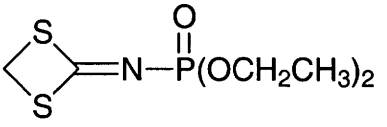
Other comments

Decomposes above 200°C without melting (1).
The carcinogenic potential of fosetyl-aluminium has been reviewed (5).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. William, D. J. et al *Br. Crop Prot. Conf. – Pests Dis. Proc.* 1977, 565.
4. *Peer Review of Aliette* 1986, US EPA, Office of Pesticide Programs, Health Effects Division, Washington, DC, USA.
5. Quest, J. A. et al *Regul. Toxicol. Pharmacol.* 1991, **14**, 3-11.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *Fed. Regist.* 23 Mar. 1990, **55**(57), 10932-10935.
9. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F109 fosthietan



$C_6H_{12}NO_3PS_2$ **Mol. Wt.** 241.27 **CAS Registry No.** 21548-32-3

Synonyms cyclic methylene-diethoxyphosphinodithiomidocarbonate; 2-(diethoxyphosphinylimino)-1,3-dithietane; diethyl 1,3-dithietan-2-ylidene phosphoramidate; Acconem; Geofos; Nem-a-tak

EINECS No. 244-437-7 **RTECS No.** NJ 6490000

Uses Superseded nematicide and insecticide.

Physical properties

Specific gravity 1.3 at 25°C **Volatility** v.p. 6.5×10^{-6} mmHg at 25°C
Solubility Water: 50 g l^{-1} at 25°C. Organic solvents: acetone, chloroform, methanol, toluene

Occupational exposure

Supply classification very toxic
Risk phrases Very toxic in contact with skin and if swallowed (R27/28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Environmental fate

Degradation studies
$t_{1/2}$ in soil 10-42 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 5, 18 mg kg^{-1}, respectively (2,3).
LD_{50} dermal rabbit 27 mg kg^{-1} (3).

Genotoxicity

Reported to be non-mutagenic in bacterial test system (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

References

1. Spencer, E. Y. *Guide to the Chemicals Used in Crop Protection* 7th ed., 1982, 313, Information Canada, Ottawa, Canada.
2. Whitney, W. K. et al *Br. Insectic. Fungic. Conf.* 1975, **2**, 625.
3. *Farm Chemicals Handbook* 1983, C167, Meister Publishing Co., Willoughby, OH, USA.
4. *The Pesticide Manual* 7th ed., 1983, British Crop Protection Council, Croydon, UK.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F110 francium

Fr

Fr **Mol. Wt.** 223.02 **CAS Registry No.** 7440-73-5

Synonyms Eka-cesium
Occurrence In uranium minerals. ^{223}Fr, the most stable isotope, is formed from α-decay of actinium.

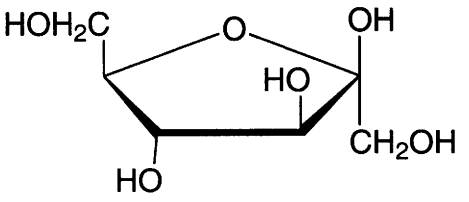
Other comments

^{223}Fr is the most stable isotope with a $t_{1/2}$ 21 min. It is a β-emitter. The properties of francium have been reviewed (1).
Francium salts have been used to influence activity of *Clostridium caproicum Prevot*, used in production of butanoic acid from ethanol by fermentation (2).

References

1. Sun, Z. et al *Weishengwuxue Zazhi* 1989, **9**(2), 9-13 (Ch.) (*Chem. Abstr.* **112**, 117296y).
2. Bailar, J. C. et al (Eds.) *Comprehensive Inorganic Chemistry* 1973, **1**, Pergamon Press, Oxford, UK

F111 D-fructose



$C_6H_{12}O_6$ **Mol. Wt.** 180.16 **CAS Registry No.** 57-48-7

Synonyms β-D-fructose; laevulose; levulose; fruit sugar; fructosan; Laevosan; Ethulose; Laevuflex

EINECS No. 200-333-3 **RTECS No.** LS 7000000

Uses As a sweetener, and to prevent sandiness in ice cream. Therapeutically as a fluid and nutrient replenisher and in veterinary medicine in treatment of bovine ketosis.

Occurrence In a large number of fruits and in honey. As part of disaccharides such as sucrose. As the sole sugar in the semen of several species, typical concentrations being 0.9-5 g l^{-1} in man, and in some other body fluids including cerebrospinal fluid (1,2).

Physical properties

M. Pt. 102-104°C (decomp.) **Specific gravity** 3300 g l^{-1}

Solubility Water: 3.3 g ml^{-1}. Organic solvents: ethanol, methanol

Mammalian & avian toxicity

Metabolism and toxicokinetics

Fructose is rapidly absorbed from the gastro-intestinal tract, but more slowly than glucose (3,4).

In the liver, most fructose is converted almost immediately into glucose, and enters the glucose metabolic pathways. Other metabolites include pyruvic acid and lactic acid (3,5).

Other effects

Other adverse effects (human)

A hereditary condition of fructose intolerance occurs in man (6).

Any other adverse effects

Diets including fructose (dose and duration unspecified) fed to rats cause dental caries, but this can be reduced by adding xylitol to diet (7).

Other comments

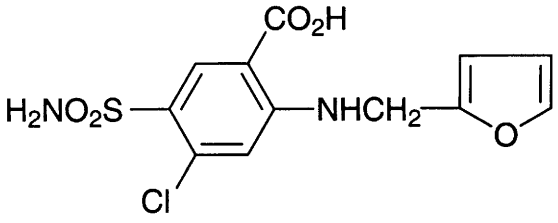
The metabolism and pharmacokinetics of fructose have been reviewed.

Fructose occurs both in furanose and pyranose forms. In aqueous solutions at 20°C, about 20% is in furanose form.

References

1. Mann, T. *The Biochemistry of Semen of the Male Reproductive Tract* 1964, Methuen, London, UK.
2. Papadopoulos et al *Arch. Biochem.* 1960, **88**, 167.
3. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
4. Ugolev, A. M. et al *Comp. Biochem. Physiol., A: Comp. Physiol.* 1986, **85A**(4), 593-612.
5. Vander et al *Human Physiology: The Mechanisms of Body Function* 1980, McGraw Hill, New York, NY, USA.
6. Hallfrisch, J. L. *FASEB J.* 1990, **4**(9), 2652-2660.
7. Karle, E. J. et al *Dtsch. Zahnaerztl. Z.* 1987, **42**(9), 835-840 (Ger.) (*Chem. Abstr.* **107**, 235322y)

F112 frusemide



$C_{12}H_{11}ClN_2O_5S$ **Mol. Wt.** 330.75 **CAS Registry No.** 54-31-9

Synonyms 5-aminosulfonyl-4-chloro-2-[(2-furanylmethyl)amino]benzoic acid; 4-chloro-*N*-furfuryl-5-sulfamoylanthranilic acid; Aisemide; Beronald; Furanthril; Furosemide; Lasix; Rosemide; Salix

EINECS No. 200-203-6 **RTECS No.** CB 2625000

Uses Diuretic and antihypertensive drug.

Physical properties

M. Pt. 220°C (decomp.)

Solubility Organic solvents: acetone, chloroform, dimethylformamide, ethanol, methanol

Environmental fate

Abiotic removal

Undergoes photolytic dechlorination under sunlight and artificial light and undergoes hydrolysis. Both mechanisms follow apparent first-order kinetics (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, mouse, rat 800, 2200, 2600 mg kg^{-1}, respectively (2-4).

LD_{50} intravenous rabbit, rat 400, 800 mg kg^{-1}, respectively (4).

LD_{50} intraperitoneal rat 800 mg kg^{-1} (5).

Intraperitoneal ♂ mouse, single dose of 400 mg kg^{-1} produced massive necrosis in the midzonal and centrilobular areas of the liver. The damage was prevented by prior administration of cytochrome P_{450} inhibitors (6).

Sub-acute and sub-chronic data

Oral rat (14 day) 13,000-46,000 mg kg^{-1} diet was fatal to 3/5 high-dose animals within 14 days. Minimal to mild nephrosis was observed in rats in all treated groups (7).

Oral rat (13 wk) 625-15,000 mg kg^{-1} diet. ♂ rats given 12,500 mg kg^{-1} or more and ♀ rats given 15,000 mg kg^{-1} diet had increased liver: body weight ratios. Dose-related diuresis was also observed. Minimal to moderate nephrosis occurred in ♂ rats administered 5000 or 10,000 mg kg^{-1} diet and in ♀ rats administered 7,500 or 15,000 mg kg^{-1} diet. Mineralisation was observed at the corticomedullary junction in ♂ rats given 625 mg kg^{-1} diet or more (7).

Subcutaneous rat (15 days) 5 or 15 mg kg^{-1} day^{-1} on days 4-28 after birth. Increased urinary calcium and magnesium excretion was observed and total calcium and magnesium in bone was lower. Growth was also inhibited in a dose-dependent manner (8).

Carcinogenicity and chronic effects

Inadequate evidence for the evaluation of carcinogenicity to humans and animals, IARC classification group 3 (9).

Oral rat and mouse (2 yr) 0, 350 or 700 ppm diet in rats, 0, 700 or 1400 ppm diet in mice. Survival of dosed ♀ mice was lower than for controls. Nephropathy was increased in ♂ rats and in ♀ and ♂ mice. In ♀ mice, treatment-related increase in malignant tumours of the mammary gland was observed. In ♂ rats, insignificant marginal increases in tubular cell neoplasms of the kidney and meningioma of the brain were observed in treated animals (10).

As part of study on the combined administration with the known carcinogen *N*-nitrosobutyl-*N*-(4-hydroxybutylamine), rats were administered 2.5 mg kg^{-1} by gavage 3 × wk^{-1} for 32 wk. At the end of the experiment all bladders were histologically examined. No significant difference in the incidence of bladder lesions was observed in frusemide-treated versus other groups. Treatment with frusemide alone did not induce any lesions of the bladder (11).

Teratogenicity and reproductive effects

Dosage of 37.5, 75, 150 or 300 mg kg^{-1} to rats (route unspecified) 2 × day^{-1} on days 6-17 of gestation caused a dose-related increase in the frequency of wavy ribs. Also 5/176 foetuses in the 150 mg kg^{-1} group had malformations of the scapula. The two higher doses caused some maternal fatalities and resulted in increased resorption rates and decreased foetal weights (12).

Metabolism and toxicokinetics

Following oral administration of 10, 20, 30 or 40 mg to human volunteers, frusemide was rapidly absorbed from the gastro-intestinal tract with a 1st-order rate constant k_a of 2.33 hr^{-1} after a lag time of 6.45 min. Elimination was rapid and was mainly via the urine (13).

30-70% absorption was reported in humans, rats and dogs following oral administration (14-16).

~4% of an intravenous dose to rats was recovered from the gut (16).

In rats, frusemide is cleared from the plasma by the kidneys, is biotransformed by the liver, or is excreted unchanged in the bile with subsequent intestinal reabsorption (17).

Glucuronidation of frusemide appears to take place in the kidney. Removal of the liver did not affect clearance of frusemide in dogs (17,18).

Covalent binding to mouse liver proteins has been demonstrated and was enhanced by administration of an infiltration of epoxide hydratase, indicating the formation of an arene oxide intermediate involving the furan ring (19).

In vitro human liver microsomes can convert frusemide into metabolites which bind irreversibly to microsomal proteins (20).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation marginally positive (21).

In vitro mouse lymphoma L5178Y cells, induction of mutations to trifluoro-thymidine resistance, with metabolic activation positive (7).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges positive (7).

In vitro Chinese hamster lung fibroblasts, chromosomal damage without metabolic activation positive (22,23).

In vitro human diploid fibroblasts, HE2144, sister chromatid exchanges negative (24).

In vitro human lymphocytes, chromosomal aberrations positive (25).

Intraperitoneal administration to mice of 0.3-50 mg kg^{-1} caused an increase in chromosomal aberrations of meiotic cells throughout the whole spermatic cycle (26).

Other effects

Other adverse effects (human)

The most common side-effect associated with frusemide therapy is fluid and electrolyte imbalance, including hyponatraemia, hypokalaemia and hypochloraemic alkalosis. Unlike the thiadiazole diuretics, it increases the urinary excretion of calcium. Nephrocalcinosis has been reported when treating pre-term infants. Hyperglycaemia and glycosuria may be provoked. It has been reported to cause hyperuriaemia and precipitate attacks of gout in some patients (27).

In a cohort study designed to screen a large number of drugs for possible carcinogenicity, 2302 persons prescribed frusemide at least once during 1969-1973 were followed for up to 15 yr. A two-fold increase in risk was noted for lung cancer and 1.5-fold increase for cancers at all other sites. These could, however, have been accounted for by smoking and/or chance (28).

Tinnitus and deafness may rarely occur, in particular during rapid high-dose parenteral frusemide therapy. Rarely, deafness may be permanent if other ototoxic drugs are taken as well (27).

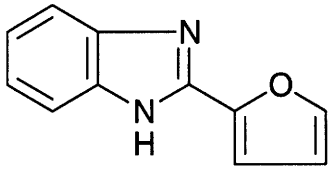
Other comments

Physical properties, use, analysis, carcinogenicity, metabolism, mammalian toxicity and teratogenicity reviewed (9).

References

1. Yagi, M. et al *Chem. Pharm. Bull.* 1991, **39**(2), 454-457.
2. Goldenthal, E. I. *Toxicol. Appl. Pharmacol.* 1971, **18**, 185.
3. Pomanora, T. V. et al *Pharm. Chem. J.* 1985, **19**, 706.
4. Horioka, M. et al *Drugs in Japan: Ethical Drugs* 6th ed., 1982, 725, Jakugyo Jiho Co, Tokyo, Japan.
5. *Acta. Pol. Phar.* 1985, **42**, 199.
6. Mitchell, J. R. et al *Nature (London)* 1974, **251**, 508-511.
7. *National Toxicology Program Research and Testing Division* 1989, Report No.TR-356, NIEHS, Research Triangle Park, NC, USA.
8. Koo, W. W. K. et al *Pediatr. Res.* 1986, **20**, 74-78.
9. *IARC Monograph* 1990, **50**, 277-291.
10. Bucher, J. R. et al *J. Appl. Toxicol.* 1990, **10**(5), 369-378.
11. Shabata, M. A. et al *J. Toxicol. Environ. Health* 1989, **26**, 255-265.
12. Robertson, R. T. et al *Toxicol. Appl. Pharmacol.* 1981, **60**, 142-150.
13. Zhu, J. et al *J. Pharmacobio-Dyn.* 1987, **10**(8), 370-376.
14. Yakatan, G. J. et al *Res. Commun. Chem. Pathol. Pharmacol.* 1979, **24**, 465-482.
15. Tilstone, W. J. et al *Clin. Pharmacol. Ther.* 1978, **23**, 644-650.
16. Lee, M. G. et al *J. Pharmacokinet. Biopharm.* 1983, **11**, 623-640.
17. Kitani, M. et al *Chem. Pharm. Bull.* 1988.
18. Verbeek, R. K. et al *J. Pharmacol. Exp. Ther.* 1981, **216**, 479-483.
19. Wirth, P. J. et al *Mol. Pharmacol.* 1976, **12**, 759-768.
20. Dybing, E. *Acta Pharmacol. Toxicol.* 1977, **41**, 89-93.
21. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
22. Matsuoka, A. et al *Mutat. Res.* 1979, **66**, 277-290.
23. Ishidate, M. *Data Book of Chromosomal Aberrations Test In Vitro* 1988, Elsevier, Amsterdam, Netherlands.
24. Sasaki, M. et al *Senshokutai* 1980, **II-20**, 574-584.
25. Jameela, X. et al *Mutat. Res.* 1979, **66**, 69-74.
26. Subranamyam, S. et al *Indian J. Med. Res.* 1977, **66**, 104-113.
27. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
28. Selby, J. V. et al *Cancer Res.* 1989, **49**, 5736-5747

F113 fuberidazole



$C_{11}H_8N_2O$ **Mol. Wt.** 184.20 **CAS Registry No.** 3878-19-1

Synonyms 2-(2′-furyl)benzimidazole; 2-(2-furanyl)-1*H*-benzimidazole; Voronit

EINECS No. 223-404-0 **RTECS No.** DD 9010000

Uses Fungicide.

Physical properties

M. Pt. 292°C (decomp.) **Partition coefficient** log P_{ow} 2.67 at 22°C **Volatility** v.p. 7.52×10^{-6} mmHg at 20°C **Solubility** Water: 71 mg l^{-1} at 25°C. Organic solvents: dichloromethane, diethyl ether, ethanol, isopropanol, light petroleum, toluene

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust (S2, S22)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) mosquito fish, sailfin molly >1 mg l^{-1} (1).

Environmental fate

Abiotic removal
Unstable to light (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 500, 825 mg kg^{-1}, respectively (1-3).
LC_{50} (4 hr) inhalation rat 330 mg m^{-3} (4).
LD_{50} dermal rat 500 mg kg^{-1} (4).
LD_{50} intraperitoneal rat 100 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral rat (90 days) 1500 mg kg^{-1} diet caused no adverse effects (1).

Carcinogenicity and chronic effects
In 2-yr feeding studies NOEL for dog, ♂ rat, mouse, ♀ rat 20, 80, 100, 400 mg kg^{-1} diet, respectively (2).

Metabolism and toxicokinetics
Following oral administration to mammals, fuberidazole is rapidly metabolised by hydrolysis and hydroxylation. Elimination is mainly in the urine (1).

Genotoxicity

Salmonella typhimurium TA1530, LT-2 with and without metabolic activation positive (5).

Legislation

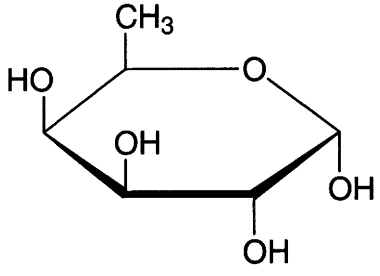
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
WHO Toxicity Class III (8).
ADI 0.006 mg kg^{-1} body weight (2).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *Farm Chemicals Handbook* 1991, C148, Meister Publishing Co., Willoughby, OH, USA.
4. Perkow, W. *Wirksubstanzen der Pflanzenschutz und Schaedlings-bekaempfungsmittel* 1971-76, Verlag Paul Parey, Berlin, Germany.
5. Seiler, J. P. et al *Mutat. Res.* 1972, **15**, 273-276.

6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F114 D-fucose



$C_6H_{12}O_5$ **Mol. Wt.** 164.16 **CAS Registry No.** 3615-37-0

Synonyms 6-deoxy-D-galactose; D-galactomethylose; rhodeose

EINECS No. 222-792-9

Uses As a sweetener.

Occurrence In glucosides found in various species of Convolvulaceae. In jalap resin.

Physical properties

M. Pt. 144°C

Solubility Organic solvents: ethanol

Mammalian & avian toxicity

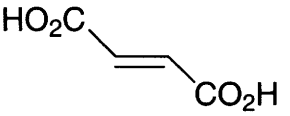
Metabolism and toxicokinetics

Can compete with D-glucose for facilitated transport uptake system into rat liver lysosomes and may compete for a variety of other sugar binding and transport sites (1).

References

1. Jonas, A. J. *Biochem. J.* 1990, **272**(2), 323-326

F115 fumaric acid



$C_4H_4O_4$ **Mol. Wt.** 116.07 **CAS Registry No.** 110-17-8

Synonyms (*E*)-2-butenedioic acid; *trans*-2-butenedioic acid; allomaleic acid; boletic acid; *trans*-1,2-ethylenedicarboxylic acid; lichemic acid

EINECS No. 203-743-0 **RTECS No.** LS 9625000

Uses Antioxidant. Organic synthesis. Mordant in dyeing. Flavouring agent. Food additive. Treatment of skin disorders. Substitute for tartaric acid in beverages.
Occurrence In many plants.

Physical properties

M. Pt. 299-300°C (sublimes) **B. Pt.** 165°C at 1.7 mmHg **Flash point** 230°C **Specific gravity** 1.635 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.3 (1) **Volatility** v.p. 1.7 mmHg at 165°C
Solubility Water: 6.3 g l^{-1} at 25°C. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

Supply classification irritant
Risk phrases Irritating to the eyes (R36)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S26)

Environmental fate

Degradation studies
Oxidised to acetate by *Desulfovibrio* in the presence of sulfate (2).
ThOD 0.827 mg l^{-1} O_2, BOD_5 0.175 mg l^{-1} O_2 (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 10,700 mg kg^{-1} (4).
LD_{50} dermal rabbit 20,000 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 100 mg kg^{-1} (5).

Metabolism and toxicokinetics
Intermediate metabolite in the tricarboxylic acid cycle. Concentrations of fumarate in muscle increased in humans during prolonged exercise (6).

Irritancy
Dermal rabbit (24 hr) caused mild irritation and 100 mg instilled into rabbit eye (24 hr) caused moderate irritation (7).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (8).

Other effects

Other adverse effects (human)

Reports of acute renal failure have been associated with the administration of fumaric acid. Other adverse effects with oral therapy have included disturbances of liver function, gastro-intestinal effects, and flushing (9).

Legislation

Because fumaric acid is a normal constituent of tissues and is metabolised by the body, the FAO/WHO committee considered that the establishment of an acceptable daily intake for man was unnecessary for fumaric acid and its salts (10).

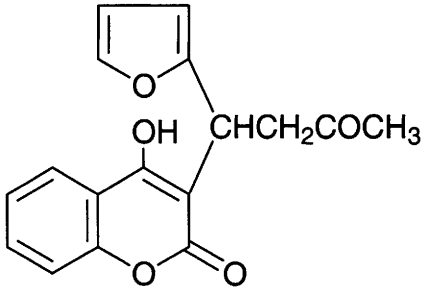
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (11).
Autoignition temperature 375°C

References

1. *Chemical Safety Sheets* 1991, 436, Kluwer Academic Publishers, Dodrecht, Netherlands.
2. Kremer, D. R. et al *Arch. Microbiol.* 1989, **151**(1), 34-39.
3. Meinck, F. et al *Les Eaux Residuaires Industrielles* 1970.
4. *Toxicol. Appl. Pharmacol.* 1977, **42**, 417.
5. *National Technical Information Service* AD277-689, Springfield, VA, USA.
6. Shlin, K. et al *Am. J. Physiol.* 1990, (5, Part 1), C834-C841.
7. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 51, Prague, Czechoslovakia.
8. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
9. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
10. *Evaluation of Certain Food Additives and Contaminants: 35th Report of the Joint FAO/WHO Expert Committee of Food Additives* 1990, WHO Tech. Rep. Ser. 789, Geneva, Switzerland.
11. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F116 fumarin



$C_{17}H_{14}O_5$ **Mol. Wt.** 298.30 **CAS Registry No.** 117-52-2

Synonyms 3-(α-acetonylfurfuryl)-4-hydroxycoumarin; 3-(1-furyl-3-acetylethyl)-4-hydroxycoumarin; Coumafuryl; Krumkil; Ratofin; Rat-a-Way

EINECS No. 204-195-5 **RTECS No.** GN 4850000

Uses Superseded rodenticide.

Physical properties

M. Pt. 124°C
Solubility Organic solvents: ethanol

Occupational exposure

Supply classification toxic
Risk phrases Toxic if swallowed – Toxic: danger of serious damage to health by prolonged exposure if swallowed (R25, R48/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S37, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 15, 25 mg kg^{-1}, respectively (1).

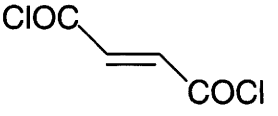
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *Farm Chemicals Handbook* 1980, D146, Meister, Willoughby, OH, USA.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F117 fumaryl chloride



$C_4H_2Cl_2O_2$ **Mol. Wt.** 152.96 **CAS Registry No.** 627-63-4
Synonyms fumaric acid, dichloride
EINECS No. 211-005-4 **RTECS No.** LT 2800000
Uses Chemical intermediate.

Physical properties

B. Pt. 161-164°C **Flash point** 73°C **Specific gravity** 1.408 at 20°C with respect to water at 4°C
Solubility Water: miscible

Occupational exposure

UN No. 1780 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 810 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 500 ppm (1).
LD_{50} dermal rabbit 1410 mg kg^{-1} (1).

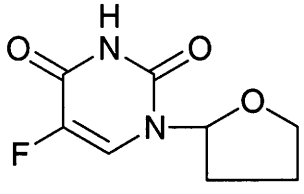
Irritancy

Dermal rabbit (24 hr) 500 mg caused severe irritation and 5 mg instilled into rabbit eye caused severe irritation (2).

References

1. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
2. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 53, Prague, Czechoslovakia

F118 furafluor



$C_8H_9FN_2O_3$ **Mol. Wt.** 200.17 **CAS Registry No.** 17902-23-7

Synonyms 5-fluoro-1-(tetrahydro-2-furanyl)-2,4(1*H*,3*H*)-pyrimidinedione; 5-fluoro-1-(tetrahydro-2-furyl)uracil; *N*′-(2′-furanidyl)-5-fluorouracil; Tegafur; FT207

EINECS No. 241-846-2 **RTECS No.** YR 0450000

Uses Antineoplastic agent used particularly for cancers of gastro-intestinal tract and breast by oral or intravenous route (1).

Physical properties

M. Pt. 164-165°C
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1000 mg kg^{-1} (2).
LD_{50} oral mouse 775 mg kg^{-1} (3).
LD_{50} oral dog 34 mg kg^{-1} (4).
LD_{50} intraperitoneal rat 740 mg kg^{-1} (2).

Teratogenicity and reproductive effects

The active metabolite 5-fluorouracil causes a variety of teratogenic and reproductive effects (5).

Metabolism and toxicokinetics

Compound is absorbed from rat intestinal tract at a rate independent of luminal concentration. Absorption is influenced by its lipophilicity (6,7).
The compound is a pro-drug and is converted, in part by blood enzymes, into 5-fluorouracil (1,8).

When administered to rats with cancer of the lung, the intravenous route results in lower blood, liver and tissue concentrations than the oral route, but blood levels of 5-fluorouracil are maintained at higher levels by the intravenous route (9).
Compound can cross the blood-brain barrier and can be detected in CSF (1).
In humans, when administered intravenously, $t_{1/2}$ 6-16 hr (1).
Animal studies have shown some reduction in cardio- and neurotoxicity of the compound when uracil is given to animals at the same time. A metabolic or biochemical interaction has been suggested (1).

Genotoxicity

Mice receiving up to 1100 mg kg^{-1} orally and sacrificed after 24 hr showed no significant mutagenicity in bone marrow cells (10).

Other effects

Other adverse effects (human)
Adverse effects are similar to those of 5-fluorouracil and are those commonly seen with antineoplastic and immunosuppressant agents. Neurotoxicity is greater than with 5-fluorouracil, but bone marrow damage is less. Gastro-intestinal damage is similar (1).

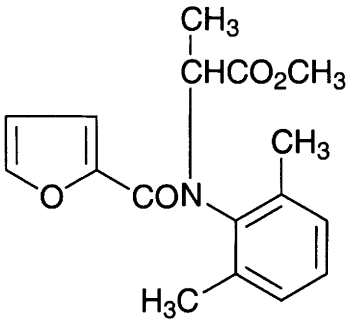
Other comments

Pharmacokinetics and metabolism in humans reviewed (11).
The efficacy and toxicity have been assessed (12).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
2. *Drugs in Japan: Ethical Drugs* 1982, **6**, 472.
3. *Yaoxue Tongbao* 1987, **22**, 27.
4. *Oyo Yakuri* 1980, **20**, 1009.
5. Shah, R. M. et al *J. Embryol. Exp. Morphol.* 1978, **43**, 47-54.
6. Sasaki, H. et al *Chem. Pharm. Bull.* 1986, **34**(10), 4265-4272.
7. Novodney, L. et al *Cancer Chemother. Pharmacol.* 1989, **24**(4), 238-242.
8. Jaeger, W. et al *Sci. Pharm.* 1991, **59**(2), 101-106.
9. Kimoto, M. et al *Gan to Kagaku Ryoho* 1987, **14**(1), 135-139 (Japan.) (*Chem. Abstr.* **106**, 168457k).
10. Lu, D. *Shenyang Yaoxueyuan Xuebao* 1988, **5**(1), 58 (Ch.) (*Chem. Abstr.* **108**, 215922m).
11. Au, J. L. *Cancer Treat. Rep.* 1979, **63**, 343.
12. Smart, C. R. et al *Cancer (Philadelphia)* 1979, **44**, 48

F119 furalaxyl



$C_{17}H_{19}NO_4$ **Mol. Wt.** 301.34 **CAS Registry No.** 57646-30-7

Synonyms methyl *N*-(2-furoyl)-*N*-(2,6-xylyl)-D,L-alaninate; methyl *N*-(2,6-dimethylphenyl)-*N*-(2-furanylcarbonyl)-DL-alaninate; methyl *N*-(2,6-dimethylphenyl)-*N*-(2-furoyl)-DL-alaninate; Fonganil; Fongarid

EINECS No. 260-875-1 **RTECS No.** AY 6320000

Uses Fungicide.

Physical properties

M. Pt. 70 and 84°C (dimorphic) **Specific gravity** 1.223 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.7 **Volatility** v.p. 5.3×10^{-7} mmHg at 20°C
Solubility Water: 230 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, dichloromethane, hexane, methanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R52/53)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing, gloves and eye/face protection – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S36/37/39, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, crucian carp 32-38 mg l^{-1} (1).

Environmental fate

Abiotic removal
Estimated $t_{1/2}$ for hydrolysis at 20°C >200 days at pH 1, >200 days at pH 9, 22 days at pH 10 (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 940 mg kg^{-1} (1).
LD_{50} dermal rabbit 5500 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral rat and dog (90 days) no-adverse-effect level for dogs 50 mg kg^{-1} and for rats 1250 mg kg^{-1} diet (1).

Sensitisation
Did not cause skin sensitisation to guinea pigs (1).

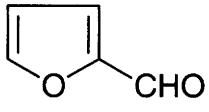
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class III (5).
EPA Toxicity Class III (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F120 2-furaldehyde



$C_5H_4O_2$ **Mol. Wt.** 96.09 **CAS Registry No.** 98-01-1

Synonyms furfural; 2-furancarboxaldehyde; 2-furancarbonal; artificial ant oil; furole; pyromucic aldehyde

EINECS No. 202-627-7 **RTECS No.** LT 7000000

Uses In the manufacture of plastics and varnishes. In solvent refining of petroleum oils. As solvent for nitrocellulose, cellulose acetate, gums, shoe dyes and nitrated cotton. Insecticide. Fungicide. Germicide. Analytical reagent. Flavouring.
Occurrence Some essential oils.

Physical properties

M. Pt. -38°C **B. Pt.** 161.8°C **Flash point** 60°C (closed cup), 68°C (open cup) **Specific gravity** 1.1563 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.81 (1) **Volatility** v.p. 1.0 mmHg at 20°C ; v.den. 3.31
Solubility Water: 83,000 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VLE 2 ppm (8 mg m^{-3})
JP-OEL 2.5 ppm (9.8 mg m^{-3})
SE-LEVL 2 ppm (8 mg m^{-3}) **SE-STEL** 5 ppm (20 mg m^{-3})
UK-LTEL 2 ppm (8 mg m^{-3}) **UK-STEL** 10 ppm (40 mg m^{-3})
US-TWA 2 ppm (7.9 mg m^{-3})

UN No. 1199 **HAZCHEM Code** 2W **Conveyance classification** flammable liquid
Supply classification toxic

Risk phrases Harmful in contact with skin – Toxic by inhalation and if swallowed – Irritating to eyes and respiratory system – Possible risk of irreversible effects (R21, R23/25, R36/37, R40)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36/37/39, S45)

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy 11 mg l^{-1} (1).
LC_{50} (96 hr) fathead minnow 32 mg l^{-1} (2).

Invertebrate toxicity
LOEC cell multiplication inhibition test *Microcystis aeruginosa* and *Entosiphon sulcatum* 0.6-2.7 mg l^{-1} (3,4).

Environmental fate

Nitrification inhibition
Incubated with soil for 10 days with 5-10% and 15-20% of ammonium sulfate caused 10- and 20-fold decrease in nitrification, respectively (5).

Carbonaceous inhibition
EC_{50} activated sludge microorganisms 760 mg l^{-1} (exposure unspecified) (6).

Anaerobic effects
IC_{50} methanogenic bacteria 180 mg l^{-1} anaerobic toxicity assay (7).

Degradation studies
Initial concentrations of 0.5, 5, 50 and 500 mg l^{-1} were degraded by nitrate-reducing microbes isolated from a mixture of soil and sewage. >97% degradation occurred in 0.25, 1.5, 4 and 32 days, respectively. For the same initial concentrations, methanogenic microbes, isolated from anaerobic digester sludge, 97% was metabolised in 2, 4, 48 and 144 hr, respectively. Both sets of microbes reduced levels to <20 ppb (8).
BOD_5 0.77 mg $l^{-1}O_2$ using standard dilution technique with sewage at 2-20 mg l^{-1} (9).
ThOD 1.66 (9).
As sole carbon source, with adapted bench scale activated sludge, fill and draw operations at 20°C, 96% COD removal at 37.0 mg COD g^{-1} dry inoculum hr^{-1} (10).
Waste water treatment using the method of river water oxidation at 20°C removed 100% after 2 days observation and natural acclimation in surface water. Initial concentration 1 mg l^{-1} (11).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 98 mg kg^{-1} (12).
LD_{50} oral rat 65-127 mg kg^{-1} (13-14).
LD_{50} oral mouse, dog 400, 950 mg kg^{-1}, respectively (15,16).
LC_{Lo} (6 hr) inhalation mouse, dog 370 ppm (16).
LC_{Lo} (4 hr) inhalation rat 150 ppm (17).
LD_{Lo} dermal rabbit 620 mg kg^{-1} (18).
LD_{50} intravenous mouse 150 mg kg^{-1} (18).

Carcinogenicity and chronic effects
Gavage F344/N rats 0, 30 or 60 mg kg^{-1} day^{-1} 5 day wk^{-1} for 103 wk. B6C3F1 mice were similarly given 0, 50, 100 or 175 mg kg^{-1} day^{-1}. Some evidence of carcinogenicity in ♂ rats. No evidence in ♀ rats. Increased incidence of hepatocellular adenomas and carcinomas were seen in ♂ mice. There was some evidence (hepatocellular carcinomas) of carcinogenicity in ♀ mice. Squamous cell papillomas of the forestomach in ♀ mice and all renal cortical carcinomas or adenomas in ♂ mice may have been related to exposure (19).

Metabolism and toxicokinetics

Goats fed 0.65% diet showed maximum level of 25 ppm in the ruminal fluid at 60 min (20).

Oral Sprague-Dawley rats single dose 50 mg kg^{-1}. The major urinary metabolite was 2-furoylglycine, followed by unconjugated 2-furoic acid, *trans*-2-furanacryloglycine, and *trans*-2-furanacryl acid (21).

Irritancy

50 mg instilled into rabbit eye caused well-defined erythema and slight oedema (duration unspecified) (16).

Dermal rabbit (24 hr) 500 mg caused moderate irritation, 20 mg instilled into rabbit eye for 24 hr caused mild irritation (17).

Genotoxicity

In vitro Chinese hamster V79 cells induced chromosomal aberrations and a significant lowering of mitotic activity (22).

In vitro mouse lymphoma L5178Y tk^+/tk^- without metabolic activation positive (23).

Other effects

Other adverse effects (human)

Epidemiological studies found no health effects to children (24).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (25).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (26).

Other comments

Experimental toxicology, epidemiology, human health effects, workplace experience and physico-chemical properties reviewed (27-29).

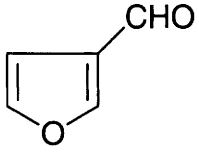
Autoignition temperature 392°C.

References

1. Deneer, J. W. et al *Aquat. Toxicol.* 1988, **12**, 185-192.
2. Vincent, R. M. et al *Acute Toxicity of Selected Organic Compounds to Fathead Minnows* 1976, EPA-600/3-76-097, EPA, Washington, DC, USA.
3. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
4. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9).
5. Khasanov, B. et al *Uzb. Biol. Zh.* 1987, (3), 7172 (Russ.) (*Chem. Abstr.* **107**, 76835z).
6. Volskay, V. T. et al *Water Res.* 1990, **24**(7), 863-874.
7. Blum, D. J. W. et al *Res. J. Water Pollut. Control Fed.* 1991, **63**(3), 198-207.
8. Knight, E. V. et al *Environ. Toxicol. Chem.* 1990, **9**(6), 725-730.
9. Lund, H. F. *Industrial Pollution Control Handbook* 1971, McGraw-Hill, New York, NY, USA.
10. Pitter, P. *Water Res.* 1976, **10**, 231-235.
11. Ludzack, I. J. et al *J. Water Pollut. Control Fed.* 1960, **32**, 1173.
12. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
13. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1964, **2**, 327.
14. *Bromatol. Chem. Toksykol. Zna* 1980, **13**, 371.
15. *Biochem. J.* 1940, **34**, 1196.
16. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
17. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
18. *Food Cosmet. Toxicol.* 1978, **16**, 759.
19. *National Toxicology Program Report* 1990, NTP-TR-382, NIH/PUB-90-2837, Research Triangle Park, NC, USA.
20. Kyuma, T. et al *Chikusan Shikenjo Kenkyu Hokoku* 1991, (51), 51-57 (Japan.) (*Chem. Abstr.* **115**, 278360s).
21. Laham, S. et al *Toxicol. Environ. Chem.* 1989, **24**(1-2), 35-47.
22. Nishi, Y. et al *Mutat. Res.* 1989, **227(2)**, 117-123.

23. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **11**(1), 91-118.
24. Hrasovec, B. et al *Wiss. Umwelt* 1987, (4), 206-209 (Ger.) (*Chem. Abstr.* **108**, 155716k).
25. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
26. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
27. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(3), 96-102.
28. *BIBRA Toxicity Profiles* 1991, British Industrial Biological Research Association, Carlshalton, UK.
29. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F121 3-furaldehyde



$C_5H_4O_2$ **Mol. Wt.** 96.09 **CAS Registry No.** 498-60-2

Synonyms 3-furfural; 3-furancarboxaldehyde

Uses Chemical intermediate.

Occurrence Product of decay of woods such as *Eucryphia cordifolia* by white and brown rot fungi (1). A pyrolysis product of humic and fulvic acids from soil (2).

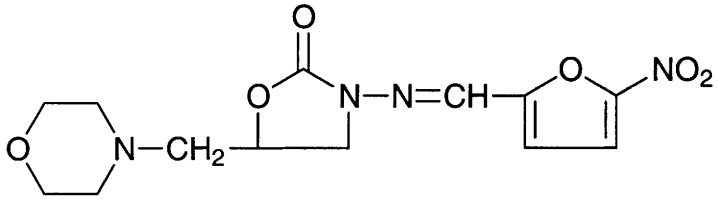
Physical properties

B. Pt. 144°C at 732 mmHg **Flash point** 48°C **Specific gravity** 1.111 at 20°C

References

1. Mulder, M. et al *J. Anal. Appl. Pyrolysis* 1991, **19**, 75-91.
2. Alcaniz, J. *Sci. Total Environ.* 1989, 81-82

F122 furaltadone



$C_{13}H_{16}N_4O_6$ **Mol. Wt.** 324.29 **CAS Registry No.** 139-91-3

Synonyms 5-(morpholinomethyl)-3-[(5-nitrofurfurylidene)amino]-2-oxazolidinone; Altabactina; Furzoline; Furmethanol; Ibifur; Sepsinol

EINECS No. 205-384-5 **RTECS No.** RQ 3620000

Uses Antibacterial agent.

Physical properties

B. Pt. 206°C (decomp.)
Solubility Water: 750 mg l^{-1} at 25°C

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 1000 mg kg^{-1} (1).
LD_{50} (route unspecified) mouse 525 mg kg^{-1} (2).

Metabolism and toxicokinetics
Oral rat 100 mg kg^{-1} body weight, plasma levels of 3.2 mg l^{-1} were observed after 4 hr. When given 138 mg kg^{-1} ~3.4% was recovered from urine within 48 hr (3).

Other effects

Any other adverse effects
In oral chicken at therapeutic levels, blebs of an electron dense substance developed in adrenal cortical mitochondria and aspartate transaminase activity was reduced (4).

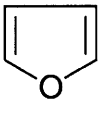
Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. *J. Pharm. Pharmacol.* 1964, **16**, 663.
2. Paul, M. F. et al *Exp. Chemother.* 1964, **2**(1), 307-370.
3. Paul, M. F. et al *Antibiot. Chemother.* 1960, **10**, 287-302.
4. Barltet, A. L. et al *J. Vet. Pharmacol. Ther.* 1990, **13**(2), 206-216.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

F123 furan



C_4H_4O **Mol. Wt.** 68.08 **CAS Registry No.** 110-00-9
Synonyms 1,4-epoxy-1,3-butadiene; divinylene oxide; furfuran; oxacyclopentadiene; oxole; tetrole
EINECS No. 203-727-3 **RTECS No.** LT 8524000
Uses Manufacture of polymers. Organic synthesis. Solvent. Herbicide.

Physical properties

M. Pt. -85.65°C **B. Pt.** 32°C at 758 mmHg **Flash point** -35°C (closed cup) **Specific gravity** 0.937 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.34 **Volatility** v.p. 602 mmHg at 25°C ; v.den. 2.35
Solubility Water: insoluble in water. Organic solvents: acetone, diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

UN No. 2389 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 61 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 103 ppm Microtox test (2).

Bioaccumulation

Estimated bioconcentration factor of 3-6 indicates that environmental accumulation is unlikely (3).

Environmental fate

Abiotic removal

Estimated $t_{1/2}$ for volatilisation from model river water 2.5 hr (3).

Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in the atmosphere 9.5 hr, and with ozone 4.7 days. During night-time, $t_{1/2}$ for reaction with nitrate radicals in the atmosphere 0.5 hr (4-6).

Estimated $t_{1/2}$ for reaction with singlet oxygen in water 1 hr (7).

Adsorption and retention

Estimated K_{oc} for soils of 27-128 indicates that adsorption to soil and sediments would not be significant (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >100 mg kg^{-1} (8).

LC_{50} (1 hr) inhalation mouse 120 mg m^{-3} (9).

LD_{50} intraperitoneal rat, mouse 5-7 mg kg^{-1} (9).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via gavage. Clear evidence of carcinogenicity (dose-related increased incidence in malignant neoplasms, combination of malignant and benign neoplasms, or benign neoplasms with an indication of the ability of such tumours to progress to malignancy) in rats and mice of both sexes (10).

National Toxicology Program classification: reasonably anticipated to be a human carcinogen (11).

Gavage rat (3 wk) 15-60 mg kg^{-1} day^{-1} 5 days wk^{-1}. High doses caused a rapid development of cholangiofibrosis characterised by the presence of bile ductular hyperplasia, intestinal metaplasia, and fibrosis. The lesion was almost exclusively localised to the caudate liver lobe. Other cellular changes in relation to the development of intrahepatic cholangiocarcinogenesis were also reported (12).

Metabolism and toxicokinetics

Absorbed through human skin (13).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (14).

Phage T7 inactivation test positive (15).

In vitro mouse lymphoma L5178Y tk^+/tk^- forward induction assay without metabolic activation positive (16).

Other effects

Any other adverse effects

Vapours are narcotic (17).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

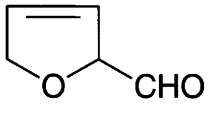
Other comments

Occurs in oil obtained by the distillation of pine wood containing rosin. Present in cigarette smoke, wood smoke and engine exhaust fumes (19).
Environmental fate and toxicology reviewed (19,20).
Preparations of furan are often stabilised with butylated hydroxytoluene to inhibit the formation of peroxides (21).

References

1. Devillers, J. et al *Chemosphere* 1988, **17**(8), 1531-1537.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
4. Atkinson, R. *Chem. Rev.* 1985, **85**, 69-201.
5. Atkinson, R. et al *Environ. Sci. Technol.* 1985, **19**, 87-89.
6. Atkinson, R. et al *Chem. Rev.* 1984, **84**, 437-470.
7. Mill, T. et al in *Environmental Exposure from Chemicals* 1985, **1**, 221, CRC Press, Boca Raton, FL, USA.
8. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
9. *Am. Ind. Hyg. Assoc. J.* 1979, **40**, 310.
10. *National Toxicology Program Research and Testing Division* 1992, Report No.TR-402, NIEHS, Research Triangle Park, NC, USA.
11. *Eighth Report on Carcinogens* 1998, National Toxicology Program, NIEHS, Research Triangle Park, NC 27709, USA.
12. Elmore, L. W. et al *Cancer Res.* 1991, **51**(20), 5752-5759.
13. Browning, E. *Toxicity of Industrial Materials* 2nd ed., 1969, 698, Appleton-Century-Crafts, New York, NY, USA.
14. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl.7), 1-119.
15. Ronto, G. et al *Mutagenesis* 1989, **4**(6), 471-475.
16. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **12**(1), 85-154.
17. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
18. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
19. Howard, P. H. (Ed.) *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 3rd ed., 1991, **2**, 267-272, Lewis Publishers, Chelsea, MI, USA.
20. *Dangerous Prop. Ind. Mater. Rep.)* 1987, **7**(3), 93-95.
21. Verschueren, K. *Handbook of Environmental Fate on Organic Chemicals* 2nd ed., 1983, 686, Van Nostrand Reinhold, New York, NY, USA

F124 2(5*H*)-furanone



$C_4H_4O_2$ **Mol. Wt.** 84.07 **CAS Registry No.** 497-23-4

Synonyms cratone; γ-crotolactone; α,β-crotolactone; γ-hydroxycrotonic acid lactone; 4-hydroxycrotonic acid γ-lactone; isocrotonolactone

EINECS No. 207-839-3 **RTECS No.** LU 3450000

Uses Appetite depressant. Organic synthesis. Fish growth promoter.

Physical properties

M. Pt. 4-5°C **B. Pt.** 86-87°C at 12 mmHg **Flash point** 101°C **Specific gravity** 1.185 at 20°C

Mammalian & avian toxicity

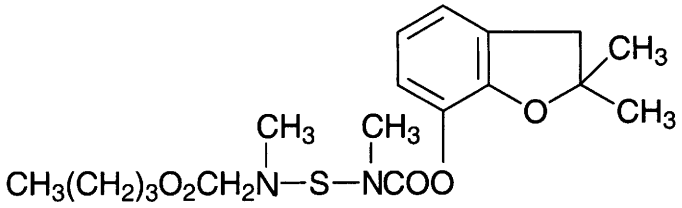
Teratogenicity and reproductive effects
Intraperitoneal rat (2 wk) 1400 mg kg^{-1} day^{-1} caused maternal toxicity. No foetoxic or teratogenic effects were reported (1).

Irritancy
Irritating to the skin. Vapour or mist irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (2).

References

1. *Acta Endocrinol.* 1990, **123**, 571.
2. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1753, Sigma-Aldrich, Milwaukee, WI, USA

F125 furathiocarb



$C_{18}H_{26}N_2O_5S$ **Mol. Wt.** 382.48 **CAS Registry No.** 65907-30-4

Synonyms butyl 2,3-dihydro-2,2-dimethylbenzofuran-7-yl *N*,*N*′-dimethyl-*N*,*N*′-thiocarbamate; 2,3-dihydro-2,2-dimethyl-7-benzofuranyl 2,4-dimethyl-5-oxo-6-oxa-3-thia-2,4-diazadecanoate; Deltanet; Promet

EINECS No. 265-974-3 **RTECS No.** DF 6652100

Uses Insecticide.

Physical properties

B. Pt. 160°C at 0.01 mmHg **Specific gravity** 1.16 at 20°C **Partition coefficient** log P_{ow} 4.6 at 25°C
Volatility v.p. 6.3×10^{-7} mmHg at 20°C
Solubility Water: 10 mg l^{-1} at 20°C. Organic solvents: acetone, hexane, isopropanol, methanol, toluene

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Toxic if swallowed – Very toxic by inhalation – Irritating to eyes and skin – May cause sensitisation by skin contact – Harmful: danger of serious damage to health by prolonged exposure if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R25, R26, R36/38, R43, R48/22, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S38, S45, S60, S61)

Ecotoxicity

Fish toxicity
LD_{50} (96 hr) carp, bluegill sunfish, rainbow trout 0.03-0.12 mg l^{-1} (1).

Environmental fate

Degradation studies

In soil rapidly decomposed to carbofuran by bacterial activity (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 53, 330 mg kg^{-1}, respectively (1,3).

LC_{50} (4 hr) inhalation rat 210 mg m^{-3} (1).

LD_{50} dermal rat >2000 mg kg^{-1} (1).

Other effects

Any other adverse effects

Cholinesterase inhibitor (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Partition coefficient exceeds European Union liit of 3.0.

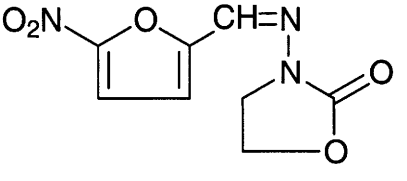
WHO Toxicity Class Ib (6).

EPA Toxicity Class II (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Rouchaud, J. et al *Toxicol. Environ. Chem.* 1990, **25**(2-3), 109-124.
3. *Farm Chemicals Handbook* 1991, C250, Meister Publishing, Willoughby, OH, USA.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

F126 furazolidone



$C_8H_7N_3O_5$ **Mol. Wt.** 225.16 **CAS Registry No.** 67-45-8

Synonyms 3-[[(5-nitro-2-furanyl)methylene]amino]-2-oxazolinone; 3-[(5-nitrofurfurylidene)amino]-2-oxazolidinone; nitrofurazolidone; nitrofurazolidonum; Furoxone

EINECS No. 200-653-3 **RTECS No.** RQ 3675000

Uses Topical anti-infective, topical antiprotozoal.

Physical properties

M. Pt. 254-256°C (decomp.)
Solubility Water: 40 mg l^{-1}

Ecotoxicity

Fish toxicity
Carp exposed to 0.1 mg $100g^{-1}$ day^{-1} underwent changes in physiochemical processes, including glycogen uptake, cholesterol levels, and lipid analysis (1).

Invertebrate toxicity
LC_{50} (24 hr) *Daphnia magna* 60 mg l^{-1} (2).
LC_{50} (24 hr) *Artemia salina* 250 mg l^{-1} (2).
LC_{50} (24 hr) *Culex pipiens* larvae 40 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2336 mg kg^{-1} (3).
LD_{50} oral mouse 1782 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 300 mg kg^{-1} (5).
LD_{Lo} oral chicken 150 mg kg^{-1} (6).
Human minimum lethal dose 11 mg kg^{-1}, effects on the blood and pulmonary system (7).

Sub-acute and sub-chronic data
♂ Ducklings 700 mg furazolidone kg^{-1} feed for 27 days. Clinical alterations of decreased feed consumption with lower weight gain and nervous signs were observed. Gross pathological changes were observed after day-8 and included cardiomegaly, pericardial effusion, pulmonary oedema and congestion, ascites and testicular enlargement (8).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (9).

Teratogenicity and reproductive effects
Oral mice 1.0 g kg^{-1} on days 7 and 10 of gestation interrupted pregnancy in 5/5 and 9/10 mice, respectively, but only 2/6 animals when dosed on day 10 (10).

Metabolism and toxicokinetics
In humans most of a dose of furazolidone passes through the gut without being absorbed but is extensively metabolised in the intestine (11).
Oral rat 100 mg kg^{-1} (single dose), only 3% of the dose was recovered in faeces as unmetabolised compound (12).
The urinary and faecal excretion of furazolidone in rats was studied by means of mutagenicity assays. <0.1% of a single dose of 1-10 mg per 100g administered by gavage to rats was recovered in urine and quickly disappeared. After prolonged (1 wk) treatments urine contained some mutagenic activity until the 5th-7th days. Faecal excretion of mutagenicity amounted to <0.1% of the administered dose and had disappeared by day-3 (13).

Irritancy
Allergic contact eczema has been reported in subjects handling animal feed containing furazolidone (14).

Sensitisation
In humans receiving furazolidone allergic reactions may occur. These are most commonly skin reactions such as rashes or angio-edema. Acute pulmonary reactions have been reported. Agranulocytosis has been reported rarely. Haemolytic anaemia may occur in patients with a deficiency of glucose-6-phosphate dehydrogenase (11).

Genotoxicity

Escherichia coli phage inhibition capacity 2 mg l^{-1} (15).
Salmonella typhimurium TA100 with and without activation strongly positive (16).

Salmonella typhimurium TA98 with and without activation strongly positive, but greatly decreased in strain TA98/1,8-DNP6 (17).
Human lymphocyte cytogenetic analysis system (72 hr) positive at 2 mg l^{-1} (18).
Induced unscheduled DNA synthesis in primary cultures of adult rat hepatocytes (19).
Predicted to be a teratogen by the *in vitro* micromass teratogen test (14).
Drosophila melanogaster, sex-linked recessive lethal mutations induced (20).

Other effects

Other adverse effects (human)

In human patients the most common adverse effects of treatment with furazolidone include nausea and vomiting. Dizziness, drowsiness, headache and a general malaise have also been reported (11).

Any other adverse effects

Dietary furazolidone at concentrations as low as 300 ppm was associated in turkey poults with death, cardiac dilation, and ascites (21).
5 μg ml^{-1} caused a marked decrease in cell viability and proliferation in three cell lines: human larynx carcinoma HEp-2, human colon adenocarcinoma CaCo-2, Chinese hamster lung V97 (22).

Legislation

In the USA, zero tolerance is established for furazolidone residues in uncooked edible tissues of swine (23).

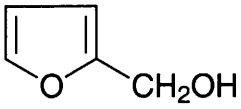
Other comments

Furazolidone is a monoamine oxidase inhibitor.
Incompatible with strong oxidising agents and strong bases.
FAO/WHO have not set a maximum daily intake because of evidence of genotoxicity and carcinogenicity *in vitro* and in animals and lack of information on the nature of metabolism (24).

References

1. Kobayashi, K. et al *Nippon Suisan Gakkaishi* 1987, **53**, 487.
2. Macri, A. et al *Ecotoxicol. Environ. Saf.* 1988, **16**, 90-94.
3. Goldenthal, E. I. et al *Toxicol. Appl. Pharmacol.* 1971, **18**, 185-207.
4. *Trans. R. Soc. Trop. Med. Hyg.* 1980, **74**, 43.
5. *Prog. Med. Chem.* 1967, **5**, 320.
6. MacDougal, J. R. *Compilation of LD_{50} Values of New Drugs*, Department of National Health and Welfare, Food and Drug Divisions, 35 John St., Ottawa, Ontario, Canada.
7. *Am. Rev. Respir. Dis.* 1972, **105**, 823.
8. Webb, D. M. et al *Am. J. Vet. Res.* 1991, **52**(9), 1531-1536.
9. *IARC Monograph* 1987, **Suppl. 7**, 63.
10. Jackson, D. et al *J. Endocrinol.* 1957, **15**, 355-359.
11. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
12. Paul, M. F. *Antibiot. Chemother.* 1960, **10**, 287-302.
13. Crebelli, R. et al *Ecotoxicol. Environ. Saf.* 1982, **6**(5), 448-456.
14. Uphill, P. F. et al *Toxicol. in Vitro* 1990, **4**(4-5), 623-626.
15. *Mutat. Res.* 1985, **156**, 156.
16. Tatsumi, K. et al *J. Pharmacobio-Dyn.* 1978, **1**(4), 256-261.
17. Ni, Y. et al *Mutat. Res.* 1987, **192**(1), 15-22.
18. *Mutat. Res.* 1979, **59**, 139.
19. Probst, G. S. et al *Environ. Mutagen.* 1981, **3**(1), 11-32.
20. Kramers, P. G. N. *Mutat. Res.* 1982, **101**(3), 209-236.
21. Jankus, E. F. et al *Avian Dis.* 1972, **16**(4), 958-964.
22. De Angelis, I. et al *Food Chem. Toxicol.* 1994, **32**(5), 481-488.
23. *US FDA. US Code Fed. Regul., Title21* 1980, part 556.290.
24. *FAO/WHO, Evaluation of Certain Veterinary Drug Residues in Food: Fortieth Report of the Joint FAO/WHO Expert Committee on Food Additives* WHO Technical Report Series 839, 1993

F127 furfuryl alcohol



$C_5H_6O_2$ **Mol. Wt.** 98.10 **CAS Registry No.** 98-00-0

Synonyms 2-furanemethanol; furyl alcohol; 2-furylcarbinol; 2-hydroxymethylfuran; FA; QO Fa-Rok

EINECS No. 202-626-1 **RTECS No.** LU 9100000

Uses Organic synthesis. Manufacture of polymers. Solvent. Flavouring agent.
Occurrence Aroma component of plants, dairy products, cooked meat and fish.

Physical properties

M. Pt. -29°C **B. Pt.** 170°C **Flash point** 65°C **Specific gravity** 1.129 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.28 (1) **Volatility** v.p. 1 mmHg at 32°C ; v.den. 3.37
Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 10 ppm (41 mg m^{-3})
FR-VME 10 ppm (40 mg m^{-3})
JP-OEL 5 ppm (20 mg m^{-3})
SE-LEVL 5 ppm (20 mg m^{-3}) **SE-STEL** 10 ppm (40 mg m^{-3})
UK-LTEL 5 ppm (20 mg m^{-3}) **UK-STEL** 15 ppm (61 mg m^{-3})
US-TWA 10 ppm (40 mg m^{-3}) **US-STEL** 15 ppm (60 mg m^{-3})

UN No. 2874 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful by inhalation, in contact with skin and if swallowed (R20/21/22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
No fatalities or observable adverse effects to stickleback, rainbow trout or sockeye salmon at 10 mg l^{-1} for 24 hr (2).

Invertebrate toxicity
Toxicity threshold (cell multiplication test) *Pseudomonas putida* 180 mg l^{-1}, *Scenedesmus quadricauda* 25 mg l^{-1}, *Entosiphon sulcatum* 227 mg l^{-1} (3).

Bioaccumulation
Calculated bioconcentration factor 0.96 indicated that environmental accumulation was unlikely (4).

Environmental fate

Degradation studies
BOD_5 0.532 mg l^{-1} O_2, BOD_{20} 1.314 mg l^{-1} O_2 (5).

Abiotic removal
Estimated $t_{1/2}$ for reaction with hydroxyl radicals in the atmosphere 3.7 hr (6).
$t_{1/2}$ for reaction with photochemically produced singlet oxygen 40 hr (7).

Adsorption and retention
Calculated K_{oc} 34 indicates that furfuryl alcohol will not undergo significant adsorption to soil or sediments (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 88, 275 mg kg^{-1}, respectively (8-10).
LC_{50} (4 hr) inhalation rat 233 ppm (10).
LD_{50} dermal rabbit 400 mg kg^{-1} (11).
LD_{50} intraperitoneal rat 650 mg kg^{-1} (12).
LD_{50} intravenous rabbit 650 mg kg^{-1} (13).

Sub-acute and sub-chronic data

Inhalation F344 rats and B6C3F1 mice (0, 16, 31, 63, 125, 250 ppm) 6 hr day^{-1}, 5 days wk^{-1} for 14 days or for 13 wk (0, 2, 4, 8, 16, 32 ppm). Rats and mice exposed to 125 ppm and ♀mice exposed to 63 ppm for 14 days exhibited lower final mean body weights than controls but there were no significant differences in mean body weights among exposed and control groups in the 13-wk studies. Reduced survival of both mice and rats was observed in the 14-day studies. No toxicologically significant effects on organ weights in rats or mice nor adverse changes in haematological or serum chemistry parameters in rats were seen in the 13-wk studies. In 14-day and 13-wk studies of both mice and rats microscopic lesions of the nose associated with exposure to furfuryl alcohol were seen (14).

Irritancy

100 mg instilled into rabbit eye for 24 hr caused moderate irritation (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (15).
Drosophila melanogaster sex-linked recessive lethal assay and sex-chromosome loss assay negative (16).
In vitro human lymphocytes, sister chromatid exchanges negative (17).
In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations positive (18).
Furfuryl alcohol did not increase the spontaneous frequency of sister chromatid exchanges per metaphase in exposed workers (17).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (19).

Other comments

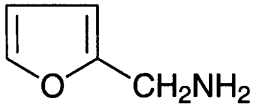
Physical properties, toxicity and environmental impact reviewed (20,21).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (22).
Autoignition temperature 491°C.

References

1. Hansch, C. et al *Medchem Project Issue No.26* 1985, Pomona College, Claremont, CA, USA.
2. McPhee, C. et al *Lethal Effects of 2014 Chemicals to Fish* 1989, EPA 560/6-89-001, PB 89-156-715, Washington, DC, USA.
3. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
4. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
5. Meinck, F. et al *Les Eaux Residuaires Industrielle* 1970.
6. Atkinson, R. *Environ. Toxicol. Chem.* 1988, **7**, 435-442.
7. Scully, F. E. *Chemosphere* 1987, **16**, 681-694.
8. Marhold, J. V. *Sbornik Vysledku Toxixologikeho Vysetreni Latek A Pripravku* 1972, 139, Prague, Czechoslovakia.
9. *Biochem. J.* 1940, **34**, 1196.
10. *Am. Ind. Hyg. Assoc. J.* 1958, **19**, 91.
11. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, 280, Academic Press, New York, NY, USA.
12. *Raw Materials Data Handbook* 1974, **1**, 64.
13. *Fed. Proc.* 1949, **8**, 294.
14. Irwin, R. D. et al *J. Appl. Toxicol.* 1997, **17**(3), 159-169.
15. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 4), 1-119.

16. Rodriguez-Arnaiz, R. et al *Mutat. Res.* 1989, **223**(3), 309-311.
17. Gomez-Arroyo, S. et al *Mutat. Res.* 1985, **156**(3), 233-238.
18. Stich, H. F. et al *Cancer Lett. (Shannon, Irel.)* 1981, **13**(2), 89-95.
19. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
20. *Dangerous Prop. Ind. Mater. Rep.* 1987, 7(6), 56-60.
21. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1993, **4**, 319-325, Lewis Publishers, Chelsea, MI, USA.
22. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F128 furfurylamine



C_5H_7NO **Mol. Wt.** 97.12 **CAS Registry No.** 617-89-0

Synonyms 2-furanmethanamine; 2-furfurylamine

EINECS No. 210-536-9 **RTECS No.** LU 9275000

Uses Organic synthesis.

Physical properties

M. Pt. -70°C **B. Pt.** 145-146°C **Flash point** 37°C (open cup) **Specific gravity** 1.099 at 20°C
Volatility v.den. 3.35
Solubility Water: miscible. Organic solvents: chloroform, diethyl ether

Occupational exposure

UN No. 2526 **HAZCHEM Code** 2W **Conveyance classification** flammable liquid, corrosive

Ecotoxicity

Fish toxicity
No fatality or observable adverse effects to stickleback, rainbow trout or sockeye salmon at 10 mg l^{-1} for 24 hr (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >96 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (3).

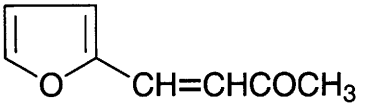
Metabolism and toxicokinetics
May be absorbed through the skin (species unspecified) (4).

Irritancy
Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (4).

References

1. McPhee, C. et al *Lethal Effects of 2014 Chemicals to Fish* 1989, EPA 560/6-89-001, PB89-156-715, Washington, DC, USA.
2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
3. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
4. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1754, Sigma-Aldrich, Milwaukee, MI, USA

F129 2-furfurylidene acetone



$C_8H_8O_2$ **Mol. Wt.** 136.15 **CAS Registry No.** 623-15-4

Synonyms furfural acetone; 4-(2-furanyl)-3-buten-2-one; furfurylideneacetone; monofurfurylideneacetone

EINECS No. 210-774-3 **RTECS No.** EM 9939000

Uses Organic synthesis.

Physical properties

M. Pt. 39-40°C **B. Pt.** 135-137°C at 33 mmHg **Specific gravity** 1.0496 at 57°C with respect to water at 4°C

Solubility Organic solvents: chloroform, diethyl ether, dimethyl sulfoxide, ethanol, petroleum ether

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (1).

Other effects

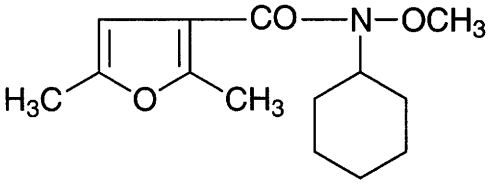
Any other adverse effects

Gavage rat, 0.67 of LD_{50} caused an increase in liver microsomal cytochrome P_{450} content (2).

References

1. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
2. Tarasov, V. V. et al *Gig. Sanit.* 1957, (4), 80-82 (Russ.) (*Chem. Abstr.* **107**, 2152c)

F130 furmecyclox



$C_{14}H_{21}NO_3$ **Mol. Wt.** 251.33 **CAS Registry No.** 60568-05-0

Synonyms *N*-cyclohexyl-*N*-methoxy-2,5-dimethyl-3-furancarboxamide; Campogran; Furmetamide

EINECS No. 262-302-0 **RTECS No.** LT 9970000

Uses Superseded fungicide (1).

Physical properties

M. Pt. 33°C **Volatility** v.p. 6.3×10^{-5} mmHg at 20°C

Solubility Water: 1.3 mg l^{-1} at 20°C. Organic solvents: acetone, chloroform, ethanol

Occupational exposure

Supply classification harmful
Risk phrases Possible risk of irreversible effects (R40)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3780 mg kg^{-1} (2).
LD_{50} dermal rat >5000 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Oral rat, mouse (2 yr) 0, 500, 2000 or 10,000 mg kg^{-1} diet. No increase in mortality occurred in treated animals. A significant dose-dependant increase in the incidence of liver tumours was observed in ♀ rats and urothelial tumours of the bladder in ♂ rats. No oncogenic effects were observed in mice (3,4).

Genotoxicity

Salmonella typhimurium mutagenicity assay with and without metabolic activation negative (strain not specified) (5).
In vitro marmoset hepatocytes, unscheduled DNA synthesis negative (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

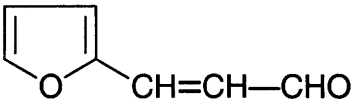
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 2nd ed., 1987, The Royal Society of Chemistry, London, UK.
3. BASF Wyandotte Corp. 1984, MRID No. 00142519, US EPA, Washington, DC, USA.
4. BASF Wyandotte Corp. 1984, MRID No. 00137839, US EPA, Washington, DC, USA.
5. BASF Wyandotte Corp. 1978, Accession No. 254304, US EPA, Washington, DC, USA.
6. BASF Wyandotte Corp. 1984, MRID No. 00142518, US EPA, Washington, DC, USA.
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
9. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

F131 β-furylacrolein



$C_7H_6O_2$ **Mol. Wt.** 122.12 **CAS Registry No.** 623-30-3

Synonyms 2-furanacrolein; 3-(2-furanyl)-2-propenal; β-(2-furyl)acrolein; 3-(2-furyl)acrolein; 3-(α-furyl)propenal

EINECS No. 210-785-3 **RTECS No.** LT 8528500

Uses Organic synthesis.

Physical properties

M. Pt. 48-50°C **B. Pt.** 58°C at 0.1 mmHg (Z-form) **Flash point** 99°C

Solubility Water: <1 g l^{-1} at 20°C. Organic solvents: dimethyl sulfoxide, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >860 mg kg^{-1} (1).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (2).

Other effects

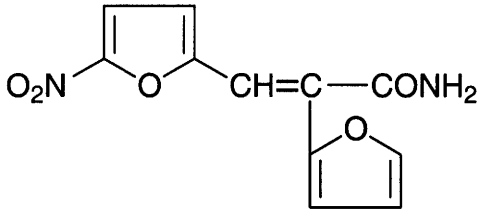
Other adverse effects (human)

Extremely destructive to tissue of the mucous membranes and upper respiratory tract. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (3).

References

1. Burdock, H. *Acute Toxicity Data* 1990, **1**, 94.
2. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
3. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1757, Sigma-Aldrich, Milwaukee, WI, USA

F132 furylamide



$C_{11}H_8N_2O_5$ **Mol. Wt.** 248.19 **CAS Registry No.** 3688-53-7

Synonyms α-2-furyl-5-nitro-2-furanacrylamide; α-[(5-nitro-2-furanyl)methylene]-2-furanacetamide; AF-2; 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide; furylfuramide; Tofuron

RTECS No. AS 3500000

Uses Formerly used as a food preservative. Preparation of pharmaceuticals.

Physical properties

M. Pt. 151-152°C

Solubility Water: <1 g l^{-1} at 18°C. Organic solvents: dimethylformamide, ethanol, methanol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 340, 1550 mg kg^{-1}, respectively (1,2).

Sub-acute and sub-chronic data

Oral mouse (60 day) 0.8 or 1.6% diet caused lymphoid atrophy and hepatic swelling. The high dose caused 100% fatality within 5 wk (3).

Oral rat 0.1-0.2% diet reduced the hepatic cytochrome P_{450} content and decreased *N*-demethylase and aniline hydroxylase activities after only 1 day of administration (4).

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, sufficient evidence of carcinogenicity to animals, IARC Classification group 2B (5).

Oral mouse (440 day) 0.08 or 0.4% diet produced glomerulonephrotic lesions in some mice (3).

Oral rat, mouse (2 yr) 0, 800 or 4000 mg kg^{-1} diet for 18 month followed by a control diet for 6 month. In mice dose-related increase in the incidence of benign forestomach neoplasms and malignant forestomach tumours was reported. Increases in the incidence of tumours of the oral cavity and metastases to liver lymph nodes, spleen and peritoneal cavity were also reported. In rats a dose-related increase in benign and malignant mammary tumours (mostly adenocarcinomas) and forestomach papillomas was reported. A non-significant increase in the incidence of haemangioendothelial sarcomas of the liver in the high-dose group was also observed (6,7).

Oral hamster (660 day) 0, 800 or 1600 mg kg^{-1} diet. A dose-related increase in the incidence of benign and malignant forestomach tumours in both sexes and squamous-cell carcinomas of the forestomach of ♂ animals was reported. An increase in the incidence of oesophageal tumours in high-dose ♂ hamsters was also reported (8).

Subcutaneous mouse (27 wk) 0 or 50 mg kg^{-1} on days 21, 22 and 23 after birth induced a statistically significant increase in the incidence of lung adenomas (9).

Pregnant mice (33 wk) were given subcutaneous injections of 0 or 50 mg kg^{-1} on days 13, 15 and 17 of gestation. A statistically significant increased incidence of lung adenomas was observed in the offspring killed at wk-32 after birth (10).

Teratogenicity and reproductive effects

Subcutaneous mouse 50 mg kg^{-1} day^{-1} on days 13, 15 and 17 of gestation caused a significant decrease in the number of live births. Only one-third of these lived to the adult stage (9).

Subcutaneous mouse 0 or 40 mg kg^{-1} day^{-1} phenobarbital on days 4-18 of gestation and a single dose of 100 mg kg^{-1} furylamide on day-10. Furylamide induced late foetal deaths only in phenobarbital pre-treated mice. A significant increase in teratogenicity, including dwarfism and anomalies of the fingers, tail and palate in foetuses of pre-treated mothers (10).
Oral mouse, 0.2% diet caused no teratogenic effects, although growth retardation was observed in foetuses of dams fed 0.6% diet (11).
Oral mice, single dose of 313 mg kg^{-1} on day-10 of gestation, or 0.5% diet on days 7-18 of gestation did not cause any significant teratogenic effect (12).
In four-generation studies no adverse effect was observed in rats or mice given 0.0125% diet (13).

Metabolism and toxicokinetics
After a single oral dose of 20 mg kg^{-1} of ^{14}C-labelled furylamide to rats on day-20 of gestation, 0.4% of the radioactivity was detected in the foetuses (11).
Following an oral dose of ^{14}C-labelled furylamide, 1.3 mg kg^{-1}, to rats, 80% of the radioactivity was excreted in the faeces and 20% in the urine within 48 hr (14).
70% degradation occurred by reduction of the nitro group during incubation with rat small intestine mucosa. This metabolism has been shown to be catalysed by milk, by rat liver xanthine oxidase, and by rat liver microsomes in the presence of an electron donor. In the presence of the latter furylamide is converted into 2-(2-furyl)-3-(5-oxo-2-pyrrolin-2-yl)acrylamide, which, it is suggested, is derived from a 5-amino derivative of furylamide by ring-cleavage and cyclisation (14-18).
The binding ability of furylamide metabolites to proteins formed in the presence of xanthine oxidase is reduced by cysteine or glutathione. The active intermediates may be the *N*-hydroxylamine derivatives, but these have not been identified. The existence of the pathway is supported by the isolation of 2-(β-carboxypropionyl)-3-(5-methyl-thio-2-furyl) acrylamide in the urine of rabbits (17-19).

Genotoxicity

Salmonella typhimurium (strain metabolic activation unspecified) positive (20).
Drosophila melanogaster sex-linked recessive lethal assay positive (metabolic activation not specified) (21).
In vitro human lymphoblast cells, sister chromatid exchanges positive (22).
In vitro primary rat and mice hepatocytes DNA repair test positive (23).
In vivo rat bone marrow reticulocytes, induction of micronuclei positive (24).
In vivo dominant lethal assay in mice negative (25).
Somatic mutations occurred following exposure of soybean seeds (26).

Other effects

Other adverse effects (human)
An epidemiological study in Japan identified a strong positive correlation between breast cancer mortality and furylamide consumption. However, the study was considered inadequate for evaluation of carcinogenicity (27,28).

Any other adverse effects
Subcutaneous mouse, single dose of 0.5 or 1.0 mg kg^{-1} simultaneously with an antigen suppressed the immune response. When a dose of 1.0 mg kg^{-1} was administered 8 or 25 hr before, or 24 hr after the antigen, antibody response was augmented (29).

Other comments

Physical properties, use, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (27).
Formerly used as a food preservative in Japan where it was estimated that on average an individual consumed ~5 mg yr^{-1}. It was withdrawn from the market in 1974 (27).

References

1. Miyaji, T. *Tohoku J. Exp. Med.* 1971, **103**, 331-369.
2. Sodemoto, Y. et al *St. Marianna Med. J.* 1976, **4**, 77-90.
3. Yokoro, K. et al *Gann* 1977, **68**, 825-828.
4. Fubuhara, M. et al *Toxicol. Appl. Pharmacol.* 1977, **42**, 571-581.
5. *IARC Monograph* 1987, **Suppl.7**, 56.
6. Takayama, S. et al *Cancer Lett. (Shannon, Irel.)* 1977, **3**, 115-120.
7. Takayama, S. et al *Toxicol. Lett.* 1977, **1**, 11-16.
8. Kinebuchi, M. et al *Food Cosmet. Toxicol.* 1979, **17**, 339-341.
9. Nomura, T. *Nature (London)* 1975, **258**, 610-611.
10. Nomura, T. et al *Mutat. Res.* 1976, **35**, 167-172.
11. Tanaka, S. et al *J. Toxicol. Sci.* 1976, **2**, 149-159.
12. Imahori, A. *J. Food Hyg. Soc. Jpn.* 1975, **16**, 301-306.
13. Miyaji, T. *Tohoku J. Exp. Med.* 1971, **103**, 381-388.
14. Tatsumi, K. et al *Chem. Pharm. Bull.* 1973, **21**, 191-201.
15. Akao, M. et al *Biochem. Pharmacol.* 1971, **20**, 3091-3096.
16. Swaninathan, S. et al *Biotransformation and Excretion of Nitrofurans* in *Carcinogenesis – A Comprehensive Survey: Nitrofurans: Chemistry Metabolism, Mutagenesis and Carcinogenesis* 1978, **4**, 59-97, Raven Press, New York, NY, USA.
17. Tatsumi, K. et al *Arch. Biochem. Biophys.* 1976, **175**, 131-137.
18. Tatsumi, K. et al *J. Pharmacobio-Dyn.* 1978, **1**, 105-113.
19. Ou, T. et al *Biochem. Biophys. Res. Commun.* 1977, **75**, 401-405.
20. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
21. Blijleven, W. G. H. et al *Mutat. Res.* 1977, **56**, 95-100.
22. Tuhda, H. et al *Cancer Res.* 1980, **40**, 4775-4780.
23. Mori, H. et al *Mutat. Res.* 1987, **190**(2), 159-167.
24. Goodman, D. R. et al *Mutat. Res.* 1977, **48**, 295-306.
25. Tutikawa, K. et al *Mutat. Res.* 1975, **31**, 271.
26. Katoh, Y. et al *Hokkaidoritsu Eisei Kenkyushoho* 1990, (40), 91-93 (Japan.) (*Chem. Abstr.* **115**, 179528w).
27. *IARC Monograph* 1983, **31**, 47-61.
28. Hirayama, T. et al *Prev. Med.* 1978, **7**, 173-195.
29. Sawada, H. et al *Gann* 1976, **67**, 693-701

G1 gadolinium

Gd

Gd **Mol. Wt.** 157.25 **CAS Registry No.** 7440-54-2

Synonyms

EINECS No. 231-162-2 **RTECS No.** LW 3850000

Uses Salts in the presence of chelating agents to create a complex for enhancing images in cranial and spinal magnetic imaging. Oxide is used in control rods of nuclear reactors.

Occurrence In minerals such as samarskite, xenotime and gadolinite, constituting 4.5–6.4 ppm of the earth's crust.

Physical properties

M. Pt. 1312°C **B. Pt.** 3233°C **Specific gravity** 7.898 at 25°C

Ecotoxicity

Bioaccumulation

Has been detected in white sucker collected from freshwater lakes (1).

Is taken up into diatom *Skeletonema costatum* from seawater. Uptake is initially rapid followed by sustained slow uptake (2).

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 25 g kg^{-1} (3).

Other effects

Any other adverse effects

Rats and mice injected with Gd^{3+} 1.2 mg l^{-1} kg^{-1} showed increased hepatic lipoperoxidation and decreased glutathione levels. Effects could be prevented by Zn^{2+} pretreatment, and could be shown to be dose and time dependent (4).

Other comments

The element has been detected in normal human breast milk (5).

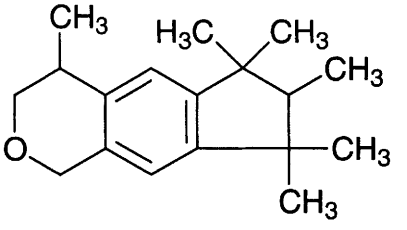
Reacts violently with air and halogens. There are seven naturally occurring isotopes ^{152}Gd, ^{154}Gd, ^{155}Gd, ^{156}Gd, ^{157}Gd, ^{158}Gd and ^{160}Gd, of which ^{152}Gd is an α-emitting radioactive isotope. The potential toxicity to man has been assessed (6).

Toxicity data refer to bioavailable forms.

References

1. Heit, M. et al *Water, Air, Soil Pollut.* 1989, **44**(1-2), 9-30.
2. Bingler, L. S. et al *Chem. Speciation Bioavailability* 1989, **1**(3), 103-110.
3. *Proc. Soc. Exp. Biol. Med.* 1970, **135**, 426.
4. Caisova, D. et al *Biologia (Bratislava)* 1986, **41**(12), 1211-1219.
5. Durrant, S. F. *J. Micronutr. Anal.* 1989, **5**(2), 111-126.
6. England, M. W. *Health Phys.* 1989, **57**(Suppl. 1), 115-119

G2 galaxolide



$C_{18}H_{26}O$ **Mol. Wt.** 258.40 **CAS Registry No.** 1222-05-5

Synonyms 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[*g*]-2-benzopyran; Abbalide

EINECS No. 214-946-9 **RTECS No.** GY 0790000

Uses Fragrance used in detergent formulations.

Mammalian & avian toxicity

Irritancy

Dermal rabbit (24 hr), 500 mg caused moderate to severe erythema and moderate oedema (1).

Genotoxicity

Human lymphocytes and human hepatoma cell line Hep G2 with and without metabolic activation, micronucleus test negative (2).

Other comments

Occurs in water samples giving unpleasant odour and taste.

References

1. *Food Cosmet. Toxicol.* 1976, **14**, 793.
2. Kevekordes, S. et al *Mutat. Res.* 1997, **395**(2,3), 145-150

G3 gallium

Ga

Ga **Mol. Wt.** 69.72 **CAS Registry No.** 7440-55-3

Synonyms gallium metal, solid; gallium metal, liquid

EINECS No. 231-163-8 **RTECS No.** LW 8600000

Uses Manufacture of light-emitting diodes, high-temperature rectifiers and thermometers, and in optical apparatus.

Occurrence Widely distributed throughout the earth's lithosphere. The richest source is the mineral germanite (0.5-0.7% Ga) (1).

Emitted into the atmosphere from metallurgical plants and from coal burning (2).

Physical properties

M. Pt. 30°C **B. Pt.** 2403°C **Specific gravity** 5.904 (solid) at 29.6°C, 6.905 (liquid) at 29.8°C

Volatility v.p. 0.004 mmHg at 1000°C

Occupational exposure

UN No. 2803 **HAZCHEM Code** 1Z **Conveyance classification** corrosive substance

Ecotoxicity

Invertebrate toxicity

Pseudomonas fluorescens ATCC 13525 grown in culture with a defined citrate medium supplemented with 69.72 mg l^{-1} gallium(III). There was an initial lag phase of 40 hr with no reduction in cellular yield. Following an initial uptake gallium was secreted in the spent fluid (3).

Environmental fate

Adsorption and retention

Gallium is immobile during weathering and diagenesis of bauxite deposits of the Mediterranean belt (4).

Mammalian & avian toxicity

Acute data

LC_{Lo} subcutaneous rat 110 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Administration to rats of 45 mg kg^{-1} (gallium nitrate) over 14 days (route not specified) caused an increase in bone calcium and phosphate levels (6).

Metabolism and toxicokinetics

Radiochemical neutron activation analysis demonstrated non-homogeneous distribution of gallium in the human brain. Concentrations detected in dry samples ranged from 0.2 ppb (in the cuneus, middle temporal gyrus and post central gyrus) to 2.2 ppb in the thalamus (7).

Intravenous mature Japanese quail ^{57}Ga, 18 hr after injection 20% of the dose was found in leg bones. Analysis of egg components over 10 days revealed 27% of the dose in egg yolk (8).

Intravenous injection of ^{67}Ga into rats, gallium was found accumulated mainly in the connective tissues (9).

Sensitisation

Patch testing did not reveal sensitisation reaction in humans although some cases of dermatitis have been reported (10).

Genotoxicity

ID_{50} (24 hr) DNA synthesis by human T-cell lymphoblasts, 8.4 mg. ID_{100}, 26 mg. The authors reported that ribonucleotide reductase was probably the major specific target (11).

Other effects

Any other adverse effects

Caused the precipitation of rat brain and liver chromatin *in vitro* (12).

Other comments

Toxicology of gallium and its compounds reviewed (2,13,14).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (15).

Exhibits anti-tumour effects (16).

Toxicity data refer to bioavailable forms.

References

1. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, **2A**, 1630, John Wiley & Sons, New York, NY, USA.
2. Filov, V. A. et al (Eds.) *Harmful Chemical Substances* 1993, **1**, 295-302, Ellis Harwood, New York, NY, USA.
3. Al-Aoukaty, A. et al *FEMS Microbiol. Lett.* 1992 **92**(3), 265-272.
4. Ozlu, N. *Miner. Deposita* 1983, **18**(3), 469-476.
5. *Toxic and Hazardous Industrial Chemicals Safety Manual* 1975, 254, International Technical Information Institute, Tokyo, Japan.
6. Repo, M. A. et al *Calcif. Tissue Int.* 1988, **43**(5), 300-306.
7. Speziali, M. et al *Biol. Trace Elem. Res.* 1989, **22**(1), 9-15.
8. Robinson, G. A. et al *Poult. Sci.* 1990, **69**(2), 300-306.
9. Ando, A. et al *Radioisotopes* **26**(6), 421-422.
10. Meek, S. F. et al *Ind. Med.* 1943, **12**, 7.
11. Hedley, D. W. et al *Cancer Res.* 1988, **48**(11), 3014-3018.
12. Walker, P. R. et al *Biochemistry* 1989, **28**(9), 3911-3915.
13. Domingo, J. L. et al *Met. Ions. Biol. Med. Proc. Int. Symp., 1st.* 1990, 415-419.
14. *Chemical Safety Data Sheets* 1989, **2**, 160-162, The Royal Society of Chemsitry, London, UK.
15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
16. Shinahara, K. *Jikken Igaku* 1987, **5**(3), 256-258 (Japan.) (*Chem. Abstr.* **107**, 89092e)

G4 gallium arsenide

AsGa

GaAs **Mol. Wt.** 144.64 **CAS Registry No.** 1303-00-0

Synonyms

EINECS No. 215-114-8 **RTECS No.** LW 8800000

Uses Semiconductor in high-temperature rectifiers.

Physical properties

M. Pt. 1238°C **Specific gravity** 5.310 at 25°C with respect to water at 4°C

Occupational exposure

SE-LEVL 0.03 mg m^{-3} (as As)
UK-LTEL MEL 0.1 mg m^{-3} (as As)
US-TWA 0.01 mg m^{-3} (as As)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse > 10,000 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 4700 mg kg^{-1} (2).

Oral ♂ albino rats administered 100, 200, or 500 mg kg^{-1} showed inhibition of erythrocyte δ-aminolevulinic acid dehydratase (ALAD) activity accompanied by elevated urinary excretion of ALA. Serum aspartate aminotransferase and γ-glutamyltranspeptidase activities increased significantly. Hepatic malondialdehyde levels increased significantly and there was a decrease in hepatic glutathione levels. Renal alkaline phosphatase activity, urinary ALA and protein excretion increased significantly. Significant alterations in almost all the immunological variables and an increase in gallium and arsenic concentration in blood and soft tissues accompanied the above changes. Most of the biochemical changes were prominent at day-7 following a single exposure to 200 or 500 mg kg^{-1}. Most of the immunological indices altered with all three doses and remained high even at day-21. These results suggest that gallium arsenide has only a moderate effect on renal and hepatic tissues, but that the immunological and haematological systems are more vulnerable to the toxic effects (3).

Carcinogenicity and chronic effects

Intraperitoneal and subcutaneous mouse, single injection of 48 or 480 mg kg^{-1} as gallium. In the subcutaneous study, no local tumours occurred at the site of injection and there was no significant difference in the survival of treated and control animals. In the intraperitoneal study, the high dose reduced the survival rate. An increased incidence in tumours in the low-dose group was reported to be spontaneous and not attributable to gallium arsenide treatment (4).

Intratracheal hamster, total dose of 3.75 mg gallium over 15 wk had no apparent carcinogenic or tumorigenic activity. Survival was significantly reduced in treated animals as compared with controls (5).

Teratogenicity and reproductive effects

Inhalation rat and mouse 0, 10, 37 or 75 mg m^{-3} 6 hr day^{-1} on days 4-17 of gestation for mice, day 4-19 of gestation for rats. Maternal and foetal toxicity and teratogenic effects were reported (6).

♂ Rats were administered gallium arsenide by repetitive intratracheal installation 7.7 mg kg^{-1} 2 × wk^{-1}, for 8 weeks. This treatment was toxic to the sperm and testis and inhibited sperm release from the seminiferous epithelium (7).

Metabolism and toxicokinetics

Syrian hamsters were administered gallium arsenide by intratracheal instillation (5 mg kg^{-1} as arsenic). Blood concentration was 0.185 ppm after 1 day, and 0.280 after 2 days. Liver concentration was 0.565% of the dose after

1 day. 5% of the dose was eliminated in the urine within 4 days. The major metabolites included dimethylarsenic acid and inorganic arsenic (8).

Other effects

Any other adverse effects

Intratracheal ♀ mouse, single dose of 2.5-200 mg kg^{-1} resulted in a dose-dependent decrease in the *in vitro* immunoglobulin-M antibody-forming cell response to the T-dependent antigen sheep red blood cells. The high dose caused a 97% decrease. Spleen cellularity was also decreased in a dose-dependent manner with a 54% decrease at the high dose (9).

Intratracheal rat, single dose of 50, 100 or 200 mg kg^{-1} caused a dose-dependent inhibition of δ-aminolevulinic acid dehydrogenase activity. Activity was decreased by 95% at the high dose, with a concomitant marked increase in the urinary excretion of aminolevulinic acid (9).

Other comments

Human health effects, experimental toxicology, physico-chemical properties reviewed (10,11).

References

1. Fadeev, A. I. *Gig. Tr. Prof. Zabol.* 1980, **3**, 45.
2. Tarasenko, N. et al *Gig. Sanit.* 1980, **45**(10), 13-16.
3. Flora, S. et al *Toxicol. Lett.* 1998, **94**(2), 103-113.
4. Tanaka, A. et al *Appl. Organomet. Chem.* 1990, **4**(3), 231-237.
5. Ohyama, S. et al *Appl. Organomet. Chem.* 1988, **2**(4), 333-337.
6. Mast, T. J. et al *Energy Res. Abstr.* 1991, **16**(3), Abstract No. 8504.
7. Omura, M. et al *Fundam. Appl. Toxicol.* 1996, **32**(1), 72-78.
8. Rosner, M. H. et al *Fundam. Appl. Toxicol.* 1987, **9**(4), 730-737.
9. Sikorski, A. A. et al *Toxicol. Appl. Pharmacol.* 1991, **110**(1), 129-142.
10. McIntrye, A. J. et al *Solid State Technol.* 1989, **32**(9), 119-126.
11. *ECETOC Technical Report No. 71* 1996, European Chemical Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G5 gallium nitrate

$$Ga(NO_3)_3$$

GaN_3O_9 **Mol. Wt.** 255.74 **CAS Registry No.** 13494-90-1

Synonyms gallium(III) nitrate

EINECS No. 236-815-5 **RTECS No.** LW 9625000

Uses Catalyst. Antineoplastic agent.

Physical properties

M. Pt. 110°C (decomp.)

Occupational exposure

UN No. 1477

UN No. 3218 (aqueous solution) **HAZCHEM Code 1Z** **HAZCHEM Code 2Z** (aqueous solution)

Conveyance classification oxidising substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2710, 4360 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous mouse 600 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse 68, 80 mg kg^{-1}, respectively (1,3).
LD_{50} intravenous mouse 55 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Treatment of rats with 45 mg kg^{-1} over 14 days (route not specified) caused an accumulation of gallium in the bone. Calcium content of the bone was also increased, with more dense bone particles accumulating in the metabolically more active metaphyseal bone (5).
Oral rabbit (18 wk) 220 mg kg^{-1} day^{-1} caused a decrease in albumin, increase in α_2- and γ-globulins, increased acetylcholinesterase activity, and inhibition of alkaline phosphatase activity. Degenerative changes in the liver parenchyma and epithelium of convoluted renal tubules, and desquamative catarrh of the pulmonary tissue were observed (6).

Irritancy

Dermal rat, 500 mg caused severe irritation (exposure not specified) (2).

Genotoxicity

Directly inhibits cytidine diphosphate and adenosine diphosphate reductase activity in a cell-free assay. Inhibition of DNA synthesis appeared to be due to a combination of a block in iron availability to ribonucleotide reductase and a direct inhibition of the enzyme by gallium (7).

References

1. Domeinger, J. L. et al *J. Toxicol. Clin. Exp.* 1987, **7**(6), 411-418.
2. Tarasenko, N. et al *Gig. Sanit.* 1980, **45**(10), 13.
3. *Environ. Qual. Saf., Suppl.* 1975, **1**, 1.
4. *Cancer Treat. Rep.* 1986, **70**, 1311.
5. Repo, M. A. et al *Calcif. Tissue Int.* 1988, **43**(5), 300-306.
6. *Harmful Chemical Substances* 1993, **1**, 295-302, Ellis Horwood, London, UK.
7. Chitamber, C. R. et al *Cancer Res.* 1991, **51**(22), 6199

G6 gallium oxide

$$Ga_2O_3$$

Ga_2O_3 **Mol. Wt.** 187.44 **CAS Registry No.** 12024-21-4

Synonyms gallium(III) oxide; digallium trioxide; gallium sesquioxide

EINECS No. 234-691-7 **RTECS No.** LW 9650000

Uses Catalyst. Corrosion inhibitor in the manufacture of electrodes. Manufacture of ceramics. Manufacture of zeolites.

Physical properties

Specific gravity 6.440

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 10 g kg^{-1} (1).

Carcinogenicity and chronic effects

Intraperitoneal and subcutaneous mouse, single injections of 48 or 480 mg kg^{-1} as gallium. In the subcutaneous study, no local tumours occurred at the site of injection and there was no significant difference in the survival rate of treated and control animals. In the intraperitoneal study the survival rate was reduced in the low-dose group. An increased incidence of tumours in treated animals was reported to be spontaneous and not attributable to gallium oxide treatment (2).

Intraperitoneal hamster, total dose of 3.75 mg (as gallium) over 15 wk had no apparent carcinogenic or tumorigenic activity. Survival was significantly reduced in treated animals compared with controls (3).

References

1. Tarasenko, N. et al *Gig. Sanit.* 1980, **45**(10), 13-16.
2. Tanaka, A. et al *Appl. Organomet. Chem.* 1990, **4**(3), 231-237.
3. Okyama, S. et al *Appl. Organomet. Chem.* 1988, **2**(4), 333-337

G7 gallium trichloride

$GaCl_3$

$GaCl_3$ **Mol. Wt.** 176.08 **CAS Registry No.** 13450-90-3

Synonyms gallium(III) chloride

EINECS No. 236-610-0 **RTECS No.** LW 9100000

Physical properties

M. Pt. 78°C **Specific gravity** 2.470 at 20°C

Solubility Water: miscible. Organic solvents: benzene, carbon disulfide, carbon tetrachloride

Ecotoxicity

Fish toxicity

Gallium chloride altered growth and ion content in acute and chronic tests on 3- and 30-day-old tilapia (1).

Environmental fate

Abiotic removal

Undergoes hydrolysis to give gallium hydroxide which is water insoluble (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4700 mg kg^{-1} (2).

LC_{Lo} (3 hr) inhalation rat 316 mg m^{-3} (3).

LD_{50} subcutaneous rat, rabbit 245-306 mg kg^{-1} (4).

LD_{50} intravenous rat, rabbit, dog 41-47 mg kg^{-1} (4).

LD_{50} intraperitoneal mouse 37-93 mg kg^{-1} (5,6).

Sub-acute and sub-chronic data
Oral rat (26 wk) 25, 250, 1250 or 2500 mg kg^{-1} diet caused no adverse effects (3).

Metabolism and toxicokinetics
Gastro-intestinal absorption of cationic gallium salts in mammals is <1% for physiological doses owing to hydrolysis to insoluble or unabsorbable gallium hydroxide (2).

Irritancy
Strong irritant to eyes and skin (species unspecified) (6,7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA102, TA2637 with and without metabolic activation negative (8).

Other comments

Physical properties, toxicity and safety precautions reviewed (9).

References

1. Lin, H. C. et al *Bull. Environ. Contam. Toxicol.* 1998, **60**(6), 931-935.
2. Venugopal, B. et al *Metal Toxicity in Mammals* 1978, 115, Plenum Press, New York, NY, USA.
3. Dudley, M. C. et al *J. Pharmacol. Exp. Ther.* 1949, **95**, 487.
4. *Environ. Qual. Saf., Suppl.* 1975, **1**, 1.
5. *C. R. Hebd. Seances Acad. Sci.* 1963, **256**, 1043.
6. *NIOSH Registry of Toxic Effects of Chemical Substances* 1976, Washington, DC, USA.
7. Tarasenko, N. Y. et al *Gig. Sanit.* 1980, (10), 13-16.
8. Iyehara Ogawa, H. et al *Jpn. J. Genet.* 1987, **62**(2), 159-162.
9. *Chemical Safety Data Sheets* 1989, **2**, 163-165, The Royal Society of Chemistry, London, UK

G8 gasoline, natural

CAS Registry No. 8006-61-9

Synonyms benzin; casinghead (natural gasoline essence); ethyl naphtha; petrol; gasohol; automotive gasoline; aviation gasoline; Avgas

EINECS No. 232-349-1 **RTECS No.** LX 3300000

Uses Fuel for internal combustion engines. Solvent.
Occurrence Component of crude oil.

Physical properties

M. Pt. <–20°C **B. Pt.** 25-220°C **Flash point** –46°C **Specific gravity** 0.7-0.8 at 20°C
Volatility v.p. 330-770 mmHg at 37.8°C ; v.den. 3.0-4.0
Solubility Organic solvents: benzene, chloroform, diethyl ether

Occupational exposure

JP-OEL 100 ppm (300 mg m^{-3})
US-TWA 300 ppm (890 mg m^{-3}) **US-STEL** 500 ppm (1480 mg m^{-3})

UN No. 1257
Supply classification toxic

Risk phrases May cause cancer – Harmful: may cause lung damage if swallowed (R45, R65)
Safety phrases 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
LC_{50} (24 or 96 hr) rainbow trout 76, 56 ppm, respectively, hard water (1)

Mammalian & avian toxicity

Acute data
LC_{50} (5 min) inhalation rat, mouse, guinea pig 300 g m^{-3} (2).
Intraperitoneal ♂ rat, single dose of 2 ml kg^{-1} induced an increase in lipid peroxidation in the liver after 24 hr (3).
Intraperitoneal ♀ rat 1 ml kg^{-1} depressed the activities of hepatic δ-aminolevulinic acid synthetase and dehydratase within 20 hr (4).

Sub-acute and sub-chronic data
Inhalation rat 110, 1600 or 12,500 mg m^{-3} for 6 hr day^{-1} 5 days wk^{-1} for 21 days induced mild renal tubular degenerative and regeneration changes, including increased levels of hyaline droplet formation, necrosis and degeneration of the proximal convoluted tubule of the renal cortex, in ♂ rat only. When exposure was extended to 90 days at 150, 1440 or 15,000 mg m^{-3} a concentration-related incidence of tubular dilatation and necrosis at the corticomedullary junction was observed in ♂ rats only (5).
Inhalation ♀ rat 300 mg m^{-3} 8 hr day^{-1} 5 days wk^{-1} for 15 days reduced levels of pulmonary surfactant, with no qualitative alteration in the phospholipid components. However, this did not result in changes in RNA or DNA synthesis in the lung tissues. Animals exposed for 12 wk exhibited a high incidence of changes in the lung parenchyma, characterised by interstitial fibrosis with associated alveolar collapse (6-8).
Gavage rat (9 days) 0.04-2.0 mg kg^{-1} unleaded gasoline markedly increased the number and size of hyaline droplets in cells of the renal proximal convoluted tubules. The renal content of the ♂ rat-specific low molecular protein α_{2u}-globulin was increased by up to 4.4-fold (9).
In electroencephalographic studies with ♂ rats given 10 ml kg^{-1} unleaded or leaded gasoline by intraperitoneal injection, animals given leaded gasoline showed excessive tension and excitement by day 6-7. Both unleaded and leaded gasoline decreased δ, θ, and α waves after 1-3 days, whereas the electrocardiogram of rats given leaded gasoline showed marked α and θ waves after 6-7 days (10).

Carcinogenicity and chronic effects
Inadequate evidence for the carcinogenicity in humans, limited evidence for the carcinogenicity in animals, IARC classification group 2B (11).
Inhalation rat, mouse (113 wk) 0, 200, 870 or 6200 mg m^{-3} unleaded gasoline (benzene content ~2%). A dose-related increase in the incidences of hepatocellular adenomas and carcinomas was observed in ♀ mice. Renal tumours were reported in 2/100 ♀ mice and in 12/100 ♂ rats. Renal sarcomas in 1/100 ♀ and 1/100 ♂ rats (12).

Teratogenicity and reproductive effects
Inhalation rat 1200 on 4800 mg m^{-3} unleaded gasoline for 6 hr day^{-1} on days 6-15 of gestation did not cause any teratogenic effects (13).

Metabolism and toxicokinetics
Gasoline was detected in human foetal and neonatal tissues, and neonatal blood concentration was double that of maternal blood, following inhalation exposure in the chemical industry (14).
Concentrations of urinary thioether were found to be increased in exposed gasoline service station attendants (15).

Irritancy
Exposure of humans to 500 ppm for 1 hr caused moderate irritation of the eyes (16).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (17).
Drosophila melanogaster somatic mutation for eye pigmentation positive (18).
In vitro mouse lymphoma L5178Y tk^+/tk^- cells mutation without metabolic activation positive (19).
In vitro human, rat and mouse hepatocytes, unscheduled DNA synthesis positive (20).
In vitro primary rat kidney cells, unscheduled DNA synthesis negative (21).
In vivo rat, mouse hepatocytes, unscheduled DNA synthesis positive in mice, negative in rats following administration by gavage. The percentage of S-cells was increased in ♂, but not ♀ mice, and in rats of both sexes (20).
In vivo rat bone marrow, chromosome aberrations negative following oral administration and by gavage (17,19).
A significant increase in the incidence of micronuclei in bone marrow cells and chromosomal aberrations in peripheral blood lymphocytes was reported in petroleum tank cleaners (22).

Other effects

Other adverse effects (human)
In a large cohort study of UK oil distribution workers, some of whom had occupational exposure to gasoline, a lower total cancer mortality was found than expected on the basis of national rates, but there was a slightly elevated number of deaths from neoplasms of the lymphatic and haematopoietic tissues (23).
A Swedish register-based cohort study on pancreatic cancer showed a moderate increase in the incidence among service station workers (24).
Two US proportionate mortality studies showed some consistency regarding elevated risks for some types of lymphopoietic cancers in motor vehicle mechanics, although not all the reported findings were significant. For service station workers, the proportionate mortality ratio for leukaemia and aleukaemia was increased in one study but not in another (25,26).
In a US case-control study on renal-cell carcinoma, there was some evidence of a positive trend in risk with duration of employment as a service station attendant (27).
A case-control study of cancer at many sites in Canada revealed an elevated risk for kidney cancer in men exposed to aviation gasoline. There were indications of a dose-response relationship (28).
In a Danish case-control study on bladder cancer, an elevated risk was associated with oil or gasoline work (29).
Non-significant increased risks of bladder cancer were reported in two US studies among motor vehicle mechanics, while no increase was seen in a third study (30-32).
A US study on cancer of the renal pelvis indicated an elevated risk for workers exposed to unspecified petroleum, tar or pitch products (33).
A Swedish study indicated an increased risk for acute non-lymphocytic leukaemia in men with occupational exposure to petroleum products (34).
One hospital-based case-control study in the USA revealed an increased risk for testicular cancer in service station attendants and garage attendants. Another study showed an increased risk for pancreatic cancer in men with occupational exposure to dry cleaning agents or gasoline. Another study demonstrated an increased risk for liver cancer among service station attendants, particularly for hepatocellular carcinoma. A case-control study of cancer at many sites in Canada revealed an elevated risk only for stomach cancer among men exposed to automotive gasoline (35-37).
Nine case-control studies from four countries provided data on parental occupations involving exposure to hydrocarbons and the risk for cancer in children. There was no consistent association between fathers' occupation and risk for childhood cancer, although significant results appeared in some studies. One study on data on maternal occupations involving exposure to hydrocarbons during pregnancy suggested an increased risk for leukaemia in their children. None of these studies specifically assessed exposure to gasoline, but parental occupations such as motor vehicle mechanics and service station attendants were not consistently associated with an increase in risk (11,38-46).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (47).

Other comments

Gasoline is a generic term used to describe volatile, flammable petroleum fuels for internal combustion engines. It is a complex mixture of hydrocarbons predominantly in the $C_4 - C_{12}$ range. Additives include anti-knock agents, lead scavengers, detergents, anti-rust agents, anti-oxidants, anti-icing agents, dyes, lubricants, metal deactivators and oxygenates (11).

Physical properties, composition, use, analysis, carcinogenicity, mammalian toxicity and mutagenicity reviewed (11).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (48).

It should be noted that the toxicology of substances of petroleum origin often depends upon the aromatic content of the original oil.

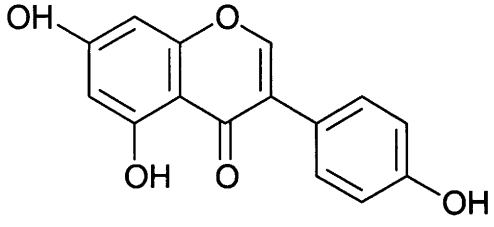
Autoignition temperature 280-462°C

References

1. Westlake, G. et al *Society of Environmental Toxicology & Chemistry 1992, European Division Conference*, Potsdam, Germany.
2. *NTIS Report* PB158-508, Natl. Tech. Inf. Service, Springfield, VA, USA.
3. Rao, G. S. et al *Environ. Res.* 1978, **16**, 174-178.
4. Rao, G. S. et al *Arch. Toxicol.* 1980, **46**, 313-317.
5. Halder, C. A. et al *Adv. Mod. Environ. Toxicol.* 1984, **7**, 73-88, Princeton Scientific Publishers, NJ, USA.
6. Lykke, A. W. J. et al *Experientia* 1978, **34**, 498.
7. Lykke, A. W. J. et al *Pathology* 1979, **11**, 71-80.
8. Stewart, B. W. et al *Chem.-Biol. Inter.* 1979, **26**, 321-338.
9. Olson, M. J. et al *Toxicol. Appl. Pharmacol.* 1987, **90**, 43-51.
10. Saito, K. *Br. J. Ind. Med.* 1973, **30**, 352-358.
11. *IARC Monograph* 1989, **45**, 159-201.
12. MacFarland, H. N. et al *J. Am. Bull. Toxicol.* 1984, **3**, 231-248.
13. Schreiner, C. A. *Adv. Mod. Environ. Toxicol.* 1984, **3**, 29-45, Princeton Scientific Publishers, NJ, USA.
14. Lipovskii, S. M. et al *Gig. Tr. Prof. Zabol.* 1979, **3**, 25-28.
15. Stock, J. K. et al *Br. J. Ind. Med.* 1986, **43**, 718-720.
16. *Arch. Environ. Health* 1960, **1**, 548.
17. Conaway, C. C. et al *Adv. Mod. Environ. Toxicol.* 1984, **6**, 89-107, Princeton Scientific Publishers, NJ, USA.
18. Nylander, P. O. et al *Mutat. Res.* 1978, **57**, 163-167.
19. Dooley, J. F. et al *Proc. 10th Annu. Symp. Polynuclear Aromatic Hydrocarbons: A Decade of Progress* 1988, 179-194, Battelle Press, Columbia, OH, USA.
20. Loury, D. J. et al *Toxicol. Appl. Pharmacol.* 1986, **85**, 11-23.
21. Loury, D. J. et al *Toxicol. Appl. Pharmacol.* 1987, **87**, 127-140.
22. Hoegstedt, B. et al *Hereditas (Lund, Swed.)* 1981, **94**, 179-187.
23. Rushton, L. et al *Br. J. Ind. Med.* 1983, **40**, 330-339.
24. Novell, S. et al *Br. J. Ind. Med.* 1986, **43**, 775-778.
25. Milham, S. *Occupational Mortality in Washington State 1950-1979*, 1983, National Institute for Occupational Safety and Health, DHSS (NIOSH) Publication No. 83-116, Cincinnati, OH, USA.
26. Schwartz, E. *Am. J. Ind. Med.* 1987, **12**, 91-99.
27. McLaughlin, J. K. et al *J. Natl. Cancer Inst.* 1984, **72**, 275-284.
28. Siemiatycki, J. et al *Scand. J. Work Environ. Health* 1987, **13**, 493-504.
29. Mommsen, S. et al *Acta Radiol. Oncol.* 1984, **23**, 147-152.
30. Smith, E. M. et al *Am. J. Public Health* 1985, **75**, 881-883.
31. Silverman, D. T. et al *J. Natl. Cancer Inst.* 1983, **70**, 237-245.
32. Schoenberg, J. B. et al *J. Natl. Cancer Inst.* 1984, **72**, 973-981.
33. McLaughlin, J. K. et al *J. Natl. Cancer Inst.* 1983, **71**, 287-291.
34. Brandt, L. et al *Br. Med. J.* 1978, **i**, 553.
35. Lin, R. S. et al *J. Am. Med. Assoc.* 1981, **245**, 147-152.
36. Steinagen, A. et al *Am. J. Epidemiol.* 1983, **117**, 443-454.

37. Siemialycki, J. et al *Scand. J. Work Environ. Health* 1987, **13**, 185.
38. Fabia, J. et al *Br. J. Prev. Soc. Med.* 1974, **28**, 98-100.
39. Hakulinen, T. et al *Br. J. Prev. Soc. Med.* 1976, **30**, 138-140.
40. Kantor, A. F. et al *J. Epidemiol. Commun. Health* 1979, **33**, 253-256.
41. Kwa, S.-L. et al *J. Occup. Med.* 1980, **22**, 792-794.
42. Zack, M. et al *Am. J. Epidemiol.* 1980, **11**, 329-336.
43. Gold, E. B. et al *J. Occup. Med.* 1982, **24**, 578-584.
44. Wilkins, J. R. et al *J. Epidemiol. Commun. Health* 1984, **38**, 7-11.
45. Van Steensel-Moll, H.A. et al *Am. J. Epidemiol.* 1985, **121**, 216.
46. Johnson, C. C. et al *Am. J. Epidemiol.* 1987, **126**, 605-613.
47. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
48. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G9 genistein



$C_{15}H_{10}O_5$ **Mol. Wt.** 270.24 **CAS Registry No.** 446-72-0

Synonyms 5,7-dihydroxy-3-(4-hydroxyphenyl)-4*H*-1-benzopyran-4-one; 4',5,7-trihydroxyisoflavone; C.I. 75610; genisteol; genisterin; prunetol

EINECS No. 207-174-9

Occurrence Isoflavone phytoestrogen occurring in numerous plants eaten by humans and food-producing animals. The aglycone of genistin and of sophoricoside.

Physical properties

M. Pt. 297-298°C slight decompn.
Solubility Water: practically insoluble. Organic solvents: soluble in usual organic solvents

Ecotoxicity

Invertebrate toxicity
Isolates of *Phytophthora sojae* were grown in cultures containing 0.01, 0.1, 1, 3, and 10 μg ml^{-1} genistein. Changes in fungal morphology were observed at all concentrations of genistein tested. Zoosporangia production and release of zoospores was decreased. Genistein in the medium containing zoospores caused a general reduction in asexual reproduction, with 10 μg ml^{-1} causing the most dramatic reduction (1).

Environmental fate

Degradation studies
Genistein was fermented by human faecal bacteria under anaerobic conditions. Dihydrodaidzein, benzopyran-4,7-diol,3-(4-hydroxyphenol) and equol were isolated from the fermentation broth (2).
Streptomyces griseus cultivated in media containing soybean meal or cottonseed meal produced the metabolites 6-chloro- and 6,8-dichloro-genistein by microbial halogenation (3).

Mammalian & avian toxicity

Teratogenicity and reproductive effects

The effect of genistein on human sperm and peripheral lymphocytes (from the same donor) were compared using the single cell gel electrophoresis assay (Comet assay). Genistein was less responsive in the peripheral lymphocytes than in the sperm. This may be due to the fact that damage induced in the elongated spermatids and consequent spermatozoa cannot be repaired. This may result from the loss of cytoplasm in the sperm in which repair enzymes are known to predominate (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1538 with and without metabolic activation negative (5).

Genistein did not affect the cytoplasmic microtubule complex or the mitotic spindle in cultured Chinese hamster V79 cells but was a strong inducer of DNA strand breaks and micronuclei containing acentric fragments (6).

Other effects

Other adverse effects (human)

Genistein, isolated from kudzu root *Radix puerariae*, has been shown to be a potent, reversible inhibitor of human alcohol dehydrogenase isoenzymes (7).

Any other adverse effects

Daidzein and genistein in the diet of captive cheetahs have been suggested as a probable cause of infertility and liver disease in these animals (8).

Sheep grazed for one day in pastures high in genistein showed significant oestrogenic activity in the cervical mucous bioassay, but the response became negligible after a grazing period of 8-10 days. After a few days of ingestion of pastures rich in genistein the phytoestrogen is catabolised to inactive *p*-ethylphenol (9).

Administration of genistein effectively lowered the total serum-cholesterol in an oestrogen-dependent animal model, the ovariectomised rat (10).

Genistein, a weak utero-vaginotropic compound, markedly inhibited uptake of oestradiol-3H by the uterus and vagina in immature mice, measured 1 hr after the injection of the genistein. This inhibition and the accompanying growth responses give further support to the conclusion that the interaction in uterine and vaginal tissue between oestradiol and the weaker utero-vaginotropic compounds involves competition for retention at receptor sites followed by expression of the activity characteristics of the compounds retained (11).

Synthetic genistein administered into the rumen of sheep was detected in the blood within 2.5 hr. Plasma levels of free genistein (excluding circulating isoflavone conjugated as glucuronide) >50 $\mu g\ l^{-1}$ were associated with maximum uterine growth response in ovariectomised ewes. Levels of 10-50 l^{-1} elicited a graded response (12).

Sixteen examples of soybean meal were examined in the mouse uterine weight bioassay and had oestrogenic activity. Genistein and daidzein were present in the extracts and the former may be responsible for most of the oestrogenic activity (13).

Genistein binds to rat α-fetoprotein with Kd *c.* 5×10^{-6} M. The authors suggest that this is sufficiently high that genistein may modulate estradiol and estrone binding to rat α-fetoprotein *in vivo* when present at dietary levels (14).

Other comments

Prepubertal ♀ rats were injected subcutaneously with genistein (500 $\mu g\ g^{-1}$) on days 16, 18 and 20 postpartum and were administered 80 $\mu g\ g^{-1}$ dimethylbenz[*a*]anthracene on day-50 postpartum. Rats treated prepubertally with genistein had reduced incidence and fewer adenocarcinomas per animal than controls not given genistein. The development of chemically induced mammary cancer was suppressed without significant toxicity to the endocrine/reproductive system (15).

Genistein is approximately 10,000 times less potent than estradiol in inducing oestrogen-responsive cell proliferation or oestrogen-specific protein in human breast tumour cell line MCF-7 (16).

Genistein is a tyrosine-kinase, angiogenesis, and topoisomerase II inhibitor and stimulates differentiation in many types of cell, including leukaemia cells (17).

Culture broths of an unidentified species of *Streptomyces* designated 85-88 showed toxicity to mosquito larvae that was traced to three compounds, tangeritin, genistein, and daidzein. The acetates of genistein and daidzein showed greater activity than that of the corresponding isoflavones (18).

Phytoestrogens, largely formononetin and genistein, are produced in the leaves of stunted desert annuals in a dry year. Ingestion of these compounds by the California quail results in inhibition of reproduction, preventing the production of young that will not have adequate food. In a wet year the plants grow vigorously and phytoestrogenic substances are largely absent (19).

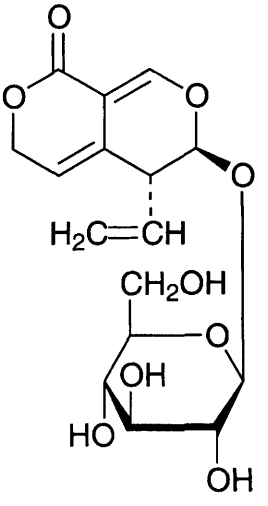
Phytochemical mimicry of reproductive hormones and modulation of herbivore fertility by phytoestrogens reviewed (20).

Endocrine disrupting effects discussed (21,22).

References

1. Vedenyapina, E. G. et al *Phytopathology* 1996, **86**(2), 144-148.
2. Chang, Y.-C. et al *J. Nat. Prod.* 1995, **58**(12), 1892-1896.
3. Anyanwutaku, I. O. et al *J. Nat. Prod.* 1992, **55**(10), 1498-1504.
4. Anderson, D. et al *Teratog. Carcinog. Mutagen.* 1997, **17**(1), 29-43.
5. Bartholomew, R. M. *Mutat. Res.* 1980, **78**(4), 317-321.
6. Kulling, S. E. et al *Food Chem. Toxicol.* 1997, **35**(6), 605-613.
7. Keung, W.-M. *Alcohol.: Clin. Exp. Res.* 1993, **17**(6), 1254-1260.
8. Setchell, K. D. R. et al *Gastroenterology* 1987, **93**, 225-233.
9. Lindsay, D. R. et al *Aust. Vet. J.* 1970, **46**(5), 219-222.
10. Dodge, J. A. et al *J. Steroid Biochem. Mol. Biol.* 1996, **59**(2), 155-161.
11. Folman, Y. et al *J. Endocrinol.* 1969, **44**(2), 213-218.
12. Lindner, H. R. *Aust. J. Agric. Res.* 1967, **18**(2), 305-333.
13. Drane, H. M. et al *Food Cosmet. Toxicol.* 1980, **18**(4), 425-427.
14. Baker, M. E. et al *Proc. Soc. Exp. Biol. Med.* 1998, **217**(3), 317-321.
15. Murrill, W. B. et al *Carcinogenesis* 1996, **17**(7), 1451-1457.
16. Mayr, U. et al *Toxicology* 1992, **74**, 135-149.
17. Adlercreutz, H. et al *Ann. Med.* 1997, **29**.
18. Rao, K. V. et al *J. Agric. Food Chem.* 1990, **38**(6), 1427-1430.
19. Leopold, A. S. et al *Science* 1976 **191**(4222), 98-100.
20. Hughes, C. L., Jr. *Environ. Health Perspect.* 1988, **78**, 171-175.
21. Mazur, W. M. in *Proc. Conf. Endocrine Disrupters in the Environment, 20-21 May 1997* 1997, IBC Conferences, 57-61 Mortimer Street, London W1N 8JX, UK.
22. *IEH Assessment on Environmental Oestrogens: Consequences to Human Health and Wildlife* 1995, Institute for Environment and Health, Leicester, UK

G10 gentiopicrin



$C_{16}H_{20}O_9$ **Mol. Wt.** 356.33 **CAS Registry No.** 20831-76-9

Synonyms gentiopicroside; 5-ethenyl-6-(β-D-glucopyranosyloxy)-5,6-dihydro-1*H*,3*H*-pyrano[3,4-*c*]pyran-1-one

EINECS No. 244-070-2

Uses Antimalarial drug.

Occurrence Occurs in *Gentiana* species.

Physical properties

M. Pt. 191°C

Solubility Organic solvents: ethanol, ethyl acetate

Mammalian & avian toxicity

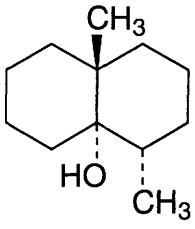
Metabolism and toxicokinetics

Metabolised anaerobically by human intestinal bacteria *in vitro*. *Veillonella parvula parvula* produced five metabolites which were identified as erythrocentaurin, gentiopicral, 5-hydroxymethylisochroman-1-one, 5-hydroxymethylisochromen-1-one, and *trans*-5,6-dihydro-5-hydroxymethyl-6-methyl-1*H*,3*H*-pyrano[3,4-*c*]pyran-1-one (1).

References

1. El-Sedaway, A. I. et al *Chem. Pharm. Bull.* 1989, **37**(9), 2435-2437

G11 geosmin



$C_{12}H_{22}O$ **Mol. Wt.** 182.31 **CAS Registry No.** 19700-21-1

Synonyms *trans*-1,10-dimethyl-*trans*-9-decalol; octahydro-4,8a-dimethyl-4a(2*H*)-naphthalenol

EINECS No. 243-239-8 **RTECS No.** QK 4249000

Occurrence Formed by algae, bacteria and fungi in potable waters, causing earthy odours. Volatile component of beet essence.

Physical properties

B. Pt. 270°C

Environmental fate

Degradation studies

Biodegraded 100% by *Pseudomonas* sp. no. 34, immobilised in gel beads of α-carrageenan in 20 hr (1).

A solution containing 200 μg l^{-1} was treated with a bio-activated carbon filter with *Bacillus cereus* at 25°C. The degradation rate was 39% at a filtration rate of 382 m day^{-1} (2).

>70% degradation after an initial concentration of 1.5 mg l^{-1}, after 2.4 min contact with bioactivated carbon filter seeded with *Bacillus subtilis* (3).

Abiotic removal

50% removal reported in distilled water; 80-100% in pilot plant studies with ozone treatment (4,5).

For an initial concentration of 0.1 μg l^{-1}, 100% removal by treatment with 15 mg l^{-1} powdered activated carbon (6).

Genotoxicity

Salmonella typhimurium Ames mutagenicity assay negative (details unspecified) (7).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

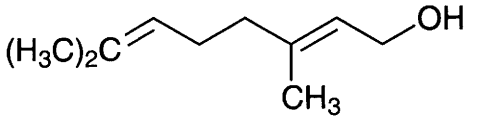
Odour threshold 0.004-2.0 μg l^{-1} in water, and 0.6-6.5 μg l^{-1} in fish (9,10).

References

1. Kitano, M. et al *Bokin Bobai* 1991, **19**(6), 275-280 (Japan.) (*Chem. Abstr.* **115**, 230504q).
2. Yagi, M. et al *Nogaku Kenkyu* 1991, **64**(4), 247-252, (Japan.) (*Chem. Abstr.* **115** 213971x).
3. Yagi, M. et al *Water Sci. Technol.* 1988, **20**(8-9), 255-260.
4. Tamsumi, S. *Proc. 8th Ozone World Congress* September 1987, Zurich, Switzerland.
5. Yasutake, S. et al *Proc. 8th Ozone World Congress* September 1987, Zurich, Switzerland.
6. Lalezary-Craig, S. et al *J. Am. Water Works Assoc.* 1988, **80**(3), 73-80.

7. *US EPA Genotoxicity Program* 1988.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
9. Persson, P. *Water Res.* 1980, **14**, 1113-1118.
10. Mallevialle, A. et al *Identification and treatment of tastes and odours in drinking water* 1987, American Water Works Association, Denver, CO, USA

G12 geraniol



$C_{10}H_{18}O$ **Mol. Wt.** 154.25 **CAS Registry No.** 106-24-1

Synonyms (*E*)-3,7-dimethyl-2,6-octadien-1-ol; 2,6-dimethyl-2,6-octadien-8-ol; Lemonol; (*E*)-geraniol; Meranol

EINECS No. 203-377-1 **RTECS No.** RG 5830000

Uses In perfumery. Insect attractant.
Occurrence Chief part of Oil of Rose and Oil of Palmarosa. Also in citronella, lemon grass and other aromatic oils.

Physical properties

M. Pt. 15°C **B. Pt.** 229-230°C at 757 mmHg **Flash point** 76°C **Specific gravity** 0.8894 at 20°C with respect to water at 4°C
Solubility Organic solvents: miscible with diethyl ether, ethanol

Environmental fate

Degradation studies
Pseudomonas putida variants can develop an enhanced ability to metabolise geraniol (1).
Bacteria from sewage can be induced to use geraniol as their sole carbon source (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3.6 g kg^{-1} (3).
The olfactory epithelium of dogs exposed for 4 hr to 0.5 g m^{-3} showed no change in enzyme acitivity. Some evidence for impairment in discrimination of ♀ pheromones in ♂ dogs was seen (4).

Teratogenicity and reproductive effects
Chick embryos injected with 190 μg on day-3 of incubation. Weak positive embryotoxic effects were seen. Malformations mostly involved skeletal or limb structures (5).

Metabolism and toxicokinetics
Compound is metabolised in rat and guinea pig microsomal preparations by uridine diphosphate-glucuronyl transferase activity induceable by phenobarbitone pretreatment, but not by 3-methyl cholanthrene pretreatment (6).

Sensitisation
No potentiation of the immediate allergic reaction was seen in an *in vitro* test using basophilic leukaemic cells (7). Hypersensitivity had been reported (8).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with metabolic activation negative (9).
Salmonella typhimurium TA100 with and without metabolic activation negative (10).
In vitro Chinese hamster fibroblasts chromosomal aberrations without metabolic activation positive with evidence of polyploidism (9).
In vitro mouse micronucleus test negative (11).

Other comments

Antibacterial action against *Clostridium botulinum* has been reported (12).

References

1. Vadenbergh, P. A. *U.S. Patent Applic.* 496.140 19 May 1983.
2. Shukla, O. P. et al *Can. J. Microbiol.* 1987, **33**(6), 489-497.
3. *Food Cosmet. Toxicol.* 1964, **2**, 327.
4. Kostrodymov, N. N. et al *Gig. Sanit.* 1987 (12), 79-80 (Russ.) (*Chem. Abstr.* **110**, 2073432).
5. Abramovici, A. et al *Toxicology* 1983, **29**, 143-156.
6. Boutin, J. A. et al *Biochem. Pharmacol.* 1985, **34**, 2235-2249.
7. Tanaka, Y. *Eisei Kagaku* 1991, **37**(5), 370-378.
8. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
9. Ishidate, M. *Food Chem. Toxicol.* 1984, **22**(8), 623-636.
10. Lutz, D. et al *Mutat. Res.* 1982, **93**, 305-315.
11. Hayashi, M. et al *Hen'igen to Dokusei* 1981, **4**, 80.
12. Ueda, S. *Nippon Shokuhin Kogyo Gakkaishi* 1982, **29**(7), 389-392

G13 germanium tetrahydride

GeH_4

GeH_4 **Mol. Wt.** 76.64 **CAS Registry No.** 7782-65-2

Synonyms germane; germanium hydride; monogermane; tetrahydrogermane

EINECS No. 231-961-6 **RTECS No.** LY 4900000

Uses Catalyst. In chemical vapour deposition of silicon-germanium films in the manufacture of semi-conductors.

Physical properties

M. Pt. –165°C **B. Pt.** –90°C **Specific gravity** 1.523 at –142°C with respect to water at 4°C

Occupational exposure

FR-VME 0.2 ppm (0.6 mg m^{-3})
UK-LTEL 0.2 ppm (0.64 mg m^{-3}) **UK-STEL** 0.6 ppm (1.9 mg m^{-3})
US-TWA 0.2 ppm (0.63 mg m^{-3})

UN No. 2192 **Conveyance classification** toxic gas, danger of fire (flammable gas)

Environmental fate

Abiotic removal

Gaseous germanium tetrahydride is removed from industrial waste gases by sorption into a porous oxide carrier (silica gel or alumina) coated with hydrated copper sulfate which is then dehydrated at 150-200°C (1).

Mammalian & avian toxicity

Acute data

Inhalation mouse (1 hr) 480 mg m^{-3} lethal (2).
Inhalation mouse (1/2 hr) 610 mg m^{-3} ultimately lethal (2).

Sub-acute and sub-chronic data

Inhalation rat (30 day) 13-170 mg m^{-3} 4 hr day^{-1} did not cause visible signs of intoxication. Autopsy revealed occasional haemorrhages with gliotic nodules in the brain (3).

Genotoxicity

Germanium compounds are not mutagenic, and under certain circumstances may inhibit the mutagenic activity of other substances (4).

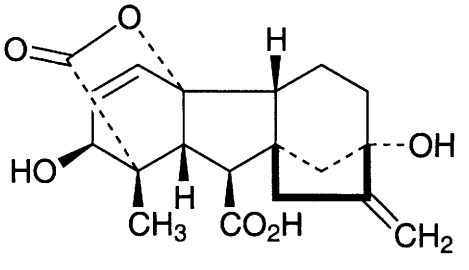
Other comments

Mutagenicity, carcinogenicity and teratogenicity of germanium compounds reviewed. Germanium is considered to be an element of rather low risk to man (4).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).
Miscible with aqueous sodium hypochlorite and hot hydrochloric acid.

References

1. Goekcek, C. (Messer Griesheim GmbH) Ger. Offen. DE 3,802, 496 (bl. Bo1J20/02) 10 Aug. 1989.
2. Paneth, F. et al *Ber. Dtsch. Chem. Ges.*1924, **57**, 1925.
3. Filov, V. A. et al (Eds.) *Harmful Chemical Substances* 1993, **1**, 531-538.
4. Garber, G. B. et al *Mutat. Res.* 1997, **387**(3), 141-146.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G14 gibberellic acid



$C_{19}H_{22}O_6$ **Mol. Wt.** 346.38 **CAS Registry No.** 77-06-5

Synonyms (+)-gibberellic acid; gibberellin A3; 3*S*,3a*S*,4*S*,4a*S*,7*S*,9a*R*,9b*R*,12*S*)-7,12-dihydroxy-3-methyl-6-methylene-2-oxoperhydro-4a,7-methano-9b,3-propeno[1,2-*b*]furan-4-carboxylic acid; (1α,2β,4aα,4bβ,10β)-2,4a,7-trihydroxy-1-methyl-8-methylenegibb-3-ene-1,10-dicarboxylic acid, 1,4a-lactone; 2β,4α,7-trihydroxy-1-methyl-8-methylene-4aα,4bβ-gibb-3-ene-1α,10β-dicarboxylic acid 1,4*a*-lactone; Acibel; Activol; Fitostim; Fructyben; Gibefol; Gibrel

EINECS No. 201-001-0 **RTECS No.** LY 8990000

Uses Plant growth regulator. Additive in the malting of barley.
Occurrence Plant growth hormone, produced by *Giberella fujikuroi* and present in higher plants.

Physical properties

M. Pt. 227°C (decomp.)
Solubility Water: 5 g l^{-1} at 20°C. Organic solvents: acetone, diethyl ether, ethanol, ethyl acetate, methanol

Ecotoxicity

Fish toxicity
No fatality or observable adverse effects to stickleback and rainbow trout exposed to 10 ml l^{-1} for 24 hr (1).

Environmental fate

Abiotic removal
Hydrolysis $t_{1/2}$ ~14 days at pH 3-4, 14 days at pH 7 (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 6300 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral rat, dog (90 day) no-adverse-effect level > 1000 mg kg^{-1} diet (4).
Inhalation rat (21 day) 400 g m^{-3} 2 hr day^{-1} caused no adverse effects (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (5,6).
In vitro human lymphocytes, chromosomal aberrations positive (metabolic activation not stated) (7).
Induced gene regulation elements in barley aleurone cells *in vitro* (8).

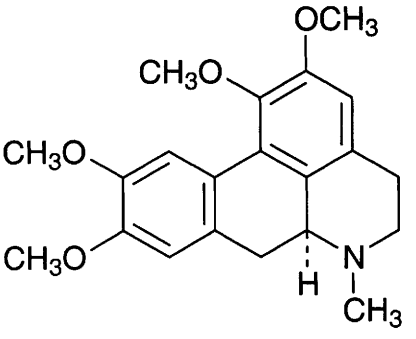
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).
WHO Class Table 5 (11).
EPA Toxicity Class III (2).

References

1. McPhee, C. et al *Lethal Effects of 2014 Chemicals to Fish* 1989, EPA 560/6-89-001; PB89-156-715, Washington, DC, USA.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Thomson, W. T. et al *Agricultural Chemicals* 1976/77, **3**, 43.
4. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
5. Zeiger, E. et al *Environ. Mol. Mutagen.* 1987, **9**(Suppl.9), 1-109.
6. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
7. Zalinyan, G. G. et al *Tsitol. Genet.* 1990, **24**(3), 31-34, (Russ.) (*Chem. Abstr.* **114**, 96582n).
8. Salemenkallio, M. et al *Monogr. – Eur. Brew. Conv.* 1990, **15**, 32-35.
9. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

G15 D-glaucine



$C_{21}H_{25}NO_4$ **Mol. Wt.** 355.43 **CAS Registry No.** 475-81-0

Synonyms 5,6,6a,7-tetrahydro-1,2,9,10-tetramethoxy-6-methyl-4*H*-dibenzo[*de,g*]quinoline; 1,2,9,10-tetramethoxyaporphine; boldine dimethyl ether; Bromcholitin; *O,O*-dimethylboldine

EINECS No. 207-501-5 **RTECS No.** CE 0925000

Uses Strong activity as cough suppressant, usually used as hydrobromide or hydrochloride.

Occurrence In species such as *Glaucium flavum* and in varieties of Papaveraceae and *Dicentra* species.

Physical properties

M. Pt. 120°C

Solubility Organic solvents: acetone, chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 434, 545 mg kg^{-1}, respectively (1).

LD_{50} intraperitoneal rat, mouse 143, 167 mg kg^{-1}, respectively (1).

Other effects

Any other adverse effects

Reduces nociception (2).

It also affects α-adrenoceptors in mice and rats and influences mono-amino oxidase (2-4).

Other comments

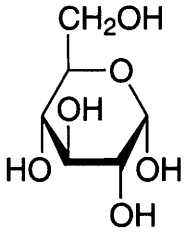
Can suppress cell growth in culture in mouse cell lines leukaemia P388 and L1210, melanoma B16, bladder cancer MBC_2 and colon cancer (colon 26) (5).

The therapeutic use and potential have been reviewed (6,7).

References

1. *Farmakol. Toksikol. (Moscow)* 1983, **46**(4), 100.
2. Zetler, G. *Arch. Int. Pharmacodyn. Ther.* 1988, **296**, 255-281.
3. Han, B. Y. et al *Yaoxue Xuebao* 1988, **33**(1), 806-811 (Ch.) (*Chem. Abstr.* **111**, 126804u).
4. Stancheva, S. et al *Dokl. Bolg. Akad. Nauk* 1989, **42**(9), 107-109.
5. Kondo, Y. et al *J. Pharmacobiodyn.* 1990, **13**(7), 426-431.
6. Gastpar, H. et al *Curr. Med. Res. Opin.* 1984, **9**, 21-27.
7. Ruhle, K. H. *Br. J. Clin. Pharmacol.* 1984, **17**, 521-524

G16 α-glucose



$C_6H_{12}O_6$ **Mol. Wt.** 180.16 **CAS Registry No.** 492-62-6

Synonyms α-D-glucose; α-D-glucopyranose

EINECS No. 207-757-8 **RTECS No.** LZ 6600000

Uses As a fluid and nutrient replenisher by oral and intravenous routes.

Occurrence The α-form of D-glucose is the principal monosaccharide of plants, animals and microorganisms. Occurs free and in di-, oligo- and polysaccharides.

Physical properties

M. Pt. 153-156°C

Solubility Water: 0.9 g ml^{-1}. Organic solvents: acetone, aniline, ethanol, pyridine

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rabbit 35 g kg^{-1} (1).

Metabolism and toxicokinetics

The metabolism of α-D-glucose by isolated rat liver has been reviewed (2).

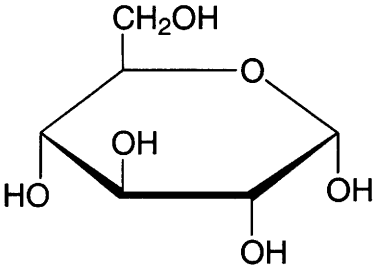
Other comments

When dissolved in water, some converts to β-D-glucose (64%) and a small amount to the open-chain form (0.02%). The physiological, biochemical and functional differences between α-D-glucose and β-D-glucose have been reviewed (3).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. Canioni, P. *Diabetes Metab.* 1987, **13**(4), 395-403 (Fr.) (*Chem. Abstr.* **108**, 18692k).
3. Okuda, J. *J. Clin. Biochem. Nutr.* 1986, **61**(3), 189-199

G17 D-glucose



$C_6H_{12}O_6$ **Mol. Wt.** 180.16 **CAS Registry No.** 50-99-7

Synonyms dextrose; blood sugar

EINECS No. 200-075-1 **RTECS No.** LZ 6600000

Uses As a fluid and nutrient replenisher, both by oral and intravenous routes. In confectionery.

Occurrence Principal monosaccharide of animals, plants and microorganisms. Occurs in free state, and in di-, oligo- or polysaccharides.

Physical properties

M. Pt. 83°C

Solubility Water: 1 kg l^{-1}. Organic solvents: ethanol

Environmental fate

Nitrification inhibition

In a loam clay soil, with added glucose, nitrogen originating from denitrification increased up to the 10th day of incubation (1).

Degradation studies

Glucose is mainly incorporated into soil as new carbohydrates, polymethylene and carboxyl carbon. Microbial activity is responsible for the accumulation of polymethylene in soils (2).

Wastewaters can be treated with powdered carbon and by anaerobic degradation in continuous stirred tank maintained at pH 6.9-7.2 (3,4).

When present in stream water at 1.8 μg l^{-1}, 22% has been found to be converted into CO_2 within 3 days (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 26 g kg^{-1} (6).

LD_{50} intravenous mouse 9 g kg^{-1} (7).

LD_{50} intravenous rabbit 35 g kg^{-1} (8).

Teratogenicity and reproductive effects

In studies with cultured rat embryos, 48 hr exposure to 9500 mg l^{-1} glucose caused growth retardation and severe malformations (9).

Hamsters injected on days 6, 7 and 8 of pregnancy with 4 g kg^{-1} on five occasions developed alternating hypo- and hyperglycaemia. The placentas were enlarged and foetuses developed small urinary bladders, microphalmia and skeletal abnormalities (10).

Metabolism and toxicokinetics

Glucose is present in human blood, normally at a concentration in adults of 600-1000 mg l^{-1} (11).

When orally administered, glucose is rapidly absorbed by carrier-mediated transport. Transport into tissues of the

body is similarly mediated except for transport into brain tissue, which is by passive diffusion (12,13).
The major fate of glucose in the body is catabolism to yield energy, CO_2 and water, but by virtue of entering the carbohydrate and fat pool, it may be utilised in a variety of biochemical processes (14).
Glucose is not normally eliminated in urine, but in subjects with diabetes mellitus, high plasma glucose levels result in high levels of glucose being filtered by the kidney and an inability of kidney tubules to reabsorb all filtered glucose (14).
Glucose present in the small intestine has the ability to enhance water absorption and to affect the passive absorption of drugs such as salicylates and sulfanilamide (15,16).
Glycolysis, which gives rise to lactic acid, can be anaerobic or aerobic (17).

Other effects

Other adverse effects (human)

Metabolism of glucose by microorganisms such as *Streptococcus sanguis* in plaque present on teeth, results in acid-mediated damage to dental enamel (18).
Infusion of hyperosmotic solutions of glucose can cause vein irritation and thrombophlebitis (19).

Other comments

In the absence of normal physiological control, excessively low levels of glucose in plasma do not allow the CNS to receive sufficient glucose, and coma followed by death can result. Excessively high glucose levels lead to loss of glucose in urine, ketosis and water and sodium loss, cardiovascular effects followed by death (14).
In rats maternal hyperketonaemia in early gestation contributes to increased embryo resorption (20).
Below 50°C α-D-glucose hydrate is the stable form. Above 50°C the anhydrous form is obtained and at higher temperatures β-D-glucose is formed. When dissolved in water an equilibrium is established with 64% as β-D-glucose, 0.02% open chain form and 36% α-D-glucose.

References

1. Drazdak, K. et al *Sci. Agric. Bohemoslov.* 1987, **19**(2), 81-86.
2. Baldock, J. A. et al *Environ. Sci. Technol.* 1990, **24**(4), 527-530.
3. *U.S. Dept. Interior FWPCA Summary Report* 1968 Publ. WP-20-AWTR-19.
4. Nakamura, M. et al *Sci. Technol.* 1991, **24**(5), 141-147.
5. Boethling, R. S. *Environ. Sci. Technol.* 1979, **13**(8), 989-991.
6. Boyd, E. M. *Toxicology of Pure Foods* CRC Press, Cleveland, OH, USA.
7. *Arzneim.-Forsch.* 1968, **18**, 666.
8. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
9. Eriksson, U. V. et al *Diabetologia* 1991, **34**(5), 325-331.
10. Gale, T. F. et al *Teratology* 1991, **44**(2), 193-202.
11. Fales et al *Stand. Methods Clin. Chem.* 1963, **4**, 101.
12. Csaky, T. Z. et al *Proc. Soc. Exp. Biol. Med.* 1966, **122**, 860.
13. Ugolev, A. M. et al *Comp. Biochem. Physiol., A: Comp. Physiol.* 1986, **85A**(4), 593-612.
14. Vander et al (Eds.) *Human Physiology: The Mechanisms of Body Function* 1980, McGraw-Hill, New York, NY, USA.
15. Ombaka, E. M. A. et al *J. Pharm. Pharmacol.* 1989, **41**(11), 737-742.
16. Mayersohn, M. et al *J. Pharm. Sci.* 1971, **60**, 225.
17. Hata, S. et al *J. Dent. Res.* 1990, **69**(6), 1244-1247.
18. De Jong, M. H. *FEMS Microbiol. Ecol.* 1986, **38**(6), 341-345.
19. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
20. Chang, S. et al *Nutr. Res. (NY)* 1988, **8**(7), 777-787

G18 glufosinate-ammonium

$$CH_3P(O)(OH)CH_2CH_2CH(NH_2)CO_2NH_4$$

$C_5H_{15}N_2O_4P$ **Mol. Wt.** 198.16 **CAS Registry No.** 77182-82-2

Synonyms 4-[(hydroxymethyl)phosphinoyl]-DL-homoalanine; ammonium-DL-homoalanin-4-yl(methyl)-phosphinic acid; ammonium (±)-2-amino-4-(hydroxymethylphosphinyl)butanoate; Basta; Buster; Challenge; Dash; Eagle; Finale; Harvest; Ignite

EINECS No. 278-636-5 **RTECS No.** EK 7713600

Uses Fungicide. Herbicide.

Physical properties

M. Pt. 215°C **Specific gravity** 1.4 at 20°C

Solubility Water: 1370 g l^{-1} at 22°C. Organic solvents: low solubility in acetone, ethanol, ethyl acetate, hexane, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 320-580 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} contact bee >100 µg bee^{-1} (1).

10 mg l^{-1} caused a transient reduction in live phytoplankton cells, which was particularly apparent in the small (1-2 and 2-3 µm) classes. The impact on live cell numbers was mirrored by a reduction in dissolved oxygen content in the treated enclosures (2).

Environmental fate

Degradation studies

Soil $t_{1/2}$ 3-20 days (1).

Adsorption and retention

The degradation and leaching of glufosinate-ammonium was studied in a forest environment. The maximum leaching depth was 10 cm (humic layer) and the DT_{50} was 4.3 days. At 32 days 10-20% of the parent compound and its metabolites (3-methylphosphinylpropionic acid and 2-methylphosphinylacetic acid) remained in the soil. Metabolites did not leach beyond 10 cm. The following season (day-295) residue levels were near to zero (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂ mouse 430 mg kg^{-1} (1).

LD_{50} oral dog 200-400 mg kg^{-1} (1).

LD_{50} oral rat 1600-2000 mg kg^{-1} (1).

LC_{50} (8 day) oral bobwhite quail >5000 mg kg^{-1} in diet (1).

LD_{50} dermal rat >4000 mg kg^{-1} (1).

LD_{50} subcutaneous rat, mouse 60-100 mg kg^{-1} (4).

LD_{50} intraperitoneal rat, mouse 80-100 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Oral mouse (2 yr) 0, 20 or 80 (in ♂ only) or 160 (in ♀ only) mg kg^{-1} diet. Survival rate in the high-dose ♂ mice was reduced. Glutathione levels which were only studied in ♂ animals, were reduced in a dose-dependent manner. There was no increase in the incidence of tumours (5).

Teratogenicity and reproductive effects

Oral rat, 2-generation study, 0, 40, 120 or 360 mg kg^{-1} diet. The only treatment-related effect observed was a reduction in the number of live pups for the high-dose group (6).

Gavage rat 0, 10, 50 or 250 mg kg^{-1} day^{-1} on days 6-15 of gestation. Maternal toxicity, enlarged adrenal glands and smaller spleens, was observed in the 50 and 250 mg kg^{-1} groups. Evidence of embryrotoxicity was also shown in the groups by more frequent distension of the renal pelvis and ureter. Retented ossification was also evident in foetuses in the high-dose group (7).

Mouse embryos (8-12 days old) were cultured (24-48 hr) in medium containing glufosinate-ammonium (10-20 μg ml^{-1}). The results indicate that glufosinate-ammonium is embryotoxic *in vitro*. In addition to causing growth retardation, it specifically altered the neuroepithelium of the brain vesicle and neural tube, leading to neuroepithelial cell death (8).

Metabolism and toxicokinetics

Following oral administration of ^{14}C-labelled substance, maximum blood levels were attained after 1 hr. Elimination $t_{1/2}$ was 4 hr, principally via the urine (~90%) and the faeces (~10%). After 7 days 0.1-1.3% of radioactivity was found incorporated, particularly in the liver and kidneys. Metabolism involved oxidative deamination yielding 3-methylphosphinico-propionic acid (4).

Sensitisation

Found to be non-sensitising in guinea pig patch test (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (10).

Escherichia coli WP2 with and without metabolic activation reverse mutation assay negative (10).

In vitro primary rat hepatocytic, unscheduled DNA synthesis negative (11).

In vitro mouse lymphoma L5178Y tk^+tk^- with and without metabolic activation forward mutation assay negative (12).

Mouse bone marrow micronucleus test negative in ♂ and ♀ mice (13).

In vitro human lymphocytes chromosomal aberrations negative (14).

In vivo mouse micronucleated polychromatic erythrocytes negative (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (16).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (17).

WHO Toxicity Class III (glufosinate) (18).

EPA Toxicity Class III (1).

Tolerable human daily intake 0.02 mg kg^{-1} day^{-1} (4).

Other comments

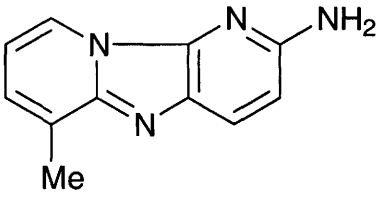
Toxicity of glufosinate reviewed (4).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Faber, M. J. et al *Environ. Toxicol. Chem.* 1998, **17**(7), 1282-1290.
3. Faber, M. J. et al *J. Agric. Food Chem.* 1997, **45**(9), 3672-3676.
4. Ebert, E. et al *Food Chem. Toxicol.* 1990, **28**(5), 339-349.
5. Suter, P. et al *2-Year Oncogenicity Study in Mice. Dietary Administration* 1986, Research and Consulting Co., AG Report No. 018527.
6. Becker, H. et al *Multiple Generation Study in Rats* 1986, Research and Consulting Co., AG Report No.018483.
7. Baedr, C. et al *Testing for the Embryotoxicity in Wistar Rats Following Oral Administration* 1985, Hoechst Report Nos. 85-748 and 85.0771.
8. Watanabe, T. et al *Teratog., Carcinog., Mutagen.* 1997, **16**(6), 287-299.

9. Ullman, L. et al *Contact Hypersensitivity in Albino Guinea Pigs – Buehler Test* 1985, Research and Consulting Co., AG Report No.053010.
10. Othaki, Y. et al *In Vitro Microbial Assay for Mutagenicity Testing* 1981, Nomura Research Institute, Report No.81-7359.
11. Cifone, M. A. et al *Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay* 1984, Litton Bionetics Inc. Report No.20991.
12. Cifone, M. A. et al *Mouse Lymphoma Forward Muatation Assay* 1985, Litton Bionetics Inc., Report No. 20989.
13. Gebel, T. et al *Arch. Toxicol.* 1997, **71**(3), 193-197.
14. Pirovano, R. et al *In Vitro Study of Chromosome Aberrations in Cultured Human Lymphocytes* 1985, Institute di Ricerche Biomedichi, Report No. M711.
15. Jung, R. et al *Micronucleus Test in Male and Female NMRI Mice after Oral Administration* 1986, Hoechst Report No.86. 1307.
16. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
17. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
18. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

G19 Glu-P-1



$C_{11}H_{10}N_4$ **Mol. Wt.** 198.23 **CAS Registry No.** 67730-11-4

Synonyms 2-amino-6-methyldipyrido[1,2-*a*:3′,2′-*d*]imidazole; 6-methyldipyrido[1,2-*a*:3′,2′-*d*]imidazol-2-amine

Occurrence Not known to occur in nature.

Physical properties

M. Pt. 226°C

Solubility Organic solvents: chloroform, dimethyl sulfoxide

Environmental fate

Abiotic removal

Degraded by chlorinated tap water with loss of mutagenicity towards *Salmonella typhimurium* TA98 and TA100. Half-life of 10 μM Glu-P-1 in the presence of 1.5 ppm Cl, $t_{1/2}$ 30-60 secs (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification Group 2B (2).

Oral F344 rats (104 wk) administered 500 ppm Glu-P-1 in pellet diet daily developed tumours in the colon, small intestine, liver, Zymbal gland, clitoral gland and brain (3,4).

Intraperitoneal neonatal ♂ B6C3F1 mice administered Glu-P-1 at two dose levels (5-10,000-fold less than employed in standard chronic bioassays) on days 1, 8 and 15 after birth exhibited a significant incidence of hepatic adenomas at 8 and 12 months compared with DMSO controls (5).

Oral CDF1 mice, 500 ppm in a pellet diet daily, developed a high incidence of hepatocellular carcinomas and haemangioendothelial sarcomas in the brown adipose tissues (6).

Metabolism and toxicokinetics

Rats administered [^{14}C]Glu-P-1 by gavage excreted *c.* 50% in the faeces and *c.* 35% in the urine within 24 hr. The excretion of radioactive label in the bile increased gradually with time to *c.* 60% of the total by 24 hr. *N*-Acetyl-Glu-P-1 was the major metabolite found in bile. The level of radioactivity found in plasma protein fractions reached a maximum at *c.* 24 hr and fell to non-detectable levels 6 days later. Glu-P-1 was found bound to erythrocyte β-globulins and serum proteins, including albumins (7).

The mean levels of Glu-P-1 and *N*-acetyl-Glu-P-1 in human 24-hr urine samples were 0.53 and 0.41 pmol, respectively. *N*-Acetyltransferase activity with Glu-P-1 occurs in the cytosolic fractions from rat kidneys and human autopsy kidney speciments, which suggests that tissues other than those of the liver may carry out significant *N*-acetylation of Glu-P-1 (6).

Genotoxicity

Salmonella typhimurium/C57BL/6N mouse hepatocyte system weakly positive (8).

Salmonella typhimurium TA98, TA100 with metabolic activation positive (9).

Salmonella typhimurium TA98 with metabolic activation (S-9 fraction prepared from liver of untreated ♂ rhesus monkey) positive (10).

Induction *in vivo* of chromosome aberrations and sister chromatid exchange in F433 rat hepatocytes positive (11).

Chinese hamster lung cells (using diphtheria toxin resistance as the marker of mutagenicity) with metabolic activation positive (12).

Other effects

Any other adverse effects

Experimental evidence suggests that administration of Glu-P-1 to ♂ F344 rats induces P-448 isoenzymes, particularly cytochrome P-448H (P450LA2), which mediate mutagenic activation of the compound (13).

Other comments

Pyrolysis product of D-glutamic acid. Found in cooked food.

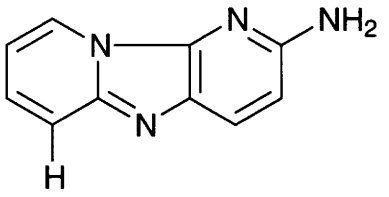
N-Hydroxylation of aromatic amines by hepatic microsomes and their conversion to mutagens reviewed (14).

Occurs in Japanese ranyu (oil of charred egg yolk) at a minimum content of 4.8 ng g^{-1} (15).

References

1. Tsuda, M. et al *Mutat. Res.* 1983, **119**(1), 27-34.
2. *IARC Monograph* 1986, **40**, 230.
3. Masuda, M. et al *Exp. Pathol.* 1984, **26**(3), 123-129.
4. Takayama, S. et al *Gann* 1984, **75**(3), 207-213.
5. Dooley, K. L. et al *Cancer Lett. (Shannon, Irel.)* 1992, **62**(3), 205-209.
6. Kanai, Y. et al *Nippon Eiseigaku Zasshi* 1991, **46**(4), 922-929.
7. Sato, S. et al *EHP, Environ. Health Perspect.* 1986, **67**, 105-109.
8. Hayashi, S. et al *Jpn. J. Cancer Res. (Gann)* 1985, **76**(9), 835-845.
9. Takeda, K. et al *Carcinogenesis (N.Y.)* 1980, **1**(11), 889-892.
10. Ishida, Y. et al *Toxicol. In Vitro* 1987, **1**(1), 45-48.
11. Sawada, S. et al *Mutat. Res.* 1991, **251**(1), 59-69.
12. Terada, M. et al *EHP, Environ. Health Perspect.* 1986, **67**, 117-119.
13. Degawa, M. et al *Carcinogenesis (London)* 1989, **10**(6), 1119-1122.
14. Kato, R. et al *EHP, Environ. Health Perspect.* 1983, **49**, 21-25.
15. Kato, T. et al *Mutat. Res.* 1990, **240**(4), 259-266

G20 Glu-P-2



$C_{10}H_8N_4$ **Mol. Wt.** 184.20 **CAS Registry No.** 67730-10-3

Synonyms dipyrido[1,2-*a*:3′,2′-*d*]imidazol-2-amine; 2-aminodipyrido[1,2-*a*:3′,2′-*d*]imidazole

Physical properties

M. Pt. 286-287°C (hydrobromide salt)

Solubility Organic solvents: chloroform, dimethyl sulfoxide

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No data for carcinogenicity to humans, sufficient evidence for carcinogeneicity to animals, IARC classification Group 2B (1).

Oral F344 rats (104 wk) administered 500 ppm Glu-P-2 in pellet diet daily developed tumours in the colon, small intestine, liver, Zymbal gland, clitoral gland and brain (2,3).

Metabolism and toxicokinetics

The mean levels of Glu-P-2 and *N*-acetyl-Glu-P-2 in human 24-hr urine samples were 2.12 and 4.60 pmol, respectively. *N*-Acetyltransferase activity with Glu-P-2 occurs in the cytosolic fractions from rat kidneys and human autopsy kidney specimens as well as those from liver specimens, which suggests that tissues other than those of the liver may carry out significant *N*-acetylation of Glu-P-2 (4).

Genotoxicity

Chinese hamster V79 cells (using 6-thioguanine resistance as the marker of mutagenicity) with metabolic activation positive (5).

Salmonella typhimurium TA98 with metabolic activation (S-9 fraction prepared from liver of untreated ♂ rhesus monkey) weakly positive (6).

Chinese hamster lung cells (using diptheria toxin resistance as the marker of mutagenicity) with metabolic activation positive (7).

Induction of *in vivo* chromosome aberrations and sister chromatid exchange in F433 rat hepatocytes positive (8).

Salmonella typhimurium/C57BL/6N mouse hepatocyte system positive (9).

Other effects

Any other adverse effects

Experimental evidence suggests that administration of Glu-P-2 to ♂ F344 rats induces P-448 isoenzymes, particularly cytochrome P-448H (P450LA2) which mediate mutagenic activation of the compound (10).

Other comments

Pyrolysis product of L-glutamic acid. Found in cooked foods.

Detected in grilled cuttlefish at 350 μg kg^{-1} (11).

References

1. *IARC Monograph* 1986, **40**, 240.
2. Masuda, M. et al *Exp. Pathol.* 1984, **26**(3), 123-129.
3. Takayama, S. et al *Gann* 1984, **75**(3), 207-213.
4. Kanai, Y. et al *Nippon Eiseigaku Zasshi* 1991, **46**(4), 922-929.
5. Lawson, T. et al *Mutat. Res.* 1994, **325**(4), 125-128.
6. Ishida, Y. et al *Toxicol. In Vitro* 1987, **1**(1), 45-48.
7. Terada, M. et al *EHP, Environ. Health Perspect.* 1986, **67**, 117-119.
8. Sawada, S. et al *Mutat. Res.* 1991, **25**(1), 59-69.
9. Hayashi, S. et al *Jpn. J. Cancer Res. (Gann)* 1985, **76**(9), 835-845.
10. Degawa, M. et al *Carcinogenesis (London)* 1989, **10**(6), 1119-1122.
11. Yamaguchi, K. et al *Gann* 1980, **71**, 743-744

G21 glutaraldehyde

$$OHC(CH_2)_3CHO$$

$C_5H_8O_2$ **Mol. Wt.** 100.12 **CAS Registry No.** 111-30-8

Synonyms glutaric dialdehyde; glutaral; 1,5-pentanedial; Cidex; Sonacide; Protectol GDA; Ucaricide 225

EINECS No. 203-856-5 **RTECS No.** MA 2450000

Uses Acetylating agent. Cross-linking agent. Disinfectant.

Physical properties

M. Pt. -14°C **B. Pt.** 187-189°C (decomp.) **Specific gravity** 0.72 at 20°C with respect to water at 4°C
Volatility v.p. 17 mmHg at 20°C ; v.den. 1.0
Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

DE-MAK 0.1 ppm (0.42 mg m^{-3})
FR-VME 0.1 ppm (0.4 mg m^{-3}) **FR-VLE** 0.2 ppm (0.8 mg m^{-3})
SE-CEIL 0.2 ppm (0.8 mg m^{-3})
UK-LTEL MEL 0.05 ppm (0.2 mg m^{-3}) **UK-STEL** 0.05 ppm (0.2 mg m^{-3})
US-STEL ceiling limit 0.05 ppm
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases Toxic by inhalation and if swallowed – Causes burns – May cause sensitisation by inhalation and skin contact – Very toxic to aquatic organisms (R23/25, R34, R42/43, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S26, S36/37/39, S45, S61)

Ecotoxicity

Invertebrate toxicity
EC_{50} (5 min) *Photobacterium phosphoreum* 76 ppm, Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, guinea pig 50-600 mg kg^{-1} (2-4).
LC_{50} (4 hr) inhalation rat ~10,000 ppm (3).
LD_{50} dermal rabbit 2560 mg kg^{-1} (5).
LD_{50} subcutaneous rat, mouse 1430-2390 mg kg^{-1} (4).
LD_{50} intravenous rat, mouse 15 mg kg^{-1} (4).
LD_{50} intraperitoneal rat, mouse 14-18 mg kg^{-1} (6).
Intranasal rat, instillation of single doses of 2000 or 4000 mg l^{-1} induced extensive lesions including inflammation, epithelial degeneration, respiratory epithelial hypertrophy and squamous metaplasia. 1000 mg l^{-1} did not induce any significant epithelial changes (7).

Carcinogenicity and chronic effects

Inhalation mouse (6 hr day^{-1}, 5 days wk^{-1} for 52 or 78 wks) 100 ppb. In the nasal passage, hyperplasia of the squamous epithelium lining was observed. Epidermal erosion and ulceration as well as squamous inflammatory exfoliation were also observed. The severity of these observations varied with length of exposure (8).

Teratogenicity and reproductive effects

Oral rat (6 month) (sex unspecified) 0.003 mg kg^{-1} day^{-1} did not cause any toxic, embryotoxic or teratogenic effects (2).

Irritancy

Dermal rabbit (24 hr) 500 mg caused severe irritation and 250 µg instilled into rabbit eye caused severe irritation (9).

Genotoxicity

Salmonella typhimurium TA102 and *Escherichia coli* WP2 without metabolic activation positive (10).
Drosophila melanogaster sex-linked recessive lethal assay negative (11).
In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations positive (12).
In vitro mouse lymphoma L5178Y tk^+/tk^- forward mutation assay positive (13).

Other effects

Other adverse effects (human)

Caused skin and upper respiratory irritation, headache, nausea and fatigue in a dose-dependent manner among exposed hospital workers. No case of contact allergy was observed (14).

Legislation

Recommended maximum admissible concentration for reservoir water in former USSR 0.07 mg l^{-1} (2).

Other comments

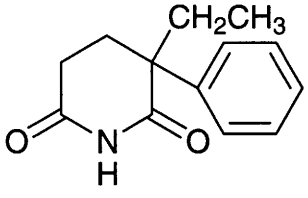
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (15).
Polymerises in water to a glassy form which regenerates the dialdehyde on vacuum distillation (2).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Nichiponenko, V. P. et al *Gig. Sanit.* 1987, (3), 77-79 (Russ.) (*Chem. Abstr.* **107**, 34487g).
3. Kennedy, G. L. et al *Toxicol. Lett.* 1991, **56** (3), 317-326.
4. *Oyo Yakuri* 1980, **19**, 503.
5. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
6. *Iyakuhin Kenkyu* 1979, **10**, 232.
7. St Clair, M. B. G. et al *Toxicol. Pathol.* 1990, **18**(3), 353-361.
8. Zissu, D. et al *Toxicol. Lett.* 1998, **95**(2), 131-139.

9. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 42, Prague, Czechoslovakia.
10. Wilcox, P. et al *Mutagenesis* 1990, **5**(3), 285-291.
11. Zimmoing, S. et al *Environ. Mol. Mutagen.* 1989, **14**(4), 245-251.
12. Rosenkranz, H. S. et al *Environ. Mol. Mutagen.* 1990, **16**(3), 149-177.
13. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **11**(1), 91-118.
14. Norbaeck, D. *Scand. J. Work, Environ. Health* 1988, 14(6), 366-371.
15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G22 glutethimide



$C_{13}H_{15}NO_2$ **Mol. Wt.** 217.27 **CAS Registry No.** 77-21-4

Synonyms 3-ethyl-3-phenyl-2,6-dioxopiperidine; 2-ethyl-2-phenylglutarimide; Alfimid; Doriden; Noxyron; Sarodormin

EINECS No. 201-012-0 **RTECS No.** MA 4725000

Uses Sedative. Hypnotic.

Physical properties

M. Pt. 84°C (*dl* form)

Solubility Organic solvents: acetone, chloroform, diethyl ether, ethanol, ethyl acetate, methanol, petroleum ether

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird and starling >100 mg kg^{-1} (1).

LD_{50} oral mouse, rat 360, 600 mg kg^{-1}, respectively (2).

LD_{50} intraperitoneal mouse 210 mg kg^{-1} (3).

Teratogenicity and reproductive effects

LD_{Lo} oral rabbit 1350 kg^{-1} day^{-1} days 8-16 of gestation caused foetal deaths and musculoskeletal malformations (4).

Metabolism and toxicokinetics

In humans it is irregularly absorbed from the gastro-intestinal tract and is extensively metabolised in the liver. It is excreted in the urine with only 2% in the unchanged form. A small amount (2%) is excreted in the faeces (5).

In humans it has a biphasic plasma $t_{1/2}$ 5-22 hr measured for the terminal phase (5).

Glutethimide can cross the placental barrier and traces have been found in breast milk (5).

Other effects

Other adverse effects (human)

Patients undergoing treatment with glutethimide have had side-effects including: nausea, headache, blurred vision, unwanted sedation and memory loss. In rare incidences hypersensitive reactions, exfoliative dermatitis and blood disorders have been reported (5).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. Usdin, E. et al *Psychotropic Drugs and Related Compounds* 2nd ed., 1972, 233, Washington, DC, USA.
3. *Acta Poloniae Pharmaceutica* 1975, **32**, 243.
4. *Toxicol. Appl. Pharmacol.* 1967, **10**, 244.
5. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK

G23 glyceraldehyde

$$HOCH_2CH(OH)CHO$$

$C_3H_6O_3$ **Mol. Wt.** 90.08 **CAS Registry No.** 56-82-6

Synonyms DL-glyceraldehyde; DL-glyceric aldehyde; (±)-glyceraldehyde; (±)-2,3-dihydroxypropanal

EINECS No. 200-290-0 **RTECS No.** MA 6475000

Physical properties

M. Pt. 144-145°C (*dl*-form) **Specific gravity** 1.455 at 18°C with respect to water at 18°C

Solubility Water: 30 g l^{-1} at 18°C. Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies

Removal from wastewater by activated sludge, 4.9% of ThOD after 6 hr; 9.4% of ThOD after 12 hr; and 20.1% of ThOD after 24 hr (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 2000 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (3).

In vitro Chinese hamster ovary cells (metabolic activation not specified) sister chromatid exchanges and chromosomal aberrations negative (4).

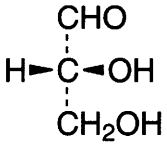
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).

References

1. Gerhold, R. M. et al *J. Water Pollut. Control Fed.* 1966, **38**(4), 562.
2. *J. Pharm. Pharmacol.* 1965, **17**, 814.
3. Yamaguchi, T. et al *Agric. Biol. Chem.* 1983, **47**(11), 2461-2465.
4. Rosenkranz, H. S. et al *Environ. Mol. Mutagen.* 1990, **16**(3), 149-177.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G24 D-glyceraldehyde



$C_3H_6O_3$ **Mol. Wt.** 90.08 **CAS Registry No.** 453-17-8

Synonyms (*R*)-(+)-glyceraldehyde; (*R*)-2,3-dihydroxypropanal

EINECS No. 207-217-1

Physical properties

Flash point > 110°C

Solubility Water: miscible

Environmental fate

Degradation studies

Supported the growth of *Euglena gracilis* as a sole carbon source (1).

References

1. Hosatani, K. et al *J. Gen. Microbiol.* 1988, **134**(1), 61-66

G25 glycerol

$CH_2OHCH(OH)CH_2OH$

$C_3H_8O_3$ **Mol. Wt.** 92.09 **CAS Registry No.** 56-81-5

Synonyms 1,2,3-propanetriol; glycerin; trihydroxypropane; incorporation factor; Ophthalgan; E422; Croderol; Glyrol; Osmoglyn; Superol

EINECS No. 200-289-5 **RTECS No.** MA 8050000

Uses Sweetener. Solvent. Antifreeze. Plastics and chemicals intermediate. Emollient and in diagnostic materials.

Occurrence Present as a component of oils and fats in a wide variety of species, and in a free form. Typical free plasma levels in man 2.9-12.1 mg l^{-1} (1).

Physical properties

M. Pt. 17.8°C **B. Pt.** 182°C at 20 mmHg **Flash point** 160°C **Specific gravity** 1.260 at 20°C

Volatility v.p. 0.0025 mmHg at 50°C ; v.den. 3.17

Solubility Water: miscible. Organic solvents: miscible with ethanol

Occupational exposure

FR-VME 10 mg m^{-3} (aerosol)
UK-LTEL 10 mg m^{-3} (mist)
US-TWA 10 mg m^{-3} (mist)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish >5 g l^{-1} (2).

Invertebrate toxicity
Cell multiplication inhibition test *Pseudomonas putida* >10 g l^{-1}, green algae >10 g l^{-1}, *Entosiphon sulcatum* 3.2 g l^{-1} (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, guinea pig 4.4-7.8 g kg^{-1} (4-6).
LD_{50} intravenous rat 4.4 ml kg^{-1} (7).
In rats, acute toxicity is associated with excitability prior to death. No gross pathological lesions are seen, but histopathological changes occur in kidney (4).
Renal failure can occur (8).

Metabolism and toxicokinetics
Readily absorbed from the gut and ultimately oxidised to CO_2 and water. Some may be excreted unchanged in urine (9).
Glycerol formed in the body by the breakdown of triacylglycerols is converted into glucose and used as an energy source by the liver (10).

Irritancy
Not irritant to skin, but as a mist it is irritant to eyes (11).

Sensitisation
No potentiation of the immediate allergic reaction was seen in an *in vitro* test using basophilic leukaemic cells (12).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with metabolic activation negative (13).
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (14).
Escherichia coli with and without metabolic activation, negative (15).
In vitro Chinese hamster fibroblasts chromosome aberration without metabolic activation negative (13).
In vitro Chinese hamster ovary cells chromosome aberration and sister chromatid exchanges with and without metabolic activation negative (14).
Unscheduled DNA synthesis in hepatocytes negative (14,16).
In vitro rat hepatocytes single strand breaks negative (16).

Other effects

Other adverse effects (human)
Large doses in man cause dizziness, nausea, vomiting, thirst and convulsions. Near fatal doses cause haemoglobinuria and renal failure (11).
An osmotic dehydrating agent. When present in plasma it draws water into the plasma from the extra-vascular space (9).

Any other adverse effects
In pregnant rats receiving a diet low in carbohydrate (4%), lipid-glycerol cannot substitute for glucose as a carbohydrate source (17).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Acute toxicity has been reviewed (7,11).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (19).

References

1. Mueller, J. *J. Lab. Clin. Med.* 1963, **61**, 953.
2. Shell Chemie *Shell Industrie Chemicalien Gids* 1.1. 1975.
3. Bringmann, G. *Water Res.* 1980, **14**, 231-241.
4. Uche, E. M. I. *Res. Commun. Chem. Pathol. Pharmacol.* 1987, **56**(1), 125-128.
5. *Farm. Zh. (Kiev)* 1977, (6), 56.
6. *J. Ind. Hyg. Toxicol.* 1941, **23**, 259.
7. Bartsch, W. et al *Arzneim.-Forsch.* 1976, **26**, 1581.
8. Luke, D. R. *Renal Failure* 1991, **13**(2), 61-69.
9. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
10. Beylot, M. et al *J. Lipid Res.* 1987, **28**(4), 414-422.
11. Caroll, R. J. *J. Pathol. Bacteriol.* 1965, **89**(3), 573-580.
12. Tanaka, Y. *Eisei Kagaku* 1991, **37**(5), 370-378.
13. Ishidate, M. *Food Chem. Toxicol.* 1984, **22**(8), 623-636.
14. Doolittle, D. J. *Food Chem. Toxicol.* 1988, **26**(7), 631-635.
15. Yamaguchi, T. *Agric. Biol. Chem.* 1982, **46**(3), 849-851.
16. Fautz, R. et al *Mutat. Res.* 1991, **260**(3), 281-294.
17. Fergusson, M. A. et al *J. Nutr.* 1990, **120**(1), 1312-1319.
18. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
19. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G26 glycerol trinitrate

$C_3H_5N_3O_9$ **Mol. Wt.** 227.09 **CAS Registry No.** 55-63-0

Synonyms 1,2,3-propanetriol trinitrate; nitroglycerin; trinitroglycerol; trinitrin; blasting gelatin; Cascade; Gelamite D; Hercol 2; Susadrin; Tridil

EINECS No. 200-240-8 **RTECS No.** QX 2100000

Uses Used in human medicine as a vasodilator, particularly in treatment of angina and to relax smooth muscle in a variety of surgical procedures. Veterinary antiasthmatic. Used in production of explosives.

Physical properties

M. Pt. 13°C (stable form) **B. Pt.** 150°C at 15 mm Hg; explodes at 270°C **Specific gravity** 1.5918 at 25°C with respect to water at 4°C **Volatility** v.p. 2.6×10^{-4} mmHg at 20°C
Solubility Water: 1.25 g l^{-1}. Organic solvents: miscible with acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 0.05 ppm (0.47 mg m^{-3}) (only applies for work areas where skin contact with the substance does not occur)
FR-VME 0.1 ppm (1 mg m^{-3})
JP-OEL ceiling limit 0.05 ppm (0.46 mg m^{-3})
SE-LEVL 0.03 ppm (0.3 mg m^{-3}) **SE-STEL** 0.1 ppm (0.9 mg m^{-3})
UK-LTEL 0.2 ppm (1.9 mg m^{-3}) **UK-STEL** 0.2 ppm (1.9 mg m^{-3})
US-TWA 0.05 ppm (0.46 mg m^{-3})
Supply classification explosive, very toxic
Risk phrases Extreme risk of explosion by shock, friction, fire or other sources of ignition – Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R3, R26/27/28, R33)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Take precautionary measures against static discharges – This material and its container must be disposed of in a safe way – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S33, S35, S36/37, S45)

Environmental fate

Degradation studies
Glycerol trinitrate (GTN) was completely mineralised in serum vials under strict anaerobiosis by mixed cultures from an anaerobic digester. Anaerobic biodegredation occurred via successive denitration of GTN and production of glycerol dinitrate (BDN) and glycerol mononitrate (GMN), which were converted into a utilisable carbon source, most likely glycerol. The rates of biodegredation were significantly decreased at each successive denitration, with conversion of GMN into glycerol being the rate limiting step (1).

Abiotic removal
Removal from wastewater associated with manufacture of explosives can be effected by biodegradation following saponification with sodium hydroxide (2).
In the environment degradation is by slow photolysis and biodegradation (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 100-120 mg kg^{-1} (4).
LD_{50} intravenous mouse 11 mg kg^{-1} (5).

Metabolism and toxicokinetics
Subject to virtually complete first-pass metabolism by the liver with consequently little activity when taken orally with $t_{1/2}$ ~2 min. The compound is therefore used therapeutically as a sub-lingual tablet or as an aerosol (3,6,7).
Prolonged exposure to high plasma concentrations of nitrates is thought to result in depletion of sulfydryl groups in smooth muscle cells and a consequent reduction in ability to release the nitric oxide (the active metabolite) from the nitrate moiety (8).
Absorption can occur through the skin (6,9,10).
Metabolism involves glutathione and action by organic nitrate reductase which yields di- and mononitrates (11).

Other effects

Other adverse effects (human)
Acute poisoning produces vomiting, abdominal cramps, convulsions, hallucinations, methaemoglobinaemia and cyanosis leading to death. Chronic poisoning can also include skin rashes (10).
Headache is the most common side-effect, while other effects include flushing, palpitation and hypotension. Tolerance to the side-effects and to the therapeutic effects is well established (12-15).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).
Included in the UK List of Classified and Authorised Explosives 1994. UK Class and Division (5% solution) 3.1. Competent Authority Reference GB 31484 (17).

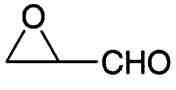
Other comments

Therapeutically, oral activity can be greatly prolonged by use of sustained-release preparations (6).
Metabolism, genotoxicity and carcinogenicity reviewed (3).
Explodes on rapid heating or on concussion. Dynamite includes 75% glycerol trinitrate.

References

1. Christodoulatos, C. et al *Water Res.* 1997, **31**(6), 1462-1470.
2. *Int. Jahrestag. – Frauenhofer-Inst. Treib – Explosivst.* 1987, **18th** (Technol. Energ. Mater.) 76/1-76/8 (Ger.) (*Chem. Abstr.* **107**, 2419492).
3. Smith, J. G. *Energy Res. Abstr.* 1987, **11**(22), Abstr. No. 51876.
4. *Yakuri to Chiryo* 1985, **13**, 3649.
5. *Iyakuhin Kenkyu* 1982, **13**, 90.
6. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
7. Paratt, J. R. *J. Pharm. Pharmacol.* 1979, **31**, 801-809.
8. Francis, G. S. *J. Am. Coll. Cardiol.* 1988, **11**, 1325-1326.
9. De Mots, H. *J. Am. Coll. Cardiol.* 1989, **13**, 786-793.
10. *Patty's Industrial Hygiene and Toxicology* 1982, 3rd ed., **2C**, Wiley-Interscience, New York, NY, USA.
11. Bagaert, M. C. *Clin. Pharmacokinet.* 1987, **12**, 1-11.
12. Thadani, U. et al *Circulation* 1980, **61**, 526-535.
13. Parker, J. O. et al *Circulation* 1983, **68**, 1074-1080.
14. Steering Committee, Transdermal Nitroglycerin Co-operative Study *Am. J. Cardiol.* 1991, **68**, 1263-1273.
15. Thadani, U. et al *Am. J. Cardiol.* 1952, **49**, 411-419.
16. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
17. *UK Explosives Acts, 1875 and 1923. The Classification and Labelling of Explosives Regulations 1983 (CLER). List of Classified and Authorised Explosives 1994 (LOCAE)* 1994, HSE

G27 glycidaldehyde



$C_3H_4O_2$ **Mol. Wt.** 72.06 **CAS Registry No.** 765-34-4

Synonyms epihydrin aldehyde; 2,3-epoxy-1-propanal; 2,3-epoxypropionaldehyde; formyloxirane; glycidal; glycidyl aldehyde; oxiranecarboxaldehyde

EINECS No. 212-143-8 **RTECS No.** MB 3150000

Uses Cross-linking agent. Tanning. Protein insolubilisation.
Occurrence Occurs in sunflower oil. Glycidaldehyde has been detected in rancid samples of commercial lard (1).

Physical properties

M. Pt. –62°C **B. Pt.** 113°C **Flash point** 31°C (open cup) **Specific gravity** 1.1403 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.73 (2) **Volatility** v.p. 27 mmHg at 25°C ; v.den. 2.58
Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2622 **HAZCHEM Code** 2W **Conveyance classification** flammable liquid, toxic

Ecotoxicity

Bioaccumulation

Calculated bioconcentration factor <1 indicated that environmental accumulation is unlikely (2).

Environmental fate

Abiotic removal

Hydrolysis in water and moist soils $t_{1/2}$ estimated to be 28 days (3).

Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in the atmosphere 18 hr (4).

Adsorption and retention

Estimated K_{oc} 10 indicated that adsorption to soil and sediments would be insignificant (2).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 50 mg kg^{-1} (5).

LC_{Lo} (4 hr) inhalation rat 250 mg kg^{-1}. Death was due to lung oedema and resultant shock (6).

LD_{50} dermal rabbit 250 mg kg^{-1} (7).

LD_{Lo} intravenous rabbit 20 mg kg^{-1} (7).

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (8).

Sub-acute and sub-chronic data

Inhalation rat 30, 60, 120 or 235 mg m^{-3} 4 hr day^{-1} for 60 days. The low dose had no effect. 60 and 120 mg m^{-3} resulted in reduced body weight gain. Some effects on the haemopoietic system and some fatalities. Exposure to 235 mg m^{-3} caused death of 8/10 rats before the 5th exposure, with focal necrosis of the liver and kidney. The number of nucleated bone marrow cells was also significantly reduced (7).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (9).

Dermal mouse (18 month) 10 mg 3 × wk^{-1} for life. Skin papillomas developed in 6/41 mice; 3 of these had squamous-cell carcinomas of the skin after 308 days. No skin tumours occurred in 300 acetone-treated controls (10).

Subcutaneous rat, mouse (19 month) wkly injections 3.3 or 0.1 mg to mice, 33 or 1.0 mg to rats induced local sarcomas in 5/30 and 3/50 mice at the two doses, respectively, and 5/20 and 1/50 in rats at the two dose levels, respectively. No local tumours developed in controls (11,12).

Irritancy

Exposure of humans to 1 ppm for 5 min caused moderate eye irritation (7).

Sensitisation

Skin sensitisation has been reported (species not specified) (7).

Genotoxicity

Salmonella typhimurium (strain, metabolic activation unspecified) positive (13).

Saccharomyces cerevisiae S211, induction of reverse base-pair mutations positive (metabolic activation not specified) (14).

In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (15).

In vitro mouse lymphoma L5178Y tk^+/tk^- with metabolic activation positive (6).

Reported to methylate DNA at the guanine residues and at specific cytosine residues dependent upon the DNA conformation (16).

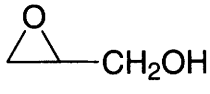
Other comments

Physical properties, use, occurrence, carcinogenicity and mammalian toxicity reviewed (1,17,18).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (19).

References

1. *IARC Monograph* 1976, **11**, 175-181.
2. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods. Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
3. Mabey, W. et al *J. Phys. Chem. Data* 1978, **7**, 383-415.
4. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
5. *Am. J. Hyg.* 1962, **76**, 209.
6. Amacher, D. E. et al *Mutat. Res.* 1982, **97**(1), 49-65.
7. Hine, C. H. et al *Arch. Environ. Health* 1961, **2**, 23-30.
8. *J. Natl. Cancer Inst.* 1979, **62**, 911.
9. *IARC Monograph* 1987, **Suppl.7**, 64.
10. Van Duuren, B. L. et al *J. Natl. Cancer Inst.* 1967, **39**, 1217-1228.
11. Van Duuren, B. L. et al *J. Natl. Cancer Inst.* 1966, **37**, 825-834.
12. Van Duuren, B. L. et al *J. Natl. Cancer Inst.* 1967, **39**, 1213-1216.
13. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
14. Izard, M. C. *C. R. Acad. Sci. (Paris)* 1973, **276**, 3037-3041.
15. Ennever, F. K. et al *Environ. Mutagen.* 1986, **8**(6), 849-865.
16. Kohivi, Y. *Carcinogenesis (London)* 1989, **10**(11), 2035-2042.
17. *Dangerous Prop. Ind. Mater.* 1987, **7**(3), 103-105.
18. *Chemical Safety Data Sheets* 1992, **5**, 148-150, The Royal Society of Chemistry, London, UK.
19. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G28 glycidol



$C_3H_6O_2$ **Mol. Wt.** 74.08 **CAS Registry No.** 556-52-5

Synonyms oxiranemethanol; allyl alcohol oxide; epihydrin alcohol; glycidyl alcohol; 2-(hydroxymethyl)oxirane; 3-hydroxypropylene oxide; oxiranylmethanol

EINECS No. 209-128-3 **RTECS No.** UB 4375000

Uses Chemical intermediate. Alkylating agent. Stabiliser.

Physical properties

M. Pt. –45°C **B. Pt.** 167°C (decomp.) **Flash point** 78°C **Specific gravity** 1.165 at 0°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.95 (1) **Volatility** v.p. 0.9 mmHg at 25°C ; v.den. 2.15
Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 50 ppm (150 mg m^{-3})
FR-VME 25 ppm (75 mg m^{-3})
US-TWA 2 ppm (6.1 mg m^{-3})

Supply classification toxic
Risk phrases Harmful in contact with skin and if swallowed – Toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by inhalation and skin contact (R21/22, R23, R36/37/38, R42/43)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S45)

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy 50 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (unspecified duration) *Selenastrum capricornutum* >100 mg l^{-1} but <1000 mg l^{-1} (2).

Environmental fate

Abiotic removal
Undergoes hydrolysis under alkaline conditions (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 420-430 mg kg^{-1} (4,5).
LC_{50} (4-8 hr) inhalation rat, mouse 450-580 mg kg^{-1} (6).
LD_{50} dermal rabbit 1980 mg kg^{-1} (6).
LD_{50} intraperitoneal rat 200 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Gavage F344 rats, B6C3F1 mice (6 day or 13 wk) both sexes, dose range 37-600 mg kg^{-1}. All high-dose animals died within 3 and 13 days. Oedema and degeneration of the epididymal stroma, atrophy of testis and granulomatous inflammation of the epididymis occurred in ♂. Focal demyelination in the medulla and thalamus of the brain occurred in all ♀ mice (7).

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice via food. Clear evidence for carcinogenicity (dose-related increase in malignant and/or benign neoplasms with an indication that such tumours would progress to malignancy) in ♂ and ♀ rats and mice (7).
Dermal mouse (18 month) 100 mg of 5% solution in acetone 3 × wk^{-1} did not induce tumours of any type (8).
Glycidol was administered orally to rats (0-75 mg kg^{-1}) and mice (0-50 mg kg^{-1}), 5 days wk^{-1} for 2 yr. Dose-related increases in the number of neoplasms were noted in both rats and mice, and mortality in rats and ♀ mice was increased. Major causes of death were due to neoplasms: in the tunica vaginalis and peritoneum in ♂ rats, in the mammary glands in ♀ rats, in the harderian gland and forestomach in ♂ mice, and the harderian gland and mammary gland in ♀ mice. Brain gliomas were increased in both sexes of rats (9).

Teratogenicity and reproductive effects
Gavage mouse, days 6-15 of gestation, 80 mg kg^{-1} caused a significant reduction in weight gain in dams, no evidence of teratogenicity in foetuses at 160 mg kg^{-1}. 120 and 160 mg kg^{-1} were toxic toward both dams and unborn offspring (10).
Oral ♂ rat (12 day) 180 mg kg^{-1} lowest toxic dose caused reproductive effects (11).

Metabolism and toxicokinetics
In mammals, metabolised to glycerol by epoxide hydratase in the liver (12).

Irritancy
Dermal rabbit (3 day) 560 mg caused moderate irritation (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (13).
Escherichia coli PG37 with and without metabolic activation positive (14).
In vitro Chinese hamster V79 cells, sister chromatid exchanges positive (15,16).

Other effects

Any other adverse effects
Can cause stimulation of the central nervous system followed by depression (17).

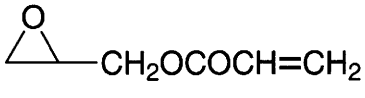
Other comments

Physical properties, safety precautions and toxicity reviewed (18,19).
Data on flammability and explosive potential provided (20).

References

1. Deneer, J. W. et al *Aquat. Toxicol.* 1988, **13**(3), 195-204.
2. Bollman, M. A. et al *Gov. Rep. Announce. Index (U. S.)* 1990, **90**(15), Abstr. No. 039169, EPA/600/3-90/041 PB90-212606.
3. Baradel, A. et al Erimicerche SpA, Eur. Pat. Appl. EP 362934 (Cl. CO2F9/00) 11 April 1990 (*Chem. Abstr.* **113**, 158084s).
4. *Food Cosmet. Toxicol.* 1981, **19**, 347.
5. *Gig. Tr. Prof. Zabol.* 1980, **24**(3), 42.
6. *Arch. Ind. Health* 1956, **14**, 250.
7. *National Toxicology Program Research and Testing Division* 1990, Report No. TR-374, NIEHS, Research Triangle Park, NC, USA.
8. van Duuren, B. L. et al *J. Natl. Cancer Inst.* 1967 **39**, 1217.
9. Irwin, R. D. et al *J. Appl. Toxicol.* 1996, **16**(3), 201-209.
10. *J. Toxicol. Environ. Health* 1982, **9**, 87.
11. *Nature (London)* 1970, **226**, 87.
12. Patel, J. M. et al *Drug Metab. Dispos.* 1980, **8**(5), 305.
13. Canter, D. A. et al *Mutat. Res.* 1986, **172**(2), 105-138.
14. von der Hude, W. *Mutat. Res.* 1990, **231**(2), 205-218.
15. Smith, R. A. et al *Carcinogenesis (London)* 1990, **11**(3), 497-498.
16. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
17. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
18. *Chemical Safety Data Sheets* 1991 **4a**, 236-239, The Royal Society of Chemistry, London, UK.
19. *ECETOC Technical Report No. 71* 1996, European Centre for Exotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
20. Piotrowski, T. et al *Organika* 1986, 55-66 (Pol.) (*Chem. Abstr.* **109**, 196344b)

G29 glycidyl acrylate



$C_6H_8O_3$ **Mol. Wt.** 128.13 **CAS Registry No.** 106-90-1

Synonyms 2,3-epoxypropyl acrylate; oxiranylmethyl 2-propenoate; glycidyl propenate; 2-propenoic acid, oxiranylmethyl ester; 2,3-epoxy-1-propanol acrylate

EINECS No. 203-440-3 **RTECS No.** AS 9275000

Uses Intermediate in organic synthesis.

Physical properties

B. Pt. 53°C at 10 mmHg **Flash point** 60.5°C **Specific gravity** 1.1 at 20°C with respect to water at 20°C
Volatility v.p. 2 mm Hg at 57°C ; v.den. 4.4
Solubility Water: insoluble. Organic solvents: acetone, dimethyl sulfoxide, diethyl ether, ethanol

Occupational exposure

Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Causes burns – May cause sensitisation by skin contact (R23/24/25, R34, R43)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36/37/39, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 210 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 125 ppm (1).
LD_{50} dermal rabbit 400 mg kg^{-1} (2).

Irritancy
Dermal rabbit (24 hr) 100 µg open caused irritation of undefined intensity (1).
Eye rabbit (24 hr) 1 mg caused severe irritation (2).

Genotoxicity

Salmonella typhimurium TA97, TA100, TA1535 with and without metabolic activation positive; TA98 with and without metabolic activation negative (3).
Escherichia coli PQ37, SOS-Chromotest, without metabolic activation positive (4).
In vitro Chinese hamster V79 cells without metabolic activation sister chromatid exchanges positive (5).

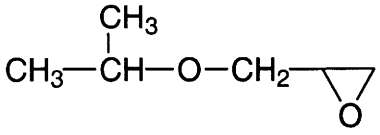
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

References

1. *Am. J. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
2. Sax, N. I. et al *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
3. Canter, D. A. et al *Mutat. Res.* 1986, **172**(2), 105-138.
4. von der Hude, W. et al *Mutat. Res.* 1990, **231**(2), 205-218.
5. von der Hude, W. et al *Mutat. Res.* 1991, **244**(1), 55-70.
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G30 glycidyl isopropyl ether



$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 4016-14-2

Synonyms 1,2-epoxy-3-isopropoxypropane; 2,3-epoxypropyl isopropyl ether; isopropyl glycidyl ether

EINECS No. 223-672-9 **RTECS No.** TZ 3500000

Uses Stabiliser for organic compounds. Intermediate in the synthesis of ethers and esters. Reactive diluent for epoxy resins.

Physical properties

B. Pt. 131-132°C **Flash point** 33°C **Specific gravity** 0.9186 at 20°C with respect to water at 4°C
Volatility v.p. 9.4 mm Hg at 25°C ; v.den. 4.15
Solubility Water: 1880 g l^{-1}. Organic solvents: alcohols, ketones

Occupational exposure

FR-VME 50 ppm (240 mg m^{-3})
UK-LTEL 50 ppm (241 mg m^{-3}) **UK-STEL** 75 ppm (362 mg m^{-3})
US-TWA 50 ppm (238 mg m^{-3}) **US-STEL** 75 ppm (356 mg m^{-3})

Mammalian & avian toxicity

Acute data
LC_{50} inhalation mouse (4 hr) 1500 ppm (1).
LC_{50} inhalation rat (8 hr) 1100 ppm (1).
LD_{50} oral mouse 1300 mg kg^{-1} (1).
LD_{50} oral rat 4200 mg kg^{-1} (1).
LD_{50} dermal rabbit 9650 mg kg^{-1} (1).

Irritancy
Exposure to 459 mg for 3 days caused moderate irritation to rabbit skin (1).
92 mg instilled into rabbit eye (72 hr) caused moderate irritation (1).

Genotoxicity

Escherichia coli PQ37 SOS response positive (2).
Salmonella typhimurium TA98, TA100, TA1535, TA1537 positive (3).
Drosophila melanogaster (2900 ppm in feed) mutagenic in the sex-linked recessive lethal (SLRL) assay, reciprocal translocations also induced (4).
Escherichia coli WP2 uvrA without metabolic activation positive (5).
Escherichia coli WP2 uvrA suffered DNA damage (5).

Other comments

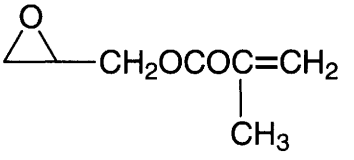
Included in Dutch occupational exposure limits (6).

References

1. Hine, C. H. et al *Arch. Ind. Hlth.* 1956, **14**, 250.
2. von der Hude, W. et al *Mutat. Res.* 1990, **231**, 205-218.

3. Canter, D. A. et al *Mutat. Res.* 1986, **172**, 105.
4. Foureman, P. et al *Environ. Mol. Mutagen.* 1994, **23**(1), 51-63.
5. Hemminki, K. et al *Arch. Toxicol.* 1980, **46**(3-4), 277-285.
6. *Gezondheidsraad Health-based Recommended Occupational Exposure Limits* Health Council of the Netherlands, Postbus 90517, NL 2509 NL Den Haag, Netherlands

G31 glycidyl methacrylate



$C_7H_{10}O_3$ **Mol. Wt.** 142.15 **CAS Registry No.** 106-91-2

Synonyms 2-propenoic acid, 2-methyl-, oxiranylmethyl ester; glycidyl α-methylacrylate; 2,3-epoxy-1-propanol methacrylate; 2,3-epoxypropyl methacrylate; SR-379

EINECS No. 203-441-9 **RTECS No.** OZ 4375000

Uses Intermediate in organic synthesis. Cross-linking agent.

Physical properties

M. Pt. 76°C **B. Pt.** 189°C **Flash point** 76°C (closed cup) **Specific gravity** 1.042 at 20°C
Solubility Water: 5-10 g l^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful by inhalation, in contact with skin and if swallowed – Irritating to eyes and skin – May cause sensitisation by skin contact (R20/21/22, R36/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water (S2, S26, S28)

Environmental fate

Nitrification inhibition
Inhibited nitrification in water at 0.445 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, guinea pig 390-700 mg kg^{-1} (2).
LD_{50} dermal rabbit 470 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 1120 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Inhalation rabbits, rats chronic study (duration unspecified) 15.3-206 mg m^{-3} caused lesions in central nervous system, cardiovascular system, liver and kidneys. At high concentrations, lesions were irreversible but at low doses, changes disappeared after 1 month (5).
Gavage rat 30 mg kg^{-1} day^{-1} for 5 days wk^{-1}, all animals died within 8 wk (6).

Carcinogenicity and chronic effects
Gavage rat (18 month) 0.003, 0.01, 0.03, 0.10 or 0.3 mg kg^{-1} day^{-1} for 5 days wk^{-1}. Effects on liver (unspecified) were observed in the high-dose group (7).

Metabolism and toxicokinetics
Showed elimination in rabbit liver and blood. Metabolism was by esterase and mixed-function oxidase enzymes (8).

Irritancy
Causes severe irritation. High concentrations are extremely destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin (9).

Genotoxicity

Salmonella typhimurium TA97, TA100, TA1535 with and without metabolic activation positive, TA98 with and without metabolic activation negative (10).
Escherichia coli PQ37, SOS chromotest, without metabolic activation positive (11).
In vitro Chinese hamster V79 cells without metabolic activation sister chromatid exchange positive (12).
In vitro unscheduled DNA synthesis induced in human, rat lymphocytes (13).
In vivo unscheduled DNA synthesis and sperm abnormality frequency tests showed 2,3-epoxypropyl methacrylate could damage DNA. Increased significantly the frequency of sperm abnormality and reduced the number of sperm (13).
Klebsiella pneumoniae positive (4).

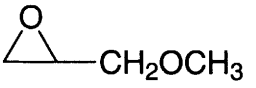
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties and exposure listed (14).

References

1. Zdrauko, B. I. et al *Gig. Sanit.* 1985, **50**(2), 67-69 (Russ.) (*Chem. Abstr.* **102**, 126801e).
2. Sax, N. I. et al *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
3. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
4. *Mutat. Res.* 1981, **89**, 269.
5. Ouyang, G. et al *Gongye Weisheng Yu Zhiyebing* 1990, **16**(1), 1-6 (Ch.) (*Chem. Abstr.* **113**, 167047j).
6. Pedrov, I. G. *Povolzh Konf. Fiziol. Uchastein. Biokhim. Farmakol. Morfol. 6th* 1973, **2**, 49-50 (Russ.) (*Chem. Abstr.* **82**, 81354m).
7. *BIBRA Toxicity Profiles* 1988, British Industrial Biological Research Association, Carshalton, UK.
8. Shi, T. et al *Zhongguo Yaolixue Yu Dulixue Zazhi* 1988, **2**(3), 226-231 (Ch.) (*Chem. Abstr.* **109**, 165295g).
9. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1785, Sigma-Aldrich, Milwaukee, WI, USA.
10. Canter, D. A. et al *Mutat. Res.* 1986, **172**(2), 105-138.
11. von der Hude, W. et al *Mutat. Res.* 1990, **231**(2), 205-218.
12. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
13. Xie, D. et al *Zhongguo Yaolixue Yu Dulixue Zazhi* 1990, **4**(3), 225-228 (Ch.) (*Chem. Abstr.* **113**, 226178c).
14. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G32 glycidyl methyl ether



$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 930-37-0

Synonyms (±)-glycidyl methyl ether; 1,2-epoxy-3-methoxypropane; 2,3-epoxypropyl methyl ether; 3-methoxy-1,2-epoxypropane; methyl glycidyl ether; (methoxymethyl)oxirane; 3-methoxypropyl oxide

EINECS No. 213-216-7 **RTECS No.** TZ 3530000

Uses Organic synthesis.

Physical properties

B. Pt. 110-111°C **Flash point** 18°C **Specific gravity** 0.982 at 20°C
Solubility Water: >100 g l^{-1} at 20°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Mammalian & avian toxicity

Irritancy
Causes skin irritation. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (1).

Sensitisation
Skin sensitisation was reported in guinea pigs (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (3).
Escherichia coli PQ37 with and without metabolic activation SOS chromotest positive (4).
In vitro Chinese hamster V79 cells, sister chromatid exchanges positive (metabolic activation not specified) (5).

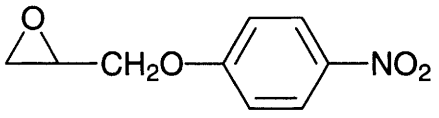
Other comments

May be absorbed through the skin (1).

References

1. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1785, Sigma-Aldrich, Milwaukee, WI, USA.
2. Rao, K. S. et al *Drug Chem. Toxicol.* 1981, **4**(4), 331.
3. Canter, D. A. et al *Mutat. Res.* 1986, **172**(2), 105-138.
4. von der Hude, W. et al *Mutat. Res.* 1990, **231**(2), 205-218.
5. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70

G33 glycidyl 4-nitrophenyl ether



$C_9H_9NO_4$ **Mol. Wt.** 195.17 **CAS Registry No.** 5255-75-4

Synonyms 1,2-epoxy-3-(*p*-nitrophenoxy)propane; 2,3-epoxy-1-(*p*-nitrophenoxy)propane; 2,3-epoxypropyl 4-nitrophenyl ether; [(4-nitrophenoxy)methyl]oxirane; 1-(4-nitrophenoxy)-2,3-propylene oxide; 1-(*p*-nitrophenoxy)-2,3-epoxypropane; 4-nitrophenyl glycidyl ether

EINECS No. 226-057-3 **RTECS No.** TZ 3650000

Physical properties

M. Pt. 67°C

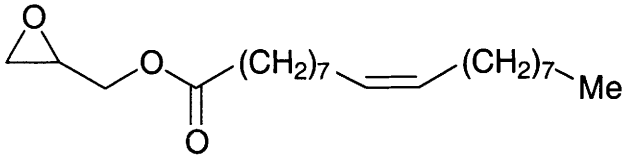
Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (1).
In vitro Chinese hamster V79 cells, sister chromatid exchanges positive (metabolic activation not specified) (2).
In vitro and *in vivo* mouse lymphocytes, chromosomal aberrations positive (3).
In vivo mouse liver DNA damage (significant increase in unwound DNA) positive (4).
In vivo mouse bone marrow, sister chromatid exchanges and chromosomal aberrations positive (5).

References

1. Sinsheimer, J. E. et al *Chem.-Biol. Interact.* 1987, **63**, 75-90.
2. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
3. Das, L. et al *Mutat. Res.* 1993, **299**(1), 19-24.
4. Giri, A. K. et al *Mutat. Res.* 1990, **242**(3), 187-194.
5. Giri, A. K. et al *Mutat. Res.* 1989, **224**(2), 253-261

G34 glycidyl oleate



$C_{21}H_{38}O_3$ **Mol. Wt.** 338.53 **CAS Registry No.** 5431-33-4

Synonyms 2,3-epoxy-1-propanol oleate; 2,3-epoxypropyl oleate; 9-octadecenoic acid, oxiranylmethyl ester; oleic acid, 2,3-epoxypropyl ester; glycidyl octadecenoate; oleic acid, glycidyl ester; glycidol oleate

EINECS No. 226-588-0

Physical properties

M. Pt. –0.5°C **B. Pt.** 185-190°C at 1mmHg

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3520 mg kg^{-1} (1).
LD_{50} dermal rabbit 8000 mg kg^{-1} (1).
LD_{Lo} intravenous mouse 15 mg kg^{-1} (2).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (3).
Subcutaneously injected to 15 BALB/c mice (8-wk-old), 0.25 mg glycidyl oleate in 0.1 ml tricaprylin for 52 wk produced local sarcomas in 5 mice after 10-11 months. 10/15 survived 9 months or more. Of 7 controls, 1 developed a local sarcoma after 13 months; 5/7 survived longer than 18 months (4).

Irritancy

Dermal rabbit (24 hr) 0.01 ml undiluted sample caused mild irritation, 0.5 ml undiluted chemical instilled into rabbit eye caused at most a very small area of necrosis (1).

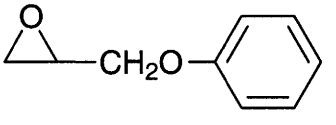
Sensitisation

In guinea pigs tested by intracutaneous injection, 2 out of 3 became sensitised to glycidyl oleate (1).

References

1. Weil, C. S. et al *Am. Ind. Hyg. Assoc. J.* 1963, **24**, 304-325.
2. *Arzneim.-Forsch.* 1967, **17**, 693.
3. *IARC Monograph* 1987, **Suppl. 7**, 64.
4. Swern, D. et al *Cancer Res.* 1970, **30**, 1037-1046

G35 glycidyl phenyl ether



$C_9H_{10}O_2$ **Mol. Wt.** 150.18 **CAS Registry No.** 122-60-1

Synonyms 1,2-epoxy-3-phenoxypropane; (phenoxymethyl)oxirane; (2,3-epoxypropoxy)benzene; 2,3-epoxypropyl phenyl ether; phenyl glycidyl ether; phenoxypropylene oxide; 1-phenoxy-2,3-epoxypropane; 3-phenyloxy-1,2-epoxypropane

EINECS No. 204-557-2 **RTECS No.** TZ 3675000

Uses Cross-linking agent for epoxy resins. Intermediate in organic synthesis.

Physical properties

M. Pt. 3.5°C **B. Pt.** 245°C **Flash point** >110°C (closed cup) **Specific gravity** 1.11 at 20°C with respect to water at 4°C **Volatility** v.p. 0.01 mmHg at 20°C ; v.den. 4.37
Solubility Water: 2.4 g l^{-1}. Organic solvents: acetone, ethanol

Occupational exposure

FR-VME 1 ppm (6 mg m^{-3})
SE-LEVL 10 ppm (60 mg m^{-3}) **SE-STEL** 15 ppm (90 mg m^{-3})

UK-LTEL 1 ppm (6.2 mg m^{-3})
US-TWA 0.1 ppm (0.6 mg m^{-3})
Supply classification harmful
Risk phrases Harmful in contact with skin – May cause sensitisation by skin contact (R21, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity
LC_{50} (24, 96 hr) goldfish 69, 43 mg l^{-1} (1).
5 ppm was not toxic when administered to trout, bluegill sunfish, perch and goldfish. Test conditions: pH 7, dissolved oxygen content 7.5 ppm, total hardness (soap method) 300 ppm, methyl orange alkalinity 310 ppm, free carbon dioxide 5 ppm, temperature 12.8°C (2).

Environmental fate

Degradation studies
BOD_5 0.14 mg l^{-1} O_2, COD 2.18 mg l^{-1} O_2 by Dutch Standard test method (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 1400, 3850 mg kg^{-1}, respectively (3).

Sub-acute and sub-chronic data
Inhalation rat (19 day) at 1.75, 5.84, 11-20 mg m^{-3}, 6 hr day^{-1} caused focal degenerative changes involving the seminiferous tubules in both gonads (4).

Teratogenicity and reproductive effects
Intraperitoneal rat (17-19 day gestation) 30 mg kg^{-1} caused reproductive effects (unspecified) (5).

Sensitisation
♀ workers patch-tested (24 hr), reading made on removal and 24, 48 and 120 hr after removal. 2 of 3 workers showed positive result (6).

Genotoxicity

Salmonella typhimurium TA97, TA100, TA1535 with and without metabolic activation positive; TA98 with and without metabolic activation negative (7).
Escherichia coli PQ37, SOS-chromotest, without metabolic activation positive (8).
In vitro Chinese hamster V79 cells without metabolic activation sister chromatid exchanges positive (9).
In vitro rat hepatocyte cells unscheduled DNA repair synthesis negative (10).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, workplace experience, epidemiology, environmental effects and exposure listed (11).
Energy of decomposition in range 360-450°C measured as 0.626 kJ g^{-1} (12).

References

1. *Shell Industrie Chemicalien Gids* 1975, Shell Nederland Chemie, Netherlands.
2. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA560/6-87-002 PB 87-200-275, Washington, DC, USA.
3. Clayton, G. D. et al (Eds.) *Patty's Industrial Hygiene and Toxicology* 1967, Vol. 2, Interscience Publishers, New York, NY, USA.
4. Tervill, J. B. et al *Haskell Laboratory Report* No. 163-75 Haskell Laboratory for Toxicology and Industrial Medicine, Wilmington, DE, USA.
5. *Teratology* 1973, **8**, 97.

6. Jolanki, R. et al *Contact Dermatitis* 1987, **16**(2), 87-92.
7. Canter, D. A. et al *Mutat. Res.* 1986, **172**(2), 105-138.
8. von der Hude, W. et al *Mutat. Res.* 1990, **231**(2), 205-218.
9. von der Hude, W. et al *Mutat. Res.* 1991, **249**(1), 55-70.
10. von der Hude, W. et al *Mutat. Res.* 1990, **245**(3), 145-150.
11. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
12. Bretherick, L. *Handbook of Reactive Chemical Hazards* 4th ed., 1990, Butterworths, London, UK

G36 glycine

$$NH_2CH_2CO_2H$$

$C_2H_5NO_2$ **Mol. Wt.** 75.07 **CAS Registry No.** 56-40-6

Synonyms aminoacetic acid; aminoethanoic acid; glyocoll; Glycosthene

EINECS No. 200-272-2 **RTECS No.** MB 7600000

Uses As a dietary supplement and in therapeutic irrigation fluids.

Occurrence Amino acid widespread in plants, animals and microorganisms. In nervous systems of mammals and other animals as a neurotransmitter. Has been identified as a pollutant in river water (1).

Physical properties

M. Pt. 232-236°C (decomp.)

Solubility Water: 250 g l^{-1}. Organic solvents: ethanol, pyridine

Ecotoxicity

Fish toxicity

LD_{50} (24 hr) trout, bluegill sunfish, goldfish >5 ppm (2).

Environmental fate

Degradation studies

Can be degraded by activated sludge (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 5, 8 g kg^{-1}, respectively (4).

LD_{50} subcutaneous rat 5.2 g kg^{-1} (4).

LD_{50} intraperitoneal mouse 4.4 g kg^{-1} (4).

LD_{50} intravenous mouse 2.4 g kg^{-1} (4).

Metabolism and toxicokinetics

Glycine is not classified as an essential amino acid since it can be synthesised within the body. As part of the amino acid pool it is used in protein, carbohydrate and fat synthesis and the synthesis of other nitrogen-containing body chemicals (5).

After oral ingestion glycine is rapidly absorbed from the small intestine by active transport and largely removed by the liver, although peripheral blood levels remain raised for some time (6-8).

Proteins ingested as part of diet are likely to yield glycine after breakdown in the gastro-intestinal tract and this is then taken up into intestinal mucosa in free or small-peptide form (6,9).

Sensitisation

In an *in vitro* test for the immediate allergic reaction using basophilic leukaemia cells, no potentiation by glycine was detected (10).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with metabolic activation negative (11).
In vitro Chinese hamster fibroblasts chromosome aberrations without metabolic activation negative (11).

Other effects

Other adverse effects (human)

Systemic absorption in man can lead to disturbances of fluid and electrolyte balance and cardiovascular and pulmonary effects (12).
It can be used for urogenital irrigation, but biochemical and physiological disturbances can occur (13,14).
Hydrolysis in water and moist soils $t_{1/2}$ estimated to be 28 days (3).

Any other adverse effects

Dietary glycine intake can influence plasma cholesterol levels in rats fed a high cholesterol diet (15).

Other comments

Exists in three polymorphic forms α, β, and γ (16).
A specific receptor for glycine exists in the central nervous system of many species, and the compound may also have actions at receptors for other mediators (17-19).

References

1. Kono, H. et al *Suishitsu Odaku Kenkyu* 1987, **10**(8), 495-502.
2. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA560/6-87-002 PB87-200-275, Washington, DC, USA.
3. Stranel, O. et al *Kozarstvi* 1988, **38**(2), 42-47 (Czech.) (*Chem. Abstr.* **109**, 236180d).
4. *Yakuri to Chiryo* 1977, **5**, 1502.
5. Vander et al (Eds.) *Human Physiology: The Mechanisms of Body Function.* 1980, McGraw-Hill, New York, NY, USA.
6. Ugolev, A. M. et al *Comp. Biochem. Physiol., A: Comp. Physiol.* 1986, **85A**(4), 593-612.
7. Craft, I. L. et al *Gut* 1968, **9**, 425-437.
8. Peters, T. J. et al *Clin. Sci.* 1970, **39**, 811-821.
9. Burston, D. et al *Clin. Sci.* 1972, **43**, 823-837.
10. Tanaka, Y. *Eisei Kagaku* 1991, **37**(5), 370-378.
11. Ishidate, M. *Food Chem. Toxicol.* 1984, **22**(8), 623-636.
12. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
13. Sinclair, J. F. *Br. Med. J.* 1985, **291**, 691-692.
14. Magos, J. L. et al *Br. Med. J.* 1990, **300**, 1097.
15. Sugiyama, K. et al *J. Nutr. Sci. Vitaminol.* 1986, **32**(6), 623-633.
16. Iitaka, *Nature (London)* 1959, **183**, 390.
17. Betz, H. *Trends Neurosci.* 1987, **10**(3), 113-117.
18. Betz, H. *Neurochem. Int.* 1988, **13**(2), 137-146.
19. Dingledine, R. et al *Adv. Exp. Med. Biol.* 1990, **268**, 17-26

G37 glycolonitrile

$HOCH_2CN$

C_2H_3NO **Mol. Wt.** 57.05 **CAS Registry No.** 107-16-4

Synonyms formaldehyde cyanohydrin; hydroxyacetonitrile; hydroxymethylnitrile; glyconitrile; glycolonitrile; USAF A-8565

EINECS No. 203-469-1 **RTECS No.** AM 0350000

Uses Chemical intermediate.

Physical properties

B. Pt. 183°C **Specific gravity** 1.10 at 19°C **Volatility** v.p. 1 mmHg at 63°C
Solubility Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies

Can be oxidised by acclimated microorganisms in wastewaters (1).

Wild type *Brevibacterium* sp. R312 strain utilised linear and branched aliphatic nitriles and β-unsaturated nitriles as both carbon and nitrogen sources, but not α-unsaturated nitriles or aromatic nitriles. A mutant strain M2 was isolated which can grow on α-unsaturated nitriles. It is suggested that this strain may be used for the biological degradation of nitriles in waste waters (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 16 mg kg^{-1} (3).
LD_{50} oral mouse 10 mg kg^{-1} (4).
TD_{Lo} inhalation (8 hr) rat 27 ppm (4).
TD_{Lo} inhalation (5 hr) mouse 27 ppm (4).
LD_{50} dermal rabbit 5 mg kg^{-1} (3,4).

Metabolism and toxicokinetics

Microsomal fractions from rat liver can metabolise the compound and liberate cyanide ions (5).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation negative (6).

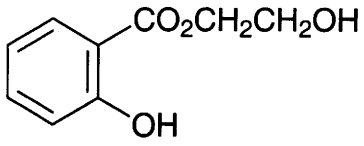
Other comments

Can result from interaction of cyanide and formaldehyde in waste waters (1), and in cooling processes from gases from coke ovens (7).

References

1. Wu, H. et al *Shanghai Huanjing Kexue* 1987, **6**(8), 8-10 (Ch.) (*Chem. Abstr.* **108**, 100510h).
2. Thiery, A. et al *Zentralbl. Mikrobiol.* 1986, **141**(8), 575-582.
3. *Annu. Meet. Am. Ind. Hyg. Assoc.* 1962, **23**, 95.
4. Deichmann, W. B. (Ed.) *Toxicology of Drugs and Chemicals* Academic Press, New York, NY, USA.
5. Freeman, J. J. *Biochem. Pharmacol.* 1987, **36**(1), 184-187.
6. Zeiger, E. *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-187.
7. Kagasov, V. M. *Koks Khim.* 1989, (9), 23-27 (Russ.) (*Chem. Abstr.* **112**, 39520a)

G38 glycol salicylate



$C_9H_{10}O_4$ **Mol. Wt.** 182.18 **CAS Registry No.** 87-28-5

Synonyms ethylene glycol monosalicylate; 2-hydroxyethyl 2-hydroxybenzoate; 2-hydroxyethyl salicylate; monoglycol salicylate; Glysal; Norgesic; Spirosal; Phlogont (salve); Dipsal

EINECS No. 201-737-2

Uses Anti-inflammatory and analgesic drug for topical application.

Physical properties

M. Pt. 37°C **B. Pt.** 169-172°C at 12 mmHg **Specific gravity** 1.2537 at 15°C with respect to water at 15°C
Solubility Water: miscible. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Metabolism and toxicokinetics
Absorbed through the skin of mammals (1).

References

1. Al-Khamis, K. et al *Int. J. Pharm.* 1987, **40**(1-2), 111-118

G39 glyoxal

OCHCHO

$C_2H_2O_2$ **Mol. Wt.** 58.04 **CAS Registry No.** 107-22-2

Synonyms biformyl; ethanedial; 1,2-ethanedione; ethane-1,2-dione; glyoxaldehyde; oxal; oxaldehyde

EINECS No. 203-474-9 **RTECS No.** MD 2700000

Uses Disinfectant. Cross-linking agent. Photographic hardening agent. In solubilisation of proteins, starch and cellulose. In leather tanning, paper sizing and textile treatment.
Occurrence Aroma component of coffee. Degradation product of carbohydrates and other organic compounds (1,2).

Physical properties

M. Pt. 15°C **B. Pt.** 51°C at 776 mm **Flash point** 220°C **Specific gravity** 1.14 at 20°C with respect to water at 44°C **Volatility** v.p. v.p 220 mmHg at 20°C ; v.den. 2.0
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful by inhalation – Irritating to eyes and skin – Possible risk of irreversible effects – May cause sensitisation by skin contact (R20, R36/38, R40, R43)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Environmental fate

Abiotic removal

Undergoes rapid polymerisation on contact with water or water-containing solvents (3).
19-23% removal by adsorption onto activated carbon at concentrations of 2 or 100 mg l^{-1} (4).
Spontaneously oxidised in water to glyoxalic acid at a rate of 8% day^{-1} at 20°C in sunlight (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig 760, 2020 mg kg^{-1}, respectively (5,6).
LD_{50} dermal guinea pig 6600 mg kg^{-1} (6).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (7).

Sub-acute and sub-chronic data

Oral rat 2000, 4000, 6000 mg l^{-1} in drinking water for 90 days, followed by administration of the same amount of glyoxal in the diet for 90 or 180 days. A dose-related decrease in body weight gain and organ weight was reported. Histopathological examination revealed only a slight papillary change in the kidneys in the high-dose group (8).

Carcinogenicity and chronic effects

Dermal mouse (1 yr) 2.5 mg $animal^{-1}$ applied 2 × wk^{-1} for 5 wk did not induce any skin tumours (9).
National Toxicology Program prechronic studies in water and /or sewage treatment completed and are under review for further evaluation (10).

Irritancy

Dermal rabbit, 545 mg caused mild irritation and 1870 μg instilled into rabbit eye caused severe irritation (exposure unspecified) (11,12).

Genotoxicity

Salmonella typhimurium TA100, TA102 (metabolic activation unspecified) positive (13).
Salmonella typhimurium TA7001-TA7006 were used to detect base-pair substitutions and the TA98 strain was employed to detect frameshift mutations. Glyoxal, a major oxidative DNA-damage product, did not induce mutations at A:T base pairs. The majority of mutations were base-pair substitutions at G:C base pairs, and a small level of frameshift mutations was detected in the TA98 strain (14).
Escherichia coli SOS chromotest without metabolic activation positive (15).
Bacillus subtilis rec assay without metabolic activation positive (16).
In vitro Chinese hamster V79 cells, chromosomal aberrations positive (2).
In vitro mouse lymphoma tk^+/tk^- forward mutation assay without metabolic activation positive (17).
In vitro primary rat hepatocytes and *in vivo* rat hepatocytes, DNA damage positive (18).
Induced unscheduled DNA synthesis in hamster TC-SV40 cells (19).
In vitro human peripheral lymphocytes, sister chromatid exchange positive. *In vitro* Chinese hamster ovary AUXBI cells, sister chromatid exchange positive (20).

Other comments

Physical properties, toxicity, environmental impact and safe handling reviewed (21).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (22).
Mixtures with air may explode and pure glyoxal may polymerise exothermically and ignite in storage (23).

References

1. Gardner, E. P. et al *J. Phys. Chem.* 1987, **91**(7), 1922-1930.
2. Nishi, Y. et al *Mutat. Res.* 1989, **227**(2), 117-123.
3. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
4. Jarret, M. et al *Sci. Eau* 1986, **5**(4), 377-400.
5. Smyth, H. F. et al *J. Ind. Hyg. Toxicol.* 1941, **23**, 259.
6. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, 291, Academic Press, New York, NY, USA.
7. *NTIS Report* AD438-895, Nat. Tech. Inf. Ser., Springfield, VA, USA.
8. Ueno, H. et al *Fundam. Appl. Toxicol.* 1991, **16**(4), 762-772.
9. Miyakawa, Y. et al *Carcinogenesis (London)* 1991, **12**(7), 1169-1173.
10. *National Toxicology Program Research and Testing Division* 1992, NIEHS, Research Triangle Park, NC, USA.
11. *Union Carbide Data Sheet* 16 March 1961 Union Carbide Corp. New York, NY, USA.
12. *Am. J. Opthalmol.* 1946, **29**, 1363.
13. Wilcox, P. et al *Mutagenesis* 1990, **5**(3), 285-291.
14. Murata-Kamiya, N. et al *Mutat. Res.* 1997, **377**(1), 13-16.
15. von der Hude, W. et al *Mutat. Res.* 1988, **203**(2), 81-94.
16. Mateni, S. et al *Water Sci. Technol.* 1989, **21**(8-9), 875-887.
17. Wangerheim, J. et al *Mutagenesis* 1988, **3**(3), 193-205.
18. Ueno, H. et al *Mutat. Res.* 1991, **260**(1), 115-119.
19. Cornago, P. et al *Biochimie* 1989, **71**(11-12), 1205.
20. Tucker, J. D. et al *Mutat. Res.* 1989, **224**(2), 269-279.
21. *Dangerous Prop. Ind. Mater. Rep.* 1987, **6**, 61-64.
22. *ECETOC Technical Report No. 30(4)* 1991, European Chemical Industry Ecology and Toxicology Centre, B-1160 Brussels, Belgium.
23. Bretherick, L. *Handbook of Reactive Chemical Hazards* 4th ed., 1990, Butterworths, London, UK

G40 glyphosate

$HO_2CCH_2NHCH_2PO_3H_2$

$C_3H_8NO_5P$ **Mol. Wt.** 169.07 **CAS Registry No.** 1071-83-6

Synonyms *N*-(phosphonomethyl)glycine; MON-0573

EINECS No. 213-997-4 **RTECS No.** MC 1075000

Uses Herbicide. Organic synthesis.

Physical properties

M. Pt. 230°C (decomp.) **Specific gravity** Bulk density: 0.5 g cm^{-3} (1) **Volatility** v.p. 3×10^{-7} mmHg
Solubility Water: 12 g l^{-1} at 25°C. Organic solvents: Insoluble in common organic solvents

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, rainbow trout, harlequin fish 86-170 mg l^{-1} (2,3).
LC_{50} (8 days) flagfish, 30 mg l^{-1} (4).
LC_{50} (96 hr) channel catfish, blugill sunfish 14.5, 13.0 mg l^{-1}, respectively (5).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 780 mg l^{-1} static bioassay (3).
EC_{50} (48 hr) midge larvae *Chironomus riparius* 5600 mg l^{-1} (6).
EC_{50} (5 min) *Photobacterium phosphoreum* 7.7 ppm Microtox test (7).

LC_{50} (96 hr) crawfish 21,632.8 mg l^{-1} (5).
LD_{50} oral and contact bee >0.1 mg bee^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ for degradation in soil ~60 days (1).
Degraded by several *Rhizobiaceae* species, *Pseudomonas* and *Arthrobacter atrocyoneus* when utilised as sole phosphorus source. Sarcosine was the immediate degradation product, indicating that the initial cleavage of glyphosate was at the C-P bond, followed by oxidation of sarcosine to glycine and formaldehyde (8-11).
Glyphosate is metabolised by two species of *Ochrobactrum anthropi* (LBAA and S5). Both species metabolise glyphosate via the aminomethylphosphonate (AMPA) pathway. The formation of *N*-methyl AMPA is common to both species, but the formation of *N*-acetyl AMPA is only observed in LBAA. *N*-methylacetamide is detected predominantly in S5 lysates (12).

Abiotic removal

75% removal from 1% solution in distilled water exposed to sunlight for 2 wk, but in polluted water only 15% was removed (13).
Effectively removed from river water by coagulation and filtration. Removal by activated carbon was less efficient from river water than from distilled water (14).

Adsorption and retention

Soil K_{oc} for clay and clay soils 8-138 (15).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rabbit, rat 470-5600 mg kg^{-1} (2,16-18).
LC_{50} (4 hr) inhalation rat >12,200 mg m^{-3} (2).
LD_{50} dermal rabbit >5000 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse 130-240 mg kg^{-1}, respectively (17,18).

Sub-acute and sub-chronic data

LC_{50} (8 days) oral quail, duck >4600 mg kg^{-1} diet (2).

Carcinogenicity and chronic effects

Oral rat and dog (2 yr) 300 mg kg^{-1} diet caused no adverse effects (2).

Teratogenicity and reproductive effects

Oral rat, three-generation study, 0, 3, 10 or 30 mg kg^{-1} day^{-1} for 60 days. No maternal or paternal toxicity or teratogenicity was observed (19).

Metabolism and toxicokinetics

Following oral administration to mammals, glyphosate is rapidly excreted unchanged (2).

Irritancy

Non-irritating to skin, mild eye irritant to rabbits (dose and duration unspecified) (2).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (20,21).
Escherichia coli WP-2 reversion assay negative (21).
In vitro Chinese hamster ovary cells, chromosomal aberrations negative (21).
In vitro rat primary hepatocytes, DNA repair assay negative (21).
In vivo rat bone marrow, chromosomal aberrations negative (21).

Legislation

WHO Toxicity Class Table 5 (22).
EPA Toxicity Class III (formulation) (1).
ADI 1.175 mg kg^{-1} (1).
UK Advisory value for drinking water 1000 μg l^{-1} (23).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (24).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (25).

Other comments

Approved for use on weeds in or near water courses and lakes in UK by MAFF (3).
Maximum permitted concentration in water under the UK Pesticide Safety Precautions Scheme 0.2 mg l^{-1} (3).
Physical properties, toxicity and health effects reviewed (26).
Metabolic pathways reviewed (27).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
3. *Guidelines for the Use of Herbicides on Weeds In or Near Watercourses and Lakes* 1985, MAFF, Alnwick, UK.
4. Holdaway, D. A. et al *Environ. Toxicol. Chem.* 1988, **7**, 63-68.
5. Abdelghani, A. A. et al *Environ. Toxicol. Water Qual.* 1997, **12**(3), 237-243.
6. Buhl, K. J. et al *Arch. Environ. Contam. Toxicol.* 1989, **18**, 530-536.
7. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
8. Liu, C. M. et al *Appl. Environ. Microbiol.* 1991, **57**(6), 1799-1804.
9. Jacob, G. S. et al *Appl. Environ. Microbiol.* 1988, **54**(12), 2953-2958.
10. Pipke, R. et al *Appl. Environ. Microbiol.* 1988, **54**(5), 1293-1296.
11. Kishore, G. M. et al *J. Biol. Chem.* 1987, **262**(25), 12164-12168.
12. Gard, J. K. et al *Xenobiotica* 1997, **27**(7), 633-644.
13. Hoie, K. et al *Bull. Environ. Contam. Toxicol.* 1986, **36**, 723-729.
14. Speth, T. F. *Proc. Am. Conf. Am. Water Works Assoc.* 1990, (Pt.2) 1877-1891.
15. *Pesticide Residues in Food* 1986, 63-76, WHO, Geneva, Switzerland.
16. Bababunmi, E. A. et al *Toxicol. Appl. Pharmacol.* 1978, **45**, 319.
17. *Toxicol. Lett.* 1980, **10**(Suppl. 1), 148.
18. *Pestic. Toxic Chem. News* 1978, **7**, 6.
19. Glass, R. L. *J. Agric. Food Chem.* 1987, **35**(4), 497-500.
20. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141.
21. Li, A. P. et al *Fundam. Appl. Toxicol.* 1988, **10**(3), 537-546.
22. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
23. *Guidance on Safeguarding the Quality of Public Water Supplies*, 1989, 91-104, HMSO, London, UK.
24. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
25. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
26. *Dangerous Properties of Industrial Materials: Report* 1990, **10**(5), 72-79.
27. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

G41 glyphosine

$$HO_2CCH_2N(CH_2PO_3H_2)_2$$

$C_4H_{11}NO_8P_2$ **Mol. Wt.** 263.08 **CAS Registry No.** 2439-99-8

Synonyms *N*,*N*-bis(phosphonomethyl)glycine; *N*-carboxymethyl-*N*,*N*-bis(methylenephosphonic acid)amine; CP-41845; Polaris

EINECS No. 219-468-4 **RTECS No.** MB 9120000

Uses Ripening agent for sugar cane. Chemical intermediate. Chelating agent. Analytical reagent.

Physical properties

M. Pt. 200°C (decomp.)

Solubility Water: 248 g l^{-1}. Organic solvents: ethanol

Occupational exposure

Supply classification irritant

Risk phrases Risk of serious damage to eyes (R41)

Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S26)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3900 mg kg^{-1} (1).

Other effects

Other adverse effects (human)

Compound binds to human apotransferrin *in vitro* (2).

Other comments

Residues have been detected in drinking water (3).

References

1. Thomson, W. T. *Agricultural Chemicals* 1977, Thomson Publ. Fresno, CA, USA.
2. Harris, W. R. *Biochemistry* 1991, **30**(28), 6930-6936.
3. Zykova, G. V. *Zavod. Lab.* 1989, **55**(6), 10-12 (Russ.). (*Chem. Abstr.* **112**, 11673d)

G42 gold

Au

Au **Mol. Wt.** 196.97 **CAS Registry No.** 7440-57-5

Synonyms

EINECS No. 231-165-9 **RTECS No.** MD 5070000

Uses In jewellery, gold plating and as a standard of currency. Catalyst. Dental material. In therapeutics in complexes such as auranofin or thio salts for rheumatic diseases and as ^{198}Au in colloid form as an antineoplastic agent. Surface colouring of confectionery.

Occurrence In rocks of almost all types and in sea water. In free form or in ores such as calavarite or sylvanite. Occurrence in Earth's crust: 0.005 ppm.

Physical properties

M. Pt. 1064.76°C **B. Pt.** 2700°C **Specific gravity** 19.3 **Volatility** v.p. 1 mmHg at 1869°C

Ecotoxicity

Bioaccumulation

39 strains of heleotrophic bacteria and fungi from natural sources have been shown capable of accumulating gold from solutions containing gold (in unspecified form) of 5 mg l^{-1}. A possible means of recovering gold from contaminated land by this method is suggested (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} intramuscular rat 200 mg kg^{-1} (implant) (2).

LD_{Lo} intravenous rat 58 mg kg^{-1} (as salts) (3).

LD_{Lo} intramuscular mouse 21 mg kg^{-1} (as salts) (2).

Teratogenicity and reproductive effects

Rats receiving 75 mg kg^{-1} intraperitoneally on days 4-6 of pregnancy showed signs of embryotoxicity (4).

Metabolism and toxicokinetics

Gold can be detected in breast milk of normal human subjects (5).

Sensitisation

Rare cases of hypersensitivity have been reported (6).

A 26-year-old man developed eczema on the eyes and fingers as a result of contact with gold-plating solutions and metallic gold. Patch testing showed a positive reaction to gold thiosulfate. The patient, who was mainly exposed to gold potassium cyanide, showed scaly dermatitis of the eyelids, chemosis of the bulbar conjunctiva, hyperaemia of the tarsal conjunctiva, follicular hypertrophy on the lower lid conjunctiva, and eosinophilia in conjunctival scrapings, consistent with an allergic reaction. The symptoms disappeared when the patient changed his job (7).

Other effects

Other adverse effects (human)

The ability of gold in various forms to cause nephropathy has been reviewed (8).

Any other adverse effects

In vitro Balb/c 3T3 fibroblasts, effects on protein production, ^{3}H-leucine incorporation, ^{3}H-thymidine incorporation and monotetrazolium-formazan production have been assessed. Low doses were stimulating, high doses cytotoxic (9).

Other comments

Natural isotope is ^{197}Au, artificial radioactive isotope ^{198}Au is used in therapeutics (6).
The dermatotoxicity associated with gold is reviewed. Hypersensitivity is recognised as a side-effect of anti-inflammatory therapy, but an increased incidence of allergic contact dermatitis due to gold is observed when it is included in routine patch testing, using gold sodium thiosulfate 0.5% in petrolatum. The risk of sensitisation is greatest when gold-containing alloy jewellery is left in permanent contact with live tissue, such as in skin piercing. Gold allergy shows a delayed reaction to challenge, persistence of clinical effects, formation of immunogenic granulomas and eczema at sites distant from the point of contact. Contact urticaria and immune complex formation can also occur (10).
The use of gold in dentistry has been reviewed (11), as has the toxicity in a variety of different species (12).
The relationship between gold and bacteria has been reviewed (13).
Metabolism and pharmacokinetics of gold salts reviewed (14).

References

1. Wnorski, A. U. *Water Sci. Technol.* 1991, **23**(1-3), 309-318.
2. *Naturwissenschaften* 1955, **42**, 75.
3. *Z. Krebsforsch.* 1960, **63**, 586.
4. *J. Pharm. Exp. Ther.* 1980, **214**, 250.
5. Durrant, S. F. *J. Micronutr. Anal.* 1989, **5**(2), 111-126.
6. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
7. Estlander, T. et al *Contact Dermatitis* 1998, **38**(1), 40-41.
8. Wantabe, J. S. *J. UOEH* 1987, **9**(Suppl.), 188-195.
9. Wataha, J. C. *J. Biomed. Mater. Res.* 1991, **25**(9), 1133-1149.
10. Hostynek, J. J. et al *Food Chem. Toxicol.* 1997, **35**(8), 839-844.
11. Brown, B. D. *Gold Bull. Gold Pat. Dig.* 1988, **21**(1) 24-28.
12. England, M. W. *Health Phys.* 1989, **57**(Suppl. 1), 115-119.
13. Ovcharenko, F. D. et al *Visn. Akad. Nauk Ukr. RSR* 1988, (2), 11-21 (Ukr.) (*Chem. Abstr.* **108**, 183330y).
14. Bianucci, G. *G. Ital. Chim. Clin.* 1987, **12**(2), (Ital.) (*Chem. Abstr.* **108**, 179358w)

G43 gold trichloride

$$AuCl_3$$

$AuCl_3$ **Mol. Wt.** 303.32 **CAS Registry No.** 13453-07-1
Synonyms auric chloride; gold chloride; gold(III) chloride
EINECS No. 236-623-1 **RTECS No.** MD 4520000

Physical properties

M. Pt. $_{760}$ 180°C (sublimes) **B. Pt.** 229°C **Specific gravity** 3.9 at 20°C with respect to water at 4°C
Solubility Water: soluble. Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} subcutaneous mouse 1500 mg kg^{-1} (1).

Teratogenicity and reproductive effects
Intratesticular injection of up to 2.5 mg kg^{-1} to rats and mice caused necrosis (2).

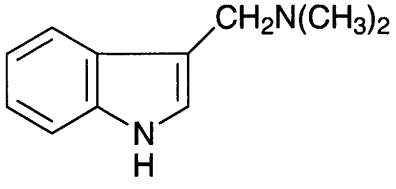
Genotoxicity

Stimulated DNA synthesis of human thymocytes and peripheral blood lymphocytes (3).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. Kamboj, V. P. et al *J. Reprod. Fertil.* 1964, **7**, 21-28.
3. Nordlind, K. *Int. Arch. Allergy Appl. Immunol.* 1985, **77**, 459-460

G44 gramine



$C_{11}H_{14}N_2$ **Mol. Wt.** 174.25 **CAS Registry No.** 87-52-5

Synonyms *N,N*-dimethyl-1*H*-indole-3-methanamine; 3-[(dimethylamino)methyl]indole; Donax; Donaxine

EINECS No. 201-749-8 **RTECS No.** NL 7525000

Occurrence In chlorophyll-deficient mutants of barley, the reed *Arundo donax*, maple species and *Phalaria aquatica*.

Physical properties

M. Pt. 138-139°C **B. Pt.** 210°C

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) goldfish 1050 mg l^{-1} (1).

Environmental fate

Degradation studies

BOD_5, 0.07 mg l^{-1} O_2; COD, 0.55 mg l^{-1} O_2 (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral sheep 400-600 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 122 mg kg^{-1} (3).

LD_{Lo} intraperitoneal rat 250 mg kg^{-1} (4).

LD_{50} intravenous mouse 46 mg kg^{-1} (5).

Other effects

Any other adverse effects

In sheep the lowest tested doses that produced clinically observable effects were 10 and 400 mg kg^{-1}

intravenously and orally, respectively. Induced nervous disorders, including tremors, hind limb paresis, recumbency and ataxia (2).

References

1. Shell Chemie *Shell Industrie Chemicalien Gids* 1975, Shell Nederland Chemie, s'Gravenhage, Netherlands.
2. Bourke, C. A. et al *Aust. Vet. J.* 1988, **65**(7), 218-220.
3. *Psychopharmacologia* 1970, **16**, 385.
4. *National Academy of Science, National Research Council, Chemical-Biological Coordination Center, Review* 1953, **5**, 11.
5. *J. Pharmacol. Exp. Ther.* 1952, **105**, 130

G45 graphite

C

C **Mol. Wt.** 12.01 **CAS Registry No.** 7782-42-5

Synonyms black lead; mineral carbon; plumbago; natural graphite

EINECS No. 231-955-3 **RTECS No.** MD 9659600

Uses Adsorbent, pigment, fuel and manufacture of explosives. Moderator in nuclear piles. Manufacture of refactory crucibles, electrodes and pencil lead.

Occurrence Obtained by mining, particularly in Canada and Sri Lanka.

Physical properties

Specific gravity 2.09-2.23 at 20°C

Occupational exposure

DE-MAK 1.5 mg m^{-3} (respirable fraction of aerosol)
FR-VME 2 mg m^{-3} (respirable dust)
SE-LEVL 5 mg m^{-3}
UK-LTEL 10 mg m^{-3} (total inhalable dust); 4 mg m^{-3} (respirable dust)
US-TWA 2 mg m^{-3} (all forms except graphite fibres)

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Inhalation rat (4 days), 100 mg m^{-3} for 4 hr day^{-1}. Bronchoalveolar lavage changes were observed 24 hr post-exposure, together with enzymatic and cytological alterations. These changes were resolved by 14 days (1).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (no specific details) (2).

Other effects

Other adverse effects (human)

Occupational exposure to graphite dusts which may contain carcinogenic PAHs, including benzo[*a*]pyrene, have been reported to pose significant health hazards (3).

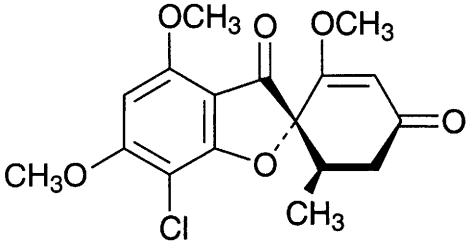
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

References

1. Thompson, S. A. et al *Report* 1988, CRD EC-TR-88161, Aberdeen Proving Ground, MD, USA.
2. Lenga, R. E. (Ed.) *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1801, Sigma-Aldrich, Milwaukee, WI, USA.
3. Dymova, E. G. et al *Gig. Tr. Prof. Zabol.* 1988, (7), 19-21 (Russ.), (*Chem. Abstr.* **109**, 134318n).
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G46 griseofulvin



$C_{17}H_{17}ClO_6$ **Mol. Wt.** 352.77 **CAS Registry No.** 126-07-8

Synonyms amudane; curling factor; (+)-griseofulvin; grisofulvin; 7-chloro-2',4,6-trimethoxy-6'-methyl-spiro [benzofuran-2(3*H*), 1'-[2]cyclohexene]-3,4'-dione; 7-chloro-4,6-dimethoxycoumarin-3-one-2-spiro-1'-(2'-methoxy-6'-methylcyclohex-2'-en-4'-one); Fulcin; Lamoryl; Spirofulrin

EINECS No. 204-767-4 **RTECS No.** WG 9800000

Uses Antifungal antibiotic.

Occurrence Isolated from *Penicillium* species (1).

Physical properties

M. Pt. 220°C

Solubility Organic solvents: acetone, acetic acid, benzene, chloroform, dimethylformamide, ethanol, methanol

Ecotoxicity

Invertebrate toxicity

LC_{50} (48 hr) *Mercenaria mercenaria* eggs <250 μg l^{-1} static bioassay (2).

LC_{50} (14 day) *Mercenaria mercenaria* larvae <1.0 mg l^{-1} static bioassay (2).

Environmental fate

Abiotic removal

Undergoes photodegradation by 1st order kinetics when irradiated by sunlight or by mercury vapour lamp. Three unidentified degradation products were formed (3).

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous mouse 1200 mg kg^{-1} (4).

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (5).

LD_{50} intravenous mouse, rat 280, 400 mg kg^{-1}, respectively (6,7).

Sub-acute and sub-chronic data

Oral rat (7 wk) 1% diet decreased the levels of erythrocytes, haemoglobin, leucocytes, neutrophils and lymphocytes. Signs of immunosuppression were demonstrated through evaluation of antibody titre, bone marrow smears, spleen plasma cell counts and skin tests. Histopathological changes were also observed in the spleen and foot pad (8).

Oral rat (14 wk) 1% diet caused a significant increase in glutamic pyruvic transaminase, glutamic oxalacetic transaminase, γ-glutamyl transferase activities, total lipids, cholesterol, urea and creatinine. A significant decrease in sperm count, motility and live sperm was observed. Marked histopathological findings were demonstrated in the liver, kidneys, heart and testes (9).

Oral mouse (82 days) 1.0-1.5 g kg^{-1} day^{-1} induced toxic liver necrosis (10).

Oral rat, dog (8 wk) 1.0-2.0 g kg^{-1} day^{-1} caused no acute toxicity (11).

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, sufficient evidence of carcinogenicity to animals, IARC classification group 2B (12).

Oral mouse (16 month) 1% of diet for 12-16 months. 19/23 ♂ mice and 7/27 ♀ mice developed hepatomas. Acute porphyria was also reported. Griseofulvin of three particle sizes was used; a lower incidence of hepatomas was observed in the group fed regular formulation which had the lowest surface area (13).

Subcutaneous mouse (1 yr) total dose of 3 mg administered on days 1, 7, 14 and 21 after birth. 24% of ♂ mice developed hepatomas compared with <5% in controls (14).

Teratogenicity and reproductive effects

Gavage mouse, 1500 mg kg^{-1} day^{-1} on days 8-12 of gestation caused no teratogenic effects (15).

Oral rat, 1250 or 1500 mg kg^{-1} day^{-1} on days 6-15 of gestation induced foetal malformations and decreased survival. Malformations included tail abnormalities, no eyes, anal atresia and exencephaly (16).

Metabolism and toxicokinetics

In rats oral doses of 100 mg kg^{-1} ^{36}Cl-griseofulvin, 10% of the activity was found in urine after 24 hr and 4% during 24-48 hr. Of the activity found in the urine 65% was 6-desmethyl griseofulvin. In another study, only 0.14% of similar oral doses was found in the urine within 24 hr, and 16% was recovered in the faeces (11,17).

Following intravenous injection to rats griseofulvin was distributed throughout the body, highest levels being found in the lungs and skin (17).

In rats 77% of an intravenous dose was excreted in the bile and 12% in the urine. The major biliary metabolite was 4-desmethyl griseofulvin (18).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (19).

Drosophila melanogaster induction of aneuploidy positive (20).

In vitro human fibroblasts inhibition of DNA synthesis positive (21).

In vitro human lymphocytes micronucleus assay positive (22).

Induced aneuploidy in the *Vicia faba* root assay system (23).

Other effects

Other adverse effects (human)

Fatal toxic epidermal necrolysis attributed to griseofulvin was reported in a 19-yr-old woman (24).

Erythema multiforme occurred in three patients taking griseofulvin for 3-10 days (25).

Other comments

Physical properties, use, occurrence, analysis, carcinogenicity and mammalian toxicity reviewed (1).

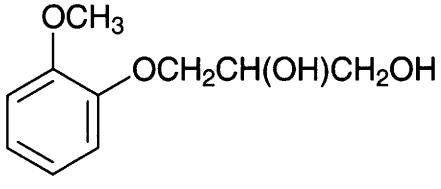
Biochemical studies on griseofulvin-induced protoporphyria reviewed (26).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (27).

References

1. *IARC Monograph* 1976, **10**, 153-161.
2. Davis, H. C. et al *Fish Bull.* 1969, **67**(2), 383-404.
3. Fernandez, B. et al *Rev. Latinoam. Quim.* 1988, **19**(1), 22-25, (Span.) (*Chem. Abstr.* **109**, 128679q).
4. *CRC Handbook of Antibiotic Compounds* 1981, **6**, 290.
5. *Report AD277-689*, Natl. Tech. Inf. Ser., Springfield, VA, USA.
6. *Nature (London)* 1958, **182**, 1320.
7. Korzyoski, T. et al *Antibiotics: Origin, Nature and Properties*, 1978, **3**, 1766, American Society for Microbiology, Washington, DC, USA.
8. Khalifa, B. A. et al *J. Egypt. Vet. Med. Assoc.* 1987, **47**(1-2), 107-116.
9. Soliman, M. M. et al *J. Egypt. Vet. Med. Assoc.* 1987, **47**(1-2), 87-95.
10. Barich, L. L. et al *Antibiot. Chemother.* 1961, **11**, 566-571.
11. Barnes, M. J. et al *Biochem. J.* 1961, **78**, 41-43.
12. *IARC Monograph* 1987, **Suppl. 7**, 391.
13. De Matteis, F. et al *Cancer Res.* 1966, **26**, 721-726.
14. Fujii, K. et al *Toxicol. Appl. Pharmacol.* 1969, **14**, 613-614.
15. Karloek, R. J. et al *Teratog., Carcinog., Mutagen.* 1987, **7**(1), 7-16.
16. Klein, M. F. et al *Science (Washington, DC, 1883-* 1972, **175**, 1483-1484.
17. Bedford, C. et al *AMA Arch. Dermatol.* 1960, **81**, 735-745.
18. Symchowicz, S. et al *Biochem. Pharmacol.* 1967, **16**, 2405-2411.
19. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**, (Suppl.21), 2-141.
20. Zimmering, S. et al *Mutat. Res.* 1990, **234**(5), 319-326.
21. Yanagisawa, K. *Nippon Hifuka Gakkai Zasshi* 1987, **97**(8), 945-952 (Japan.) (*Chem. Abstr.* **107**, 170146x).
22. Migliore, L. et al *Toxicol. In Vitro* 1991, **5**(4), 325-336.
23. Sandhu, S. S. et al *Toxicol. Ind. Health* 1988, **4**(2), 257-267.
24. Mion, G. et al *Lancet* 1989 **ii**, 1331.
25. Rustin, M. H. A. et al *Br. J. Dermatol.* 1989, **120**, 455-458.
26. Shimoyama, T. et al *Ann. N. Y. Acad. Sci.* 1987, **514**, 160-169.
27. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G47 guaiphenesin



$C_{10}H_{14}O_4$ **Mol. Wt.** 198.22 **CAS Registry No.** 93-14-1

Synonyms 3-(2-methoxyphenoxy)-1,2-propanediol; glycerin guaiacolate; glyceryl guaicafate; glycerol α-(2-methoxyphenyl) ether; Aeronesin; Creson; Glycotuss; Guaiacuran; Hustisol; Miocurin; Myocaine; Neurotone; Respenyl; Robitussin; Sinotol

EINECS No. 202-222-5 **RTECS No.** TY 8400000

Uses Antitussive and decongestant. Anaesthetic.

Physical properties

M. Pt. 78-79°C **B. Pt.** 215°C at 19 mmHg

Solubility Water: 50 g l^{-1} at 25°C. Organic solvents: benzene

Environmental fate

Degradation studies

Utilised by *Acinetobacter*, *Alcaligenes*, and *Bacillus subtilis* as sole carbon source (1,2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 690, 1510 mg kg^{-1}, respectively (3,4).

LD_{50} subcutaneous mouse, rat 800, 2550 mg kg^{-1}, respectively (5,6).

LD_{50} intraperitoneal mouse 500 mg kg^{-1} (4).

Metabolism and toxicokinetics

In humans guaiphenesin is absorbed from the gastro-intestinal tract. It is metabolised and excreted in the urine, principally as glucuronide and sulfate conjugates (7,8).

Other effects

Other adverse effects (human)

Gastro-intestinal discomfort has been reported in some patients. Very large doses can cause nausea and vomiting (7).

Administration is considered unsafe for use in patients with acute porphyria because it has been shown to be porphyrinogenic in animals (9).

References

1. Vasudevan, N. et al *Curr. Sci.* 1990, **59**(1), 52-54.
2. Vasudevan, N. et al *J. Biotechnol.* 1989, **9**(2), 107-116.
3. *Pharmacol. Res. Commun.* 1969, **1**, 413.
4. Usdin, E. et al *Psychotropic Drugs and Related Compounds* 2nd ed., 1972, 398, Washington, DC, USA.
5. *Arzneim.-Forsch.* 1965, **15**, 1355.
6. *Drugs in Japan: Ethical Drugs* 6th ed., 1987, 210, Jakugyo Jiho Co., Tokyo, Japan.
7. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
8. Gosselin, R. E. et al *Clinical Toxicology of Commercial Products* 4th ed., 1976, II-240, Williams & Williams, Baltimore, USA.
9. Moore, M. R. et al *Porphyria: Drug Lists* 1991, Porphyria Research Unit, University of Glasgow, UK

G48 guanidine hydrochloride

$$H_2NC(=NH)NH_2 \cdot HCl$$

CH_6ClN_3 **Mol. Wt.** 95.53 **CAS Registry No.** 50-01-1

Synonyms guanidine monohydrochloride

EINECS No. 200-002-3 **RTECS No.** MI 4300000

Uses Fire-proofing agent. Protein denaturant. Parasympathomimetic drug.

Physical properties

M. Pt. 185-189°C **Specific gravity** 1.354 at 20°C with respect to water at 4°C

Solubility Water: miscible. Organic solvents: ethanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to eyes and skin (R22, R36/38)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust (S2, S22)

Ecotoxicity

Fish toxicity
Not toxic to stickleback and rainbow trout at 30 mg l^{-1} for 24 hr (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 570-620 mg kg^{-1}. Clinical signs of behavioural and respiratory changes were observed (2).
LD_{Lo} subcutaneous dog, guinea pig, rat 100-400 mg kg^{-1} (3,4).
LD_{50} intraperitoneal mouse 500 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Oral rat (4 wk) 94 mg kg^{-1} caused no observable toxic effects (6).

Irritancy
Dermal rabbit (24 hr) 500 mg caused severe irritation. 81 mg instilled into rabbit eye caused moderate irritation (exposure not specified) (7,8).

Genotoxicity

Saccharomyces cerevisiae 1203, D58511C, non-chromosomal respiratory deficient mutation assay positive (9).

Other effects

Other adverse effects (human)
Therapeutic use has been associated with bone-marrow suppression in some patients (10).

Any other adverse effects
Dermal rabbit (24 hr) 2000 mg kg^{-1} applied to clipped dorsal skin surface caused no compound-related fatalities or clinical effects except dermal irritation, necrosis and eschar formation were observed (11).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

References

1. McPhee, C. et al *Lethal Effects of 2014 Chemicals to Fish* 1989, EPA 560/6-89-001; PB89-156-715, Washington, DC, USA.
2. Morgan, E. W. et al *Report* 1989, LAIR-418, Toxicology Series – 87, NTIS, Washington, DC, USA.
3. *J. Pharmacol. Exp. Ther.* 1926, **28**, 251.
4. *Abdernalden's Handbuch der Biologischen Arbeitsmethoden* 1935, **4**, 1352, Leipzig, Germany.
5. *NTIS Report AD277-689* Natl. Tech. Inf. Ser., Springfield, VA, USA.
6. *Kirk-Othmer Encyclopedia of Chemical Technology* 3rd ed., 1984, **Supplement**, 514-521.
7. *NTIS Report AD-A166-306* Natl. Tech. Inf. Ser., Springfield, VA, USA.
8. *NTIS Report AD-A184-068* Natl. Tech. Inf. Ser., Springfield, VA, USA.
9. Juliani, M. H. et al *Biochem. Biophys. Res. Commun.* 1973, **53(2)**, 531-538.
10. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
11. Hiatt, G. F. et al *Report* 1989, LAIR-419, Toxicology Series – 98, NTIS, Washington, DC, USA.
12. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G49 guanidine nitrate

$$H_2NC(=NH)NH_2 \cdot HNO_3$$

$CH_6N_4O_3$ **Mol. Wt.** 122.08 **CAS Registry No.** 506-93-4

Synonyms guanidine mononitrate; guanidinium nitrate

EINECS No. 208-060-1 **RTECS No.** MI 4350000

Uses Manufacture of explosives.

Physical properties

M. Pt. 213-215°C

Solubility Water: 10%. Organic solvents: acetone, ethanol

Occupational exposure

UN No. 1467 **HAZCHEM Code** 1Y **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1030-1200 mg kg^{-1}. Clinical signs included behavioural changes, hunched posture and changes in reflex activity (1).

LD_{50} dermal rabbit >10,000 mg kg^{-1} (2).

Irritancy

Caused severe skin and eye irritation to rabbits in modified Draize test (3,4).

Sensitisation

No evidence of skin sensitisation was reported in the Buehler patch-test on guinea pigs (5).

Other effects

Any other adverse effects

Dermal rabbit (24 hr) 2000 mg kg^{-1} applied to skin with a semi-occlusive covering caused no compound-related fatalities or clinical effects except dermal irritation (6).

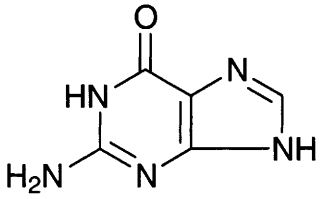
Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

References

1. Brown, L. D. et al *Report* 1988 – LAIR-276, Toxicology Series – 96, NTIS, Washington, DC, USA.
2. *Material Safety Data Sheet for Guanidine Nitrate* 1982, American Cyanamid Co., New York, NY, USA.
3. Morgan, E. W. et al *Report* 1986, LAIR-212, NTIS, Washington, DC, USA.
4. Le Tellier, Y. C. et al *Report* 1988, LAIR-280, Toxicology Series – 9, NTIS, Washington, DC, USA.
5. Hitatt, G. F. et al *Report* 1988, LAIR-282, Toxicology Series 100, NTIS, Washington, DC, USA.
6. Sano, S. K. et al *Report* 1988, LAIR-281, Toxicology Series – 85, NTIS, Washington, DC, USA.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

G50 guanine



$C_5H_5N_5O$ **Mol. Wt.** 151.13 **CAS Registry No.** 73-40-5

Synonyms C.I. Natural White 1; 2-amino-1,7-dihydro-6*H*-purin-6-one; 2-aminohypoxanthine; 2-amino-6-hydroxypurine; natural pearl essence

EINECS No. 200-799-8 **RTECS No.** MF 8260000

Uses Food colorant. In cosmetics.
Occurrence Component of nucleic acids.

Physical properties

M. Pt. 360°C (decomp., with partial sublimation)
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Metabolism and toxicokinetics
Absorbed in uric acid form from gastro-intestinal tract of the chicken. Metabolism occurs in the mucosa of the duodenum (1).

Other comments

The activity of a number of carcinogens is related to the formation of covalent adducts of guanine (2-4).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).
Soluble in aqueous ammonium hydroxide and potassium hydroxide.

References

1. Karasawa, Y. et al *Comp. Biochem. Physiol., A: Comp. Physiol.* 1991, **99A**(1-2), 235-240.
2. Fuchs, R. P. P. et al *Environ. Health Perspect.* 1990, **89**, 83-87.
3. Said, B. et al *Nucleic Acid Res.* 1991, **19**(6), 1311-1316.
4. Lyman, B. A. et al *Biochem. Pharmacol.* 1988, **37**(8), 1481-1486.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

G51 Guar Gum

CAS Registry No. 9000-30-0

Synonyms Decorpa; Emulgum 200; Fire gum G; gur flour; galactasol; Gum cyamopsis; Indalca A G; Jaguar; Supercol; E412; Edicol

EINECS No. 232-536-8 **RTECS No.** MG 0185000

Uses Absorbent for liquid spills. Gelling and binding agent. Used in the preparation of drug formulation and in food. Flocculent. Paper sizing. Antidiabetic food aid.

Occurrence Obtained from the ground endosperms of the legume *Cyamopsis tetragonolobus*.

Physical properties

Solubility Water: miscible. Organic solvents: dimethyl sulfoxide

Environmental fate

Degradation studies

Degraded by *Pseudomonas* species isolated from soil (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, rabbit, hamster 6000-8100 mg kg^{-1} (2,3).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via feed. Negative results were reported for rats and mice of both sexes (4).

Metabolism and toxicokinetics

Not metabolised by colonic bacteria in mammals (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6). *In vivo* rat dominant lethal assay negative (7).

Other effects

Other adverse effects (human)

Therapeutic use has been reported to cause gastro-intestinal disturbance with flatulence, diarrhoea or nausea, particularly at the start of treatment (8).

Other comments

Enriched diets in rats suppressed increases in plasma and liver cholesterol (9).

Consists of linear chains of (1→4)-β-D-mannopyranosyl units with α-D-galactopyranosyl units attached by (1→6) linkages. Ratio of D-galactose to D-mannose is 1:2. Molecular weight ~220,000 (10).

References

1. Yoshida, S. et al *Bokin Bobai* 1991, **19**(3), 105-110, (Japan.) (*Chem. Abstr.* **115**, 119444f).
2. Graham, S. L. et al *Food Cosmet. Toxicol.* 1981, **19**, 287.
3. *Report* 1976, **124** Food and Drug Research Laboratories, Waverly, New York, NY, USA.
4. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-229, NIEHS, Research Triangle Park, NC, USA.

5. Lancaster, C. M. et al *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.* 1989, **30**(1), 480-481.
6. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141.
7. Newell, G. W. et al *Report* 1972, ISS No.221815/4, 102, NTIS, Washington, DC, USA.
8. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
9. Takehisha, F. et al *Nippon Eiyo, Shokuryo Gakkaishi* 1990, **43**(4), 269-274 (Japan.)(*Chem. Abstr.* **114**, 17181v.).
10. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

G52 guazatine acetates

CAS Registry No. 115044-19-4

EINECS No. 254-351-1

Uses Fungicide with bird-repellant properties.

Physical properties

M. Pt. ~60°C **Specific gravity** 1.09 at 20°C **Partition coefficient** log P_{ow} –1.2 (pH 3), log P_{ow} –0.9 (pH 10)
Volatility v.p. 6×10^{-6} mmHg at 25°C
Solubility Water: >3 kg l^{-1}. Organic solvents: dimethylformamide, ethanol, methanol, 1-methylpyrrolid-2-one

Ecotoxicity

Invertebrate toxicity
LD_{50} contact >200 μg bee^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 360 mg kg^{-1} (1).
LD_{50} dermal rat 1100 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse effect level 17.5 mg kg^{-1} daily (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC.Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

Other comments

Guazatine is a mixture of the reaction products from polyamines, comprising mainly octamethylenediamine, iminodi(octamethylene)diamine and octamethylenebis(imino-octamethylene)diamine, and carbamonitrile (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

G53 Gum Arabic

CAS Registry No. 9000-01-5

Synonyms Australian gum; Cerospray; E414; gum ovaline; gum Senegal; Indian gum; NCI-C50748; wattle gum

EINECS No. 232-519-5 **RTECS No.** CE 5945000

Uses Absorbent for liquid spills. Used as a gelling, emulsifying and binding agent. Used in the preparation of drugs, food and adhesive formulations.
Occurrence Occurs in *Acacia* species.

Physical properties

Specific gravity 1.35-1.49
Solubility Water: ~50%. Organic solvents: glycerol, propylene glycol

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 8000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice via feed. Negative results were reported for rats and mice of both sexes (2).

Metabolism and toxicokinetics
Not metabolised by colonic bacteria in mammals (3).

Irritancy
Eye rabbit (5 hr) 36 mg caused severe irritation (4).

Sensitisation
Sensitisation has been reported in ~50% of exposed print workers (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6,7).
Escherichia coli WP2 tryptophan reversion assay negative (7).
In vivo ♂ mouse dominant lethal assay heritable translocation negative (8).

Other effects

Other adverse effects (human)
Examination of 37 printing workers revealed 13 cases of marked dyspnoea soon after exertion (exposure unspecified). Occasional chronic bronchitis and pulmonary congestion were also reported in 20/37 printers (5).

References

1. *Report* 1976, 124, Food and Drug Research Laboratories, Waverly, New York, NY, USA.
2. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-227, NIEHS, Research Triangle Park, NC, USA.
3. Lancaster, C. M. et al *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* 1989, **30**(1), 480-481.
4. *Arch. Otolaryngol.* 1967, **78**, 384.
5. International Labour Office *Encyclopedia of Occupational Health and Safety* 1971, 629, McGraw-Hill, New York, NY, USA.
6. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141.
7. Prival, M. J. et al *Mutat. Res.* 1991, **260**(4), 321-329.
8. Sheu, C. W. et al *Environ. Mutagen.* 1986, **8**(3), 357-367

H1 hafnium

Hf

Hf **Mol. Wt.** 178.49 **CAS Registry No.** 7440-58-6

Synonyms

EINECS No. 231-166-4 **RTECS No.** MG 4600000

Uses Hafnium and its compounds are used as neutron screens and control rod material in nuclear reactors, electrodes, in heat-resistant materials, in the manufacture of explosives and in the textile industry.
Occurrence Abundance in earth's crust ~5 ppm. Found in all zirconium containing minerals. Extracted from cyrtolite.

Physical properties

M. Pt. 2227°C **B. Pt.** 4602°C **Specific gravity** 13.31 at 20°C
Solubility Water: insoluble

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.5 mg m^{-3}
UK-LTEL 0.5 mg m^{-3} **UK-STEL** 1.5 mg m^{-3}
US-TWA 0.5 mg m^{-3}

UN No. 2545 (dry powder)

UN No. 1326 (wetted powder) **HAZCHEM Code 4W** (dry powder) **Conveyance classification** spontaneously combustible substance (dry powder) **Conveyance classification** flammable solid (wetted powder)

Mammalian & avian toxicity

Metabolism and toxicokinetics
The activity of ^{181}Hf injected into rats intravenously as a constituent of hafnium-sodium oxyphenyl acetate, was highest in the spleen, lower in the liver, bones and kidneys, and low in the adrenals, thyroid, pancreas, salivary glands and testes. Activity was detectable during 4 days post-injection, 95% occurring in the plasma. ~7% of the dose was eliminated over a period of 16 days. The rate of urinary excretion was 2.4 times higher than faecal excretion (1).

Other comments

Use, occurrence and toxicity of hafnium compounds reviewed (1).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (2).

References

1. Filov, V. A. et al (Eds.) *Harmful Chemical Substances* 1993, **1**, 614-619, Ellis Harwood, New York, NY, USA.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H2 hafnium chloride

$HfCl_4$

$HfCl_4$ **Mol. Wt.** 320.30 **CAS Registry No.** 13499-05-3

Synonyms hafnium tetrachloride

EINECS No. 236-826-5 **RTECS No.** MG 4650000

Physical properties

M. Pt. 250°C (volatilises)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Gavage rat (3 wk) 400 mg kg^{-1} day^{-1} altered protein metabolism, caused granular degeneration of the liver and kidneys and necrotic inflammatory lesions in the small intestine (1).

Metabolism and toxicokinetics

Undergoes hydrolysis in the body fluids within 30 mins with the formation of hydrochloric acid. Rate of hydrolysis was slowest in the stomach (1).

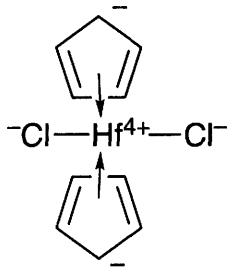
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides guide level 25 mg l^{-1} (2). Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Filov, V. A. et al (Ed.) *Harmful Chemical Substances* 1993, **1**, 614-619, Ellis Horwood, New York, NY, USA.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

H3 hafnocene dichloride



$C_{10}H_{10}Cl_2Hf$ **Mol. Wt.** 379.58 **CAS Registry No.** 12116-66-4

Synonyms hafnium dicyclopentadiene dichloride; dichlorobis(η^5-2,4-cyclopentadien-1-yl)hafnium

EINECS No. 235-177-5 **RTECS No.** MG 4815000

Uses In synthesis of a variety of early transition-metal complexes and organo-metal complexes. The compound has anti-viral and anti-tumour properties (1,2).

Physical properties

M. Pt. 230-233°C

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 100 mg kg^{-1} (3).

Genotoxicity

Binds to mammalian DNA for up to 48 hr *in vitro*, and is not released by dissolving in 1220 mg l^{-1} sodium perchlorate (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chloride guide level 25 mg l^{-1} (4).
Limited under UK Water Supply (Water Quality) Regulations, Statutory Instrument No. 1147, 1989. Chloride prescribed concentration 400 mg l^{-1} (12 monthly average) (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Soluble pharmaceutical formulations can be prepared.

References

1. Ward, S. G. *Appl. Organomet. Chem.* 1989, **3**(6), 491-497.
2. McLaughlin, M. L. *J. Am. Chem. Soc.* 1990, **112**(24), 8949-8952.
3. *US Army Armament Research and Development Command* Chemical Systems Laboratory, Aberdeen Proving Ground, MD 21010, USA.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1989 No. 1147 The Water Supply (Water Quality) Regulations* 1989, HMSO, London, UK.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

H4 halothane

$CF_3CHBrCl$

$C_2HBrClF_3$ **Mol. Wt.** 197.38 **CAS Registry No.** 151-67-7

Synonyms bromochlorotrifluoroethane; 2-bromo-2-chloro-1,1,1-trifluoroethane; Fluothane; Narcotane; Rhodialothen

EINECS No. 205-796-5 **RTECS No.** KH 6550000

Uses Inhalation anaesthetic.

Physical properties

B. Pt. 50.2°C **Specific gravity** 1.872 at 20°C with respect to water at 4°C **Volatility** v.p. 243 mmHg at 20°C
Solubility Water: 0.345%. Organic solvents: petroleum ether

Occupational exposure

DE-MAK 5 ppm (41 mg m^{-3})
SE-LEVL 5 ppm (40 mg m^{-3}) **SE-STEL** 10 ppm (80 mg m^{-3})
UK-LTEL 10 ppm (82 mg m^{-3})
US-TWA 50 ppm (404 mg m^{-3})

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, guinea pig 5700-6000 mg kg^{-1} (1).
LC_{50} (10 min) inhalation mouse 22000 ppm (2).

Sub-acute and sub-chronic data
Inhalation guinea pig, 1% halothane for 4 hr at 2-wk intervals (total exposure rate unspecified). An antibody which was cross-reactive with trifluoracetylated serum albumin was induced. The possible role of this antibody in halothane-induced hepatitis is discussed (3).
Rats exposed prenatally by inhalation administration to the dams of 80 mg m^{-3} for 8 hr day^{-1} or 5 days wk^{-1} and postnatally for 60 days to the same concentration had later impairment of hearing ability. This correlated with persistent synaptic malformation in the cerebral cortex, destruction of the rough-surfaced endoplasmic reticulum, dilation of the Golgi complex and focal cytoplasmic vacuolation (4).

Carcinogenicity and chronic effects
No adequate data for evaluation of carcinogenic activity to humans and animals, IARC classification group 3 (5).

Teratogenicity and reproductive effects
Inhalation rat, 80 mg m^{-3} 8 hr day^{-1} on 5 days wk^{-1} throughout pregnancy. Offspring had ultrastructural changes in the liver within 24 hr of birth. These changes included myelin figures and large areas of focal cytoplasmic degradation in many hepatocytes. Accumulation of lipids within hepatocytes, and leucocytic infiltration were noted in many cases. Focal necrosis was observed in >50% of tissue samples (6).

Metabolism and toxicokinetics
Trifluoroacetic acid was produced in mouse liver for at least 5 hr following inhalation exposure (7).
In dogs trifluoracetic acid and inorganic fluoride were excreted in the urine (40-60%) and in the bile (~ 30%) (8).
Gaseous loss through skin in human volunteers after inhalation exposure was 6 × and 2 × greater than that of desflurane and isoflurane, respectively (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation marginally positive (10).

Drosophila melanogaster sex-linked recessive lethal assay positive (11).
Saccharomyces cerevisiae gene conversion and homozygosis positive (12).
In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosome aberrations with and without metabolic activation negative (13,14).
In vivo mouse, induction of chromosomal aberrations in bone marrow cells, micronucleus test and dominant lethal test negative (15).

Other effects

Other adverse effects (human)
Hepatic dysfunction has been attributed to chronic inhalation of low concentrations during occupational exposure. Exacerbation of liver disease has also been related to halothane exposure (16,17).
Studies have shown a high rate of miscarriages, abortions, premature delivery and infertility among exposed female anaesthetists and nurses (18-20).
A higher rate of birth defects among children whose mothers worked in operating theatres during pregnancy was reported (21).
An increase in total malignancies, including malignant thymoma, leiomyosarcoma, hepatocellular carcinoma and carcinoma of the pancreas, was observed in a study of 621 ♀ nurse-anaesthetists (22).

Any other adverse effects
Inhalation pig, 3% halothane induced malignant hyperthermia in 1.4 min, at 2% in 2.5 min, at 1% in 5.4 min and at 0.5% in 11.8 min (23).

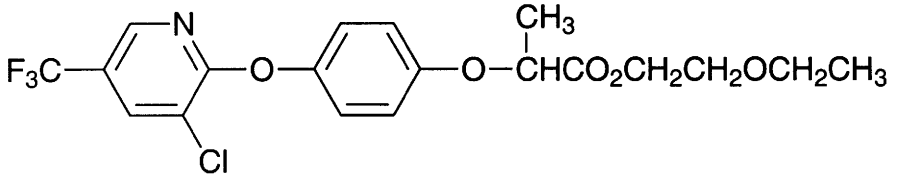
Other comments

Characterisation of hapten carrier protein conjugates associated with halothane hepatitis reviewed (24).
Halothane hepatitis and neurotoxicity reviewed (25,26).
Toxicity of inhalation anaesthetics, including halothane, reviewed (27).

References

1. *Gig. Tr. Prof. Zabol.* 1980, **24**(3), 36.
2. *J. Pharmacol. Exp. Ther.* 1946, **86**, 197.
3. Siadat-Pajouh, M. et al *Anesth. Analg. (N. Y.)* 1987, **66**(12), 1209-1214.
4. Ahern, C. P. et al *Curr. Top. Vet. Med. Anim. Sci.* 1987, **38**, 371-378.
5. Quimby, K. L. et al *Anesth. Analg. (N. Y.)* 1975, **54**, 628-633.
6. Chang, L. W. et al *Can. Anaesth. Soc. J.* 1975, **22**, 330-338.
7. Araj, K. *Masui to Sosei* 1990, **26**(4), 377-381 (Japan.) (*Chem. Abstr.* **115**, 22696p).
8. Sakai, T. et al *Drug Metab. Dispos.* 1991, **19**(2), 419-422.
9. Fassoulaki, A. et al *Anesthesiology* 1991, **74**(3), 479-483.
10. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
11. Baden, J. M. et al *Br. J. Anaesth.* 1987, **59**(6), 772-775.
12. Callen, D. F. et al *Mutat. Res.* 1980, **77**, 55-63.
13. White, A. E. et al *Anesthesiology* 1979, **50**, 426-430.
14. Galloway, S. M. et al *Environ. Mol. Mutagen.* 1987, **10**(Suppl.10), 1-175.
15. Basler, A. et al *Anesthesiology* 1981, **55**, 143-147.
16. Belfrage, S. et al *Lancet* 1966, **ii**, 1466-1467.
17. Klatskin, G. et al *New Engl. J. Med.* 1969, **280**, 515-522.
18. Vaisman, A. I. *Eksp. Khir. Anesteziol.* 1967, **3**, 44-49.
19. Askrog, V. et al *Nord. Med.* 1970, **83**, 498-500.
20. Knill-Jones, R. P. et al *Lancet* 1972, **i**, 1326-1328.
21. Corbett, T. H. et al *Anesthesiology* 1974, **41**, 341-344.
22. Corbett, T. H. et al *Anesthesiology* 1973, **38**, 260-263.
23. *IARC Monograph* 1987, **Suppl. 7**, 93-95.
24. Pohl, L. R. et al *Adv. Exp. Med. Biol.* 1991, **283** (Biol. React. Intermed. 4), 111-120.
25. Ray, D. C. et al *Br. J Anaesth.* 1991, **67**(1), 84-99.
26. Levin, E. D. et al *Neurotoxicol Teratol.* 1991, **13**(4), 461-470.
27. *IARC Monograph* 1976, **11**, 285-293

H5 haloxyfop-ethoxyethyl



$C_{19}H_{19}ClF_3NO_5$ **Mol. Wt.** 433.81 **CAS Registry No.** 87237-48-7

Synonyms 2-ethoxyethyl 2-[4-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoate; Dowco 453; Gallant; haloxyfop-etotyl; Zellek

RTECS No. UA 2458260

Uses Herbicide.

Physical properties

M. Pt. 58-61°C **Specific gravity** 1.34 **Partition coefficient** log P_{ow} 4.47 at 20°C (1)
Volatility v.p. 1.0×10^{-8} mmHg at 25°C
Solubility Water: 2.7 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, ethyl acetate, hexane, methanol, isopropanol, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, fathead minnow, trout, 280-1180 µg l^{-1} (1,2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* 4.6 mg l^{-1} (1).
LD_{50} (48 hr) oral and contact bee 100 µg bee^{-1} (1).

Environmental fate

Abiotic removal
$t_{1/2}$ for hydrolysis in water at 25°C 33 days at pH 5, 5 days at pH 7, and a few hours at pH 9. The rate of hydrolysis increases with temperature (1).
80% photodegradation under laboratory conditions, equivalent to 14.5 hr solar irradiation. 40-60% underwent isomerisation. Dealkylation and breakage of the ether bonds with recombination of the resultant fragments, and dechlorination also occurred (3).
Persisted more than 3 months in soil (4).

Adsorption and retention
K_{ow} 21,600 in silty clay loam soil (1.97% organic carbon) (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 525 mg kg^{-1} (1).
LD_{50} dermal rabbit >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (8 days) oral mallard duck, bobwhite quail >5600 mg kg^{-1} diet (1).

Metabolism and toxicokinetics
Following oral administration to rats, metabolised to haloxyfop which was excreted in the faeces and urine (1).

Irritancy
Non-irritant to skin and moderate eye irritant to rabbits (1).

Sensitisation
No skin sensitisation in guinea pigs (1).

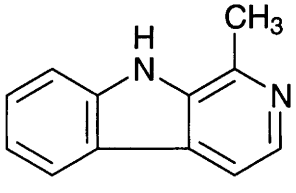
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (7).

References

1. *The Agrochemical Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Mel'nikora, N. P. et al *Izv. Timiryazevsk. S-kh. Akad.* 1990, (3), 155-160 (Russ.) (*Chem. Abstr.* **114**, 96724k).
4. Milssm, H. *Swed. Crop. Prot. Conf.* 1987, **28**(1), 207-214.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK

H6 harmane



$C_{12}H_{10}N_2$ **Mol. Wt.** 182.22 **CAS Registry No.** 486-84-0

Synonyms 1-methyl-9*H*-pyrido[3,4-*b*]indole; 1-methyl-β-carboline; Loturine; Passiflorin; Harman

EINECS No. 207-642-2 **RTECS No.** UV 0280000

Uses Anxiolytic and weak antiparasitic agent.
Occurrence In plants, including the bark of *Sickingia rubra*. In beer, wine, cooked meats and other foods and beverages (1,2).
In mammalian tissue, including human cerebrospinal fluid (3).
Identified in tobacco smoke (4,5).

Physical properties

M. Pt. 237-238°C

Occupational exposure

UN No. 2811

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 50 mg kg^{-1} (6).

Carcinogenicity and chronic effects

Rats injected with diethylnitrosamine and subsequently fed 1000 or 2000 ppm harmane for 6 wk showed no hepatotoxicity or promotion of enzyme-altered liver-foci development. Increase in relative kidney weights and some proximal tubule lesions in kidneys were observed (7).

Metabolism and toxicokinetics

Metabolism by rat liver microsomes produces 6-hydroxyharmane as the major metabolite. Types I and II binding to cytochrome P_{450} occur. Metabolism can be induced fourfold by phenabarbitone pretreatment and elevenfold by 3-methylcholanthrene pretreatment (8).

Genotoxicity

Induced SOS responses in *Salmonella typhimurium* using the *umu* test and reversion of *trp*E977 frameshift mutation in *Escherichia coli* (9).

Other effects

Any other adverse effects

Inhibits monoamine oxidase (4).

Ciliostatic activity has been observed using cilia of chicken embryo trachea *in vitro* (4).

Increased permeability of cultured human lung fibroblasts (5).

Anxiolytic activity in rats correlates with ability of the compound to potentiate neural hyperpolarising effects of 5HT (10).

Effects on benzodiazepine receptors and a putative β-carboline neuroreceptor have also been reported (11).

Other comments

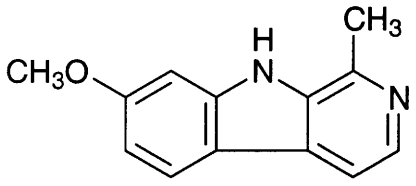
Formation within rat or human tissue is not thought to relate to alcohol ingestion (3).

Pharmacological effects have been reviewed (1,11,12).

References

1. Bosin, T. R. *Alcohol.: Clin. Exp. Res.* 1988, **12**(5), 679-682.
2. Gross, G. A. *Carcinogenesis (London)* 1990, **11**(9), 1597-1603.
3. Bosin, T. R. et al *Alcohol (N. Y.)* 1988, **5**(6), 505-511.
4. *J. Pharm. Sci.* 1968, **57**, 269.
5. Thelestam, M. et al *Toxicology* 1980, **15**, 203-217.
6. Sigg, E. B. et al *Arch. Ind. Pharmacodyn.* 1964, **149**, 164.
7. Hagiwara, A. et al *J. Toxicol. Environ. Health* 1990, **29**(2), 211-218.
8. Tweedie, D. J. *Xenobiotica* 1988, **18**(7), 785-796.
9. Oda, Y. et al *Mutat. Res.* 1988, **208**(1), 39-44.
10. Abramets, I. I. *Farmakol. Toksikol. (Moscow)* 1990, **53**(5), 13-16.
11. Dodd, R. H. et al *Encephale* 1987, **13**, 157-158 (Fr). (*Chem. Abstr.* **108**, No.179359x).
12. Cavin, J. C. *J. Ethnopharmacol.* 1987, **19**(1), 89-94.

H7 harmine



$C_{13}H_{12}N_2O$ **Mol. Wt.** 212.25 **CAS Registry No.** 442-51-3

Synonyms leucoharmine; 7-methoxyharman; 7-methoxy-1-methyl-9*H*-pyrido[3,4-*b*]indole; 7-methoxy-1-methyl-β-carboline; banisterine; telepathine

EINECS No. 207-131-4 **RTECS No.** UV 0175000

Uses Narcotic. Central stimulant.

Occurrence Alkaloid in *Banisteria caapi* and dried seeds of *Peganum harmala.*

Physical properties

M. Pt. 262-264°C (98% purity)

Solubility Water: slightly soluble. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2811

Ecotoxicity

Toxicity to other species

LD_{Lo} subcutaneous frog 300 mg kg^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous mouse 240 mg kg^{-1} (2).

LD_{Lo} intravenous rat, mouse, rabbit 10, 50, 60 mg kg^{-1}, respectively (3,4).

LD_{Lo} subcutaneous guinea pig, rabbit 100, 200 mg kg^{-1}, respectively (3).

TD_{Lo} intramuscular human 3 mg kg^{-1} (3).

LD_{Lo} intravenous rabbit 60 mg kg^{-1} (4).

Metabolism and toxicokinetics

6-Hydroxy-7-methoxyharman was the major metabolite of harmine in 3-methylcholanthrene-induced mice. The other novel metabolite was 3- or 4-hydroxy-7-methoxyharman (5).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation positive, TA1538 and TA1535 without metabolic activation positive (6).

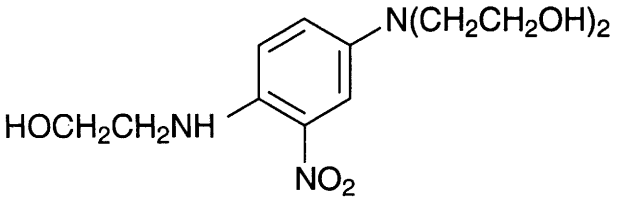
Salmonella typhimurium TA97, TA98 without metabolic activation negative, with metabolic activation weakly positive. *Escherichia coli* PQ37 chromotest without metabolic activation negative. *In vivo* micronucleus assay negative, indicating that harmine is not able to induce chromosomal mutations (7).

References

1. *J. Pharm. Pharmacol.* 1936, **9**, 37
2. *Pharm. Chem. J.* 1976, **10**, 1171.

3. *Naunyn-Schmiedebergs Arch. Exp. Pathol. Pharmakol.* 1928, **129**, 133.
4. *Neuropharmacology* 1971, **10**, 15.
5. Tweedie, D. J. et al *Drug Metab. Dispos.* 1987, **15**(1), 74-81.
6. Lin, J.-K. et al *Toxic. Assess.* 1986, **1**(3), 339-355.
7. Picada, J.N. et al *Mutat. Res.* 1997, **379**(2), 135-149.

H8 HC Blue No. 2



$C_{12}H_{19}N_3O_5$ **Mol. Wt.** 285.30 **CAS Registry No.** 33229-34-4

Synonyms 2,2′-[[4-[(2-hydroxyethyl)amino]-3-nitrophenyl]imino]diethanol; 3-nitro-N^1,N^1,N^4-tris(2-hydroxyethyl)-*p*-phenylenediamine; NCI-C54897

EINECS No. 251-410-3 **RTECS No.** KL 2880000

Uses In preparation of hair dyes.

Physical properties

Partition coefficient log P_{ow} –1.0647 (1)
Solubility Water: 1-10 g l^{-1} at 23°C. Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice via feed. No evidence of carcinogenicity was found in rats and mice of either sex (2).

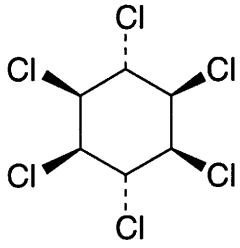
Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 (metabolic activation unspecified) positive (1,3,4).
Escherichia coli WP2 *uvr*A⁻ with and without metabolic activation positive (4).
In vitro mouse lymphoma L5178Y tk+/tk- forward mutation assay with and without metabolic activation positive (4).
In vitro Chinese hamster ovary cells, sister chromatid exchanges positive, chromosome aberrations negative (5).
In vitro primary rat, mouse, hamster and rabbit hepatocytes, unscheduled DNA synthesis positive (6).
In vivo mouse bone marrow cells, induction of micronuclei positive (7).

References

1. McCoy, G. D. et al *Carcinogenesis (London)* 1990, **11**(7), 1111-1117.
2. *National Toxicology Program Research and Testing Division* 1992, Report No.TR-293, NIEHS, Research Triangle Park, NC, USA.
3. Zeiger, E. *Cancer Res.* 1987, **47**, 1287-1296.
4. Oberly, T. J. et al *Mutat. Res.* 1990, **241**(2), 151-159.
5. Rosenkranz, H. S. et al *Mutagenesis* 1990, **5**(6), 559-571.
6. Hill, L. E. et al *Mutat. Res.* 1990, **241**(2), 145-150.
7. Parton, J. W. et al *Mutat. Res.* 1990, **241**(2), 139-144

H9 HCH



$C_6H_6Cl_6$ **Mol. Wt.** 290.83 **CAS Registry No.** 608-73-1

Synonyms hexachlorocyclohexane; 1,2,3,4,5,6-hexachlorocyclohexane, technical mixture of isomers; benzene hexachloride; BHC; benzahex; dolmix; fortified HCH; HCCH; hexachlor; hexafor; soprocide

EINECS No. 210-168-9 **RTECS No.** GV 3150000

Uses Insecticide.

Physical properties

M. Pt. 113°C **Specific gravity** 1.87 at 20°C **Volatility** v.p. 3.17×10^{-2} mmHg at 20°C
Solubility Water: 1.4 mg l^{-1} in salt water. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable dust fraction)
Supply classification toxic
Risk phrases Harmful in contact with skin – Toxic if swallowed – Possible risk of irreversible effects (R21, R25, R40)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) guppy > 1.4 mg l^{-1} (1).

Bioaccumulation
Bioaccumulation factor for guppy 500 (1).

Environmental fate

Degradation studies
Biodegradation has been studied under both aerobic and anaerobic conditions in a laboratory sediment/water system. Addition of organic nutrients greatly speeded up the biodegradation and isomerisation, especially under aerobic conditions (2).

Adsorption and retention
Highly adsorbed on sediments under both aerobic and anaerobic conditions in a laboratory sediment/water system (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat, 59, 100 mg kg^{-1}, respectively (3,4).

LD_{50} oral chicken 597 mg kg^{-1} (5).
LD_{50} dermal rat 900 mg kg^{-1} (6).
LD_{50} subcutaneous rabbit 75 mg kg^{-1} (7).

Sub-acute and sub-chronic data
Oral rat (90 day) 5 or 25 mg kg^{-1} caused some fatalities. ♂ rats were more susceptible than ♀ rats (8).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (9).
Oral mouse (24 wk) 0, 6.6, 66 or 660 mg kg^{-1} diet. Hepatomas occurred in 20/20 of the high-dose animals. No such tumours occurred at the lower doses or in controls (10).
Oral mouse (32 wk) 0, 100, 300 or 600 mg kg^{-1} diet. Hepatomas occurred in 9/9 of the high-dose group, 7/9 of the 300 mg kg^{-1} group. No such tumours occurred in the low-dose group or in controls (11).
Carcinogenicity of the metabolites 1,2,4-trichlorobenzene, 2,3,5-trichlorophenol and 2,4,5-trichlorophenol was assessed by oral administration to mice at 600 mg kg^{-1} diet for 6 months. No liver tumours occurred in these animals, in contrast to parallel experiments in which the same dose levels of the α, β, and a mixture of γ and ε gave rise to benign and/or malignant liver tumours (12).
Oral rat (2 yr) 10-1600 mg kg^{-1} diet for life. ≥800 mg kg^{-1} diet reduced weight gain and increased mortality. Fatty degeneration and focal necrosis of the liver, chronic nephritis with glomerular fibrosis and hyaline deposits was also seen in these groups (13).

Teratogenicity and reproductive effects
Oral mouse, 5, 25, 50, 100 or 200 mg kg^{-1} on day-9 of gestation caused dose-related increase in the rate of resorption and decrease in the number of live foetuses. Accumulation occurred in foetal fatty tissue, brain, liver and blood. Changes in liver enzyme activities were observed (14).
Acute administration by intraperitoneal injection to mature (90-day-old) and immature (15-day-old) rats caused oxidative stress in the testis and the percentage of dead and damaged spermatzoa was significantly increased over control (15).

Metabolism and toxicokinetics
The α, β and γ isomers of HCH are stored in the adipose tissue of rats and dogs. The α and β isomers are stored to a lesser extent in the liver, kidneys and adrenals (16).
Accumulation of residues in vital organs can be greater in ♂ than ♀ rats (8).
In vitro studies indicate that at least three mechanisms may lead to the formation of trichlorophenols in mammals. The major pathway involves direct hydroxylation and subsequent decomposition of the labile intermediate to yield 2,4,6-trichlorophenol. Dehydrochlorination to pentachlorocyclohexene or dehydrogenation to hexachlorocyclohexene with subsequent addition of oxygen and, following dehydrochlorination, formation of 2,4,5-trichlorophenol and 2,3,4,6-tetrachlorophenol also occurs. Hydroxylation of the intermediate trichlorobenzene may also occur (17-19).

Genotoxicity

Bacillus subtilis rec assay negative (20).

Other effects

Other adverse effects (human)
Aplastic anaemia has been reported in people exposed to HCH or lindane (21,22) .
An increased incidence of lung cancer was reported between 1970 and 1975 in 285 workers who were exposed to various pesticides including HCH (23).

Any other adverse effects
Oral mouse single dose of 70 mg kg^{-1} reduced the spontaneous migration rates of peripheral leukocytes (24).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (25).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (26).
Quality objective under EC Directive 84/491/EEC 0.1 μg l^{-1} (annual mean) in inland surface waters, 0.02 μg l^{-1} (annual mean) in estuary and marine waters. A 'standstill' provision applies to concentrations in sediments, molluscs, shellfish and/or fish. Limit value under EC Directive 84/491/EEC from production plant 2 g HCH per tonne produced (monthly average), 2 mg l^{-1} discharged (monthly flow-weighted average) (27).

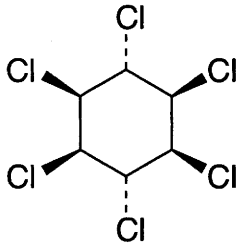
Other comments

Residues have been isolated from natural waters, soil, and in human and animal tissues (16,28).
Contains a mixture of isomers, with 14-77% of the γ-isomer. Technical grades typically contain 40-45% γ-isomer (lindane), 20-22% δ-isomer, 18-22% α-isomer, 4% β-isomer, and 1% ε-isomer, with 10% heptachlorocyclohexane (16).
Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (16,29).

References

1. Carton, J. H. et al *Water Res.* 1978, **12**, 687-690.
2. Wu, W. Z. et al *Chemosphere* 1997, **35**(9), 1887-1894.
3. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
4. *Arch. Toxikol.* 1966, **22**, 115.
5. *Poult. Sci.* 1981, **60**, 2599.
6. Perkov, W. *Wirksubstanzen der Pflanzenschutz- und Schaedlings-Bekaempfungsmittel* 1971/76, Verlag Paul Parey, Berlin, Germany.
7. *U.S. Public Health Service Publication* 1955, **414**, 273.
8. Dikshith, T. S. S. et al *Vet. Hum. Toxicol.* 1991, **33**(3), 235-237.
9. *IARC Monograph* 1987 **Suppl. 7**, 220-222.
10. Negasaki, H. *Gann* 1971, **62**, 431.
11. Hanada, M. et al *Gann* 1973, **64**, 511-513.
12. Goto, M. et al *Chemosphere* 1972, **6**, 279-282.
13. Fitzhugh, O. G. et al *J. Pharmacol. Exp. Ther.* 1950, **100**, 59-66.
14. Dikshith, T. S. S. et al *Vet. Hum. Toxicol.* 1990, **32**(6), 524-527.
15. Samanta, L. et al *Comp. Biochem. Physiol., C: Pharmacol., Toxicol. Endocrinol.* 1997, **118C**(3), 319-327.
16. *IARC Monograph* 1979, **20**, 195-239.
17. Tanaka, K. et al *Agric. Biol. Chem.* 1977, **41**, 723-725.
18. Freal, J. J. et al *J. Agric. Food Chem.* 1973, **21**, 424-427.
19. Chadwick, R. W. et al *Xenobiotica* 1977, **7**, 235-246.
20. Shirasu, Y. et al *Mutat. Res.* 1976, **40**, 19-30.
21. Hans, R. J. *J. Am. Med. Assoc.* 1976, **236**, 1009-1010.
22. Woodliff, H. J. *Med. J. Aust.* 1966, **1**, 628-629.
23. Barthel, E. Z. *Erkr. Atmungsorgane* 1976, **146**, 266-274.
24. Mikramalova, L. I. et al *Immunologiya (Moscow)* 1989, (5), 82-84 (Russ.) (*Chem. Abstr.* **112**, 93501h).
25. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
26. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
27. *DoE Circular 7/89: Water and the environment. The implementation of EC directives on pollution caused by certain dangerous substances discharged into the aquatic environment* 1989, HMSO, London, UK.
28. Goerke, H. et al *Mar. Pollut. Bull.* 1979, **10**, 127-133.
29. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H10 γ-HCH



$C_6H_6Cl_6$ **Mol. Wt.** 290.83 **CAS Registry No.** 58-89-9

Synonyms 1α,2α,3β,4α,5α,6β-hexachlorocyclohexane; 666; γ-BHC; lindane; TAP85; γ-benzene hexachloride

EINECS No. 200-401-2 **RTECS No.** GV 4900000

Uses Insecticide.

Physical properties

M. Pt. 112.8°C (γ-isomer) **B. Pt.** 288°C **Specific gravity** 1.85 **Partition coefficient** log P_{ow} 3.29-3.72 (1)
Volatility v.p. 3.26×10^{-5} mmHg at 20°C
Solubility Water: 7.3 mg l^{-1} at 25°C. Organic solvents: acetone, aromatic and chlorinated solvents, ethanol

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.5 mg m^{-3}
UK-LTEL 0.1 mg m^{-3}
US-TWA 0.5 mg m^{-3}
Supply classification toxic, dangerous for the environment
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Irritating to eyes and skin – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R36/38, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S13, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) goldfish, guppy 0.12-0.3 mg l^{-1} (2,3).
LC_{50} (96 hr) rainbow trout, perch, bluegill sunfish 0.027-0.057 mg l^{-1} (4-6).
LC_{50} (96 hr) Atlantic silverside 9 ppb static bioassay (7).
Bluegill sunfish (18 month) 0.6-9.1 μg l^{-1}, no adverse effect was observed at any of the tested concentrations.
Fathead minnow (43 wk) 1.4-23.5 μg l^{-1}, a statistically significant increase in mortality was observed at the highest dose. Growth of surviving fish was not adversely affected and spawning was normal in all test groups (8).
In freshwater and marine water fish symptoms of acute poisoning (LC_{50} for the majority of species ~ 0.05 mg l^{-1}) are gross irritability, loss of equilibrium, changes in pigmentation and localised peripheral haemorrhage (9).
Catfish *Heteropneustes fossilis* exposed to lindane (72 hr) suffered deleterious changes to ovarian histology (10).

Invertebrate toxicity
EC_{50} (15 min) *Photobacterium phosphoreum* 5.67 ppm Microtox test (11).

Microcystis aeruginosa, Cylindrospermum licheniforme 0.3-2 mg l^{-1}, no inhibition of growth. Both concentrations are higher than those that would result in adverse effects to fish or crustaceans (12,13).
Scenedesmus acutus (5 day) 5 mg l^{-1} lethal dose, concentrations of 1-5 mg l^{-1} caused a 50% reduction in growth (14).
A range of 10 common European freshwater macroinvertebrates in a continuous flow system (96 hr), LC_{50} concentration 25-430 µg l^{-1}, test conditions water temperature 11°C, pH 7.5-8.0, dissolved oxygen >96%, water hardness 93 mg l^{-1} ($CaCO_3$), *Baetis rhodani, Leuctra moselyi,* and *Protonemura meyeri* were the most sensitive species, *Physa fontinalis* and *Polycelis tenius* were the most tolerant (15).
EC_{50} (96 hr) *Daphnia magna* 516 µg l^{-1} static bioassay at 20°C (16).
LC_{50} (96 hr) *Gammarus lacustris* 48 µg l^{-1} static bioassay at 21°C (17).
LC_{50} (96 hr) *Penaeus duorarum* 0.17 µg l^{-1} flow-through bioassay 24-26°C, grass shrimp 10 µg l^{-1} static bioassay at 20°C (18).

Bioaccumulation
The bioconcentration factor is dependent on the exposure concentration, the highest concentration factors were seen with the lowest exposure concentrations (19).
Bioconcentration factors for fish 167-727; mussels (*Mytilus edulis*) 100; crustacean 25-143 (20).
Exposure via water or food in gudgeon, 0.22-142 µg l^{-1} in water, bioconcentration factors in brain, liver and muscle were 600, 200 and 100, respectively, at higher concentrations decreased to 50. Exposure via food led to accumulation 2.5 times higher (19,21).

Environmental fate

Nitrification inhibition
Nitrobacter, Nitrosomonas showed inhibited nitrification when exposed to 100 and 10 mg kg^{-1}. Nitrification was restored within 35 days (22).

Carbonaceous inhibition
100 mg kg^{-1} applied to soil inhibited carbon dioxide evolution, application of 1 and 10 mg kg^{-1} incubated for 120 days caused no or slight inhibition to CO_2 evolution (22).

Anaerobic effects
Anaerobic bacteria degraded ≤90% within 4 days, transformation to chlorine-free metabolites. CO_2 is not formed under anaerobic conditions (23).
Soils under flooded conditions at 30°C, $t_{1/2}$ 10-30 days, degradation occurred faster at higher temperatures (24).

Degradation studies
An extensive study of sandy loam, silt loam and muck soils were treated in 1954 at application rates of 1.1, 11.2. 112.1 kg ha^{-1} to a depth of 15 cm. Follow-up in 1959 found no lindane on low-dose application but ~36% remained at higher application rates. Persistence was affected by the amount of organic matter in the soil and climatic conditions (25).
Degraded by *Pseudomonas* spp. in soil. Bacterial degradation led to the accumulation of a transitory, and eventual release of covalently linked Cl^- in stoichiometric amounts (26).
Under aerobic conditions bacteria degrade lindane via dehydrochlorination of the polychlorinated cyclohexane moiety to intermediates which include chlorobenzenes and the end-product carbon dioxide (27,28).

Abiotic removal
Photooxidation by UV light in aqueous medium at 90-95°C: time for formation of carbon dioxide (% theoretical): 25% in 3 hr; 50% in ~17 hr; and 75% in ~46 hr (20).
Evaporation is an important process in the removal of lindane (29).

Adsorption and retention
Strongly absorbed onto organic soil material and weakly adsorbed onto inorganic material (30-36).
30-40% of application adsorbed onto aquifer sand at 5°C after 3-100 hr equilibrium time (20).

Mammalian & avian toxicity

Acute data

LD_{50} oral starling, bobwhite quail 100-130 mg kg^{-1} (37,2).
LD_{50} oral dog, mouse, rabbit, rat 40, 44, 60, 76 mg kg^{-1} (38-40).
LC_{50} (4 hr) inhalation rat 1600 mg m^{-3} (9).
LD_{50} dermal rabbit 200-300 mg kg^{-1} (41).
LD_{50} intraperitoneal mouse 125 mg kg^{-1} (42).
Oral ♂ rat 30, 40 or 50 mg kg^{-1} in oil caused reduced food intake and hypothermia, but death did not occur even at the highest dose. Intraperitoneal 4, 6 or 8 mg kg^{-1} in dimethylsulfoxide caused hyperthermia and convulsions. 43% of animals administered the highest dose died (43).

Sub-acute and sub-chronic data

Oral rat (3 month) 0, 0.2, 0.8, 4, 20 or 100 mg kg^{-1} diet, no effect on mortality, food consumption or haematological parameters (9).
Oral ♂ rat (2 wk) 0-800 mg kg^{-1} diet, high doses caused glucosuria and increased excretion of creatinine and urea and hypertrophy of the liver (44).
Inhalation mice (14 wk) 0, 0.3, 1.0, 5 or 10 g m^{-3} 6 hr day^{-1} 5 day wk^{-1}, significant mortality observed in ♀ mice (9).
Dermal rat (13 wk) 60 and 400 mg kg^{-1} caused reversible hypertrophy of the liver and non-reversible degeneration of the kidneys (9).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 2B (45).
National Toxicology Program (2 yr) tested rats and mice via feed. No evidence of carcinogenicity in either species (46).
Oral ♂, ♀ CF1 mice (110 wk) 400 mg kg^{-1} diet. Did not induce hepatocellular carcinoma in animals of either sex but increased the incidence of hepatocellular adenoma and hyperplastic nodules in ♂ mouse only (47).

Teratogenicity and reproductive effects

Oral ♀ mouse 0, 12, 30 or 60 mg kg^{-1} on days 6-15 or 11-12 of gestation. Foetal mortality increased and foetal weights decreased, and increased maternal mortality in high-dose animals. No effect on implantation, resorption or malformations were observed (9).
Gavage ♀ rat 5, 10 or 20 mg kg^{-1} (days 6-15 gestation). 10 and 20 mg kg^{-1} caused maternal toxicity but no evidence of embryo or foetal toxicity (48).
Gavage rabbit (days 6-18 gestation) 5, 10 and 20 mg kg^{-1} caused slight tachypnoea and lethargy. Post implantation loss and the incidence of resorptions were increased at 5 and 20 mg kg^{-1} (48).

Metabolism and toxicokinetics

After uptake, lindane is distributed to all organs and tissues in the body of laboratory animals, at measurable concentrations within a few hours. Oral rat (56 day) 1, 10 or 100 mg kg^{-1}, the highest concentrations were found in adipose tissue after 2-3 wk (49).
Inhalation rat (90 day) 0.02, 0.1, 0.5 and 5 mg m^{-3}, highest concentrations found in fatty tissues, concentrations in all organs reached control values after 4 wk (9).
Metabolism of lindane is initiated by one of four possible reactions: dehydrogenation leads to the formation of γ-HCH; dehydrochlorination leads to the formation of γ-PCCH; dechlorination to γ-tetrachlorohexene; and hydroxylation to hexachlorocyclohexanol. These compounds are considered intermediates, metabolism continues by a series of further dehydrogenating, dechlorinating, dehydrochlorinating and hydroxylating steps (50-52).

Irritancy

Dermal rabbit 0.5 g, 4 hr occlusive application, did not cause irritation (9).
Reported to cause sensory irritation in humans (53).
In 652 patients patch-tested with 1% lindane, no irritant or allergic reactions observed (54).

Sensitisation

Magnusson-Kligman maximisation test, guinea pigs unspecified dose 99.6% lindane. Animals were challenged at 24 and 48 hr. No skin sensitisation potential observed (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (55).
Bacillus subtilis H17 rec+, M45 rec^{-1} without metabolic activation negative (56).
Escherichia coli WP2, WP2 *uvr*A^{-1} with metabolic activation negative (57).
In vitro Chinese hamster V79 cells with metabolic activation negative (9).
In vitro Chinese hamster fibroblasts chromatid gaps, chromatid and chromosomal breaks equivocal (58).
Drosophila melanogaster dominant lethal mutation positive (59).
In vivo mouse bone marrow sister chromatid exchanges negative (9).

Other effects

Other adverse effects (human)

Acute symptoms include dizziness, headache, nausea, vomiting, diarrhoea, tremors, weakness, convulsions, dyspnoea and circulatory collapse (60).
No indication of a cause-effect relationship between exposure to lindane and blood dyscrasias (61).

Any other adverse effects

The binding of [3H]5α-DHT to rat androgen-binding protein was inhibited 70% by δ-HCH (100 μM) but γ-HCH (100 μM) did not reduce binding significantly (62).
May be absorbed through the skin and produce central nervous system effects, including motor excitability, muscle twitching, myoclonic jerking and convulsive seizures (63).
Even at high concentrations (687.6 μmol kg^{-1}), lindane administered intramuscularly to white leghorn roosters had neither oestrogen nor antiestrogenic activity as measured by its effect on oestrogen-related mRNA stabilising factor (64).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (65).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (66).
Included in Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (67).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (67).
WHO recommended guideline for drinking water quality 2 μg l^{-1} (68).
ADI 0.008 mg kg^{-1} body weight (2).
WHO Toxicity Class II (69).
EPA Toxicity Class II (formulation) (2).

Other comments

Environmental contamination occurred following application of lindane-containing pesticide formulations.
Emissions can cross national boundaries in water and air.
>90% exposure in non-occupationally exposed humans results from contaminated food (70).
Carcinogenicity, toxicity, toxicology and health effects reviewed (71,72).

References

1. Geyer, H. et al *Chemosphere* 1984, **13**(2), 269-284.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Hashimoto, Y. A. et al *J. Pestic. Sci.* 1981, **6**, 257.
4. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold, New York, NY, USA.
5. Macek, K. J. et al *Trans. Am. Fish Soc.* 1979, **99**(1), 20-27.
6. Randall, W. F. et al *Bull. Environ. Contam. Toxicol.* 1979, **21**, 849-854.
7. Eisler, R. *Acute Toxicities of Organochlorine and Organophosphorus Insecticides to Estuarine Fishes* 1970, Bureau of Sport Fisheries & Wildlife Tech. Paper 45, Gov. Print. Off., Washington, DC, USA.

8. Macek, K. J. et al *Bull. Environ. Contam. Toxicol.* 1969, **4**(3), 174-183.
9. *IPCS Environmental Health Criteria 124: Lindane* 1991, World Health Organisation, Geneva, Switzerland.
10. Hazarika, R. et al *Bull. Environ. Contam. Toxicol.* 1998, **60**(1), 16-21.
11. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
12. Bringmann, G. et al *Jahresher Wasser* 1978, **50**, 45-60.
13. Palmer, C. M. et al *Ohio J. Sci.* 1955, **55**(1), 1-8.
14. Krishnakumari, M. K. *Life Sci.* 1977, **20**, 1525-1532.
15. Green, D. W. J. et al *Arch. Hydrobiol.* 1986, **106**(2), 263-273.
16. Randall, W. F. et al *Bull. Environ. Contam. Toxicol.* 1979, **21**, 849-854.
17. Sanders, H. O. *Toxicity of Pesticides to the Crustacean Gammarus lacustrus* 1969, 2-18, Bureau of Sport Fisheries and Wildlife Tech. Paper No. 25, Washington, DC, USA.
18. Eisler, R. *Crustaceana Int. J. Crustacean Res.* 1969, **16**(3), 302-310.
19. Marcelle, C. et al *Bull. Environ. Contam. Toxicol.* 1983, **31**, 453-458.
20. Schimmel, S. C. et al *Arch. Environ. Contam. Toxicol.* 1977, **6**, 355.
21. Marcelle, C. et al *Bull. Environ. Contam. Toxicol.* 1984, **33**, 423-429.
22. Gaur, A. C. et al *Plant. Soil.* 1977, **46**, 5-15.
23. Haider, K. et al *Arch. Microbiol.* 1975, **104** (Ger.).
24. Yoshida, T. et al *Soil Sci. Soc. Am. Proc.* 1970, **34**, 440-442.
25. Lichtenstein, E. P. et al *J. Econ. Entomol.* 1960, **53**(1), 136-142.
26. Sahu, S. K. et al *Appl. Environ. Microbiol.* 1990, **56**(11), 3620-3622.
27. Vonk, J. W. et al *Pest. Biochem. Physiol.* 1979, **12**, 68-74.
28. Mathur, S. P. et al *Soil Sci.* 1975, **120**(4), 301-307.
29. MacKay, D. et al *Environ. Sci. Technol.* 1973, **7**, 611.
30. Baluji, G. et al *Environ. Qual. Saf. Suppl.* 1975, **3**, 243-249.
31. Kay, B. D. et al *Soil Sci.* 1967, **104**(5), 314-322.
32. Mills, A. C. et al *Soil Sci. Soc. Am. Proc.* 1969, **33**, 210-216.
33. Portmann, J. E. *Evaluation of the Impact on the Aquatic Environment of HCH Isomers* 1979, Commission of the European Communities, Brussels, Belgium.
34. Wahid, P. A. et al *J. Agric. Food Chem.* 1979, **27**(5), 1050-1053.
35. Wahid, P. A. et al *J. Agric. Food Chem.* 1980, **28**, 623-625.
36. Wirth, H. *GKSS Research Inst. Report No. GKSS 85/E/30* 1985.
37. Schafer, E. W. *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
38. *Spec. Publ. Entomol. Soc. Am.* 1974, **74**, 1.
39. *J. Econ. Entomol.* 1972, **65**, 632.
40. *J. Hyg. Epidemol. Microbiol. Immunol.* 1978, **22**, 115.
41. Izmerov, N. F. *IRPTC Scientific Review of Soviet Literature on Toxicity and Hazards of Chemicals* 1983, No. 40, CIP, Moscow, USSR.
42. *Sov. Genet.* 1966, **2**(1), 80.
43. Wolley, D. E. et al *Pharmacol. Biochem. Behav.* 1989, **33**(4), 787-792.
44. Srinivasan, K. *J. Environ. Sci. Health* 1988, **B23**(4), 367-386.
45. *IARC Monograph* 1987, **Suppl. 7**, 64.
46. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-104, NIEHS, Research Triangle Park, NC, USA.
47. Vesselinovitch, S. D. *Toxicol. Pathol.* 1983, **11**(1), 12-22.
48. Palmer, A. K. et al *Toxicology* 1978b, **9**, 239-247.
49. Oshiba, K. *Osaka Shiritsu Daigaku Igaku Zasshi* 1972, **21**(3), 1-19.
50. Engst, R. et al *Residue Rev.* 1970, **68**, 59-84.
51. Engst, R. et al *Residue Rev.* 1979, **75** (Part II), 71-95.
52. Engst, R. et al *J. Environ. Sci. Health* 1976, **B11**(2), 95-117.
53. Grasso, G. et al *J. Environ. Sci. Health* 1987, **A22**(6), 543-547.
54. Lisi, P. et al *Contact Dermatitis* 1987, **17**, 212-218.
55. Haworth, S. et al *Environ. Mutagen.* 1983, (Suppl. 1), 3-142.
56. Shirasu, Y. et al *Mutat. Res.* 1976, **40**, 19-30.
57. Probst, G. S. et al *Environ. Mutagen.* 1981, **3**, 11-32.
58. Ishidate, M. et al *Mutat. Res.* 1977, **48**, 337-354.
59. Sinha, R. R. P. et al *Comp. Physiol. Ecol.* 1983, **8**(2), 87-89.
60. Gosselin, R. E. et al (Eds.) *Clinical Toxicology of Commercial Products* 5th ed., 1984, Williams & Wilkins, Baltimore, MD, USA.
61. *Health Effects Assessment for Lindane* 1984, US EPA 540/1-86/056, Cincinnatti, OH, USA.
62. Danzo, B. J. *Environ. Health Perspect.* 1997, **105**(3), 294-301.
63. Moody, R. P. et al *J. Toxicol. Environ. Health* 1989, **28**(2), 161-169.

64. Ratnasabapathy, R. et al *Biochem. Pharmacol.* 1997, **53**(10), 1425-1434.
65. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
66. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
67. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
68. *Guidelines for Drinking Water Quality* 2nd ed., 1993, **1**, WHO, Geneva, Switzerland.
69. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
70. Geyer, H. et al *Regul. Toxicol. Pharmacol.* 1986, **6**, 313-347.
71. *Gov. Rep. Announce. Index (U. S.)* 1990, **90**(10), Abstr. No. 025089.
72. *Gov. Rep. Announce. Index (U. S.)* 1987, **87**(18), Abstr. No. 740936

H11 helium

He

He **Mol. Wt.** 4.00 **CAS Registry No.** 7440-59-7

Synonyms

EINECS No. 231-168-5 **RTECS No.** MH 6520000

Uses In cryogenic studies. Used with oxygen by divers to prevent the development of decompression sickness.
Occurrence Extracted on a commercial scale from natural gas. Produced in the decay of radioactive elements.

Physical properties

M. Pt. $_{20,000}$–272.2°C **B. Pt.** –268.9°C **Specific gravity** 0.176 g l^{-1} at 25°C and 760 mmHg; 0.147 at –270.8°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.7 (1) **Volatility** v.p. 760 mmHg at –269°C ; v.den. 0.14
Solubility Water: 9.7 ml l^{-1} at 0°C

Occupational exposure

UN No. 1046 (compressed)

UN No. 1963 (refrigerated liquid) **HAZCHEM Code** 2~ (compressed) **HAZCHEM Code** 2R (refrigerated liquid) **Conveyance classification** non-flammable non-toxic gas

Genotoxicity

Salmonella typhimurium TA98, TA100, TA102 induction of revertants by ^{4}He ions positive (2).
Saccharomyces cerevisiae induction of double strand breakage in DNA by heavy helium ions positive (3).

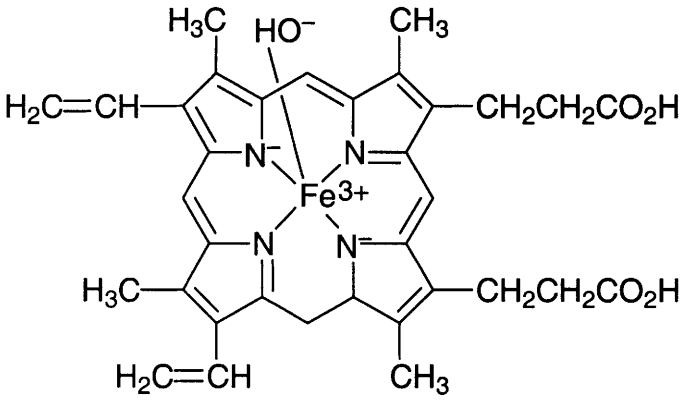
Other effects

Any other adverse effects
Acts as a simple asphyxiant (4).

References

1. *Chemical Safety Sheets* 1991, 452-453, Kluwer, Norwell, MA, USA.
2. Kozubek, S. et al *Mutat. Res.* 1989, **210**(2), 221-226.
3. Akpa, T.C. et al *GSI-Rep.* 1991, **GSI 91-1**, 217.
4. Lewis, R. J. L. (Ed.) *Sax's Dangerous Properties of Industrial Materials* 8th ed., 1992, **1**, 1824, Van Nostrand Reinhold, New York, NY, USA

H12 hematin



$C_{34}H_{33}FeN_4O_5$ **Mol. Wt.** 633.51 **CAS Registry No.** 15489-90-4

Synonyms ferrihemic acid; ferriprotoporphyrin basic; protohematin; 7,12-diethenyl-3,8,13,17-tetramethyl-21*H*,23*H*-porphine-2,18-dipropanoato(4–)-N^{21},N^{22},N^{23},N^{24}-hydroxyferate(2–)dihydrogen

EINECS No. 239-518-9 **RTECS No.** NO 6725000

Uses Catalyst. In treatment of hepatic porphyria.

Physical properties

M. Pt. >200°C

Solubility Organic solvents: hot pyridine

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat 43 mg kg^{-1} (1).

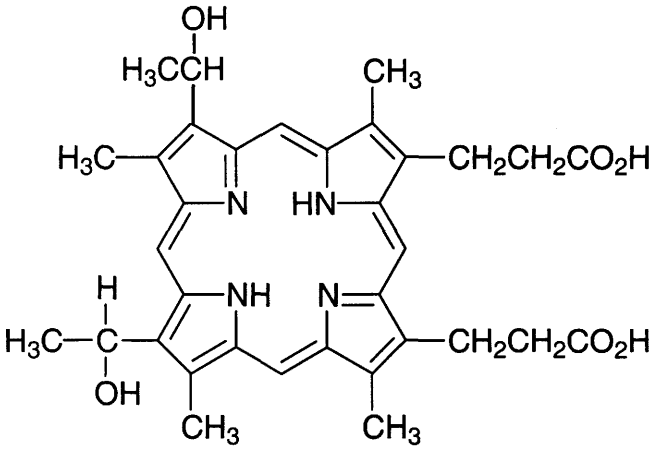
Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. Lips, D. L. et al *Toxicol. Lett.* 1978, **2**, 329.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

H13 hematoporphyrin



$C_{34}H_{38}N_4O_6$ **Mol. Wt.** 598.70 **CAS Registry No.** 14459-29-1

Synonyms 7,12-bis(1-hydroxyethyl)-3,8,13,17-tetramethyl-21*H*,23*H*-porphine-2,18-dipropanoic acid; 7,12-bis (1-hydroxyethyl)-3,8,13,17-tetramethyl-2,18-porphinedipropionic acid; 1,3,5,8-tetramethyl-2,4-bis(α-hydroxyethyl)porphine-6,7-dipropionic acid; haematoporphyrin IX; Photodyns

EINECS No. 238-450-7 **RTECS No.** TS 5500000

Uses As a photosensitising agent for malignant neoplasms. Has been used in the treatment of mental depression. Isolated from *Chlorella vulgaris*.

Physical properties

Solubility Organic solvents: acetic acid, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 307 mg kg^{-1} (1).

Metabolism and toxicokinetics

Tends to be retained by rats tumour tissue *in vivo* (2).

Genotoxicity

Derivatives can induce DNA damage in JC411 cells *in vitro* (1).

Other effects

Other adverse effects (human)

Hematoporphyrin binds to serum albumin of patients receiving the compound during therapy, and may be using a carrier system for endogenous porphyrins (3).

Any other adverse effects

Is cytotoxic to erythrocytes possibly due to generation of singlet oxygen (4).
It binds to smooth muscle cells and binds differently to the aortas of normal and Wistar Kyoto hypertensive rats (5).
Animal cells micro-injected with mitochondrial or extra mitochondrial substrates after exposure to haematoporphyrin show transient changes in NADPH (6).
Tends to be retained by rat tumour tissue *in vivo* (2).

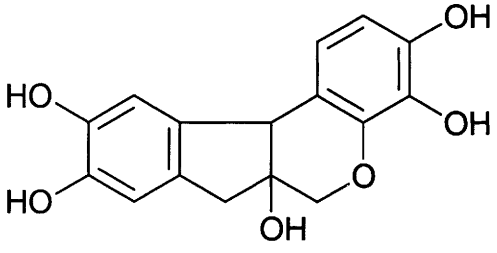
Other comments

The use of the compound as a photosensitising agent is described (7,8).
♀ wistar rats with implanted Yoshida hepatoma cells, demonstrate enhanced enzyme activity in mitochondria of implanted cells, after administration of hematoporphyrin (9).

References

1. *Cancer Res.* 1981 **41**, 3543.
2. Barabash, R. D. *Farmakol. Toksikol. (Moscow)* 1990, **53**(3), 24-26 (Russ.) (*Chem. Abstr.* **113**, 52015e).
3. Cohen, S. et al *Biochem. J.* 1990, **270**(2), 325-330
4. Lin, H. *Anal. Biochim.* 1987, **161**(2), 323-331.
5. Scannapieco, G. *Eur. J. Clin. Invest.* 1988, **18**(6), 614-618.
6. Kohen, E. et al *Photochem. Photobiol.* 1986, **44**(4), 471-475.
7. Abramson, A. L. *Arch. Otolaryngol., Head Neck Surg.* 1992, **118**, 25-29.
8. Abulati, M. M. et al *Br. Med. J.* 1992, **304**, 589-590.
9. Freitas, L. *Med., Biol., Environ.* 1988, **16**(1), 97-109.

H14 hematoxylin



$C_{16}H_{14}O_6$ **Mol. Wt.** 302.28 **CAS Registry No.** 517-28-2

Synonyms 7,11b-dihydrobenz[*b*]indeno[1,2-*d*]pyran-3,4,6a,9,10(6*H*)-pentol; hematoxiline; hydroxybrazilin; hydroxybrasilin; haematoxylin

EINECS No. 208-237-3 **RTECS No.** MH 7875000

Uses As a stain in microscopy. In dyestuffs. In detection systems.
Occurrence In heartwood of logwood (*Haematoxylin campechianum*).

Physical properties

M. Pt. 100-120°C (trihydrate)
Solubility Organic solvents: diethyl ether

Ecotoxicity

Fish toxicity
LD_{50} (24 hr) trout, bluegill sunfish, goldfish 5 ppm negative. Test conditions: pH 7, dissolved oxygen 7.5 ppm, total hardness (soap method) 300 ppm, methyl orange alkalinity 310 ppm, free carbon dioxide 5 ppm and temperature 12.8°C (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 400 mg kg^{-1} (2).

Other comments

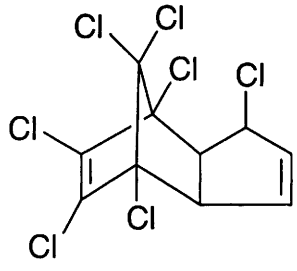
Hematoxylin has anti-inflammatory properties, as judged by its ability to inhibit carageenan-induced paw oedema in rats (3).

Hematoxylin is responsible for the sweetness of the heartwood of logwood (4).

References

1. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA560/6-87-002 PB87-200-275, Washington, DC, USA.
2. *Gastroenterology* 1953, **23**, 1.
3. Razga, Z. *Acta Pharm. Hung.* 1990, **60**(1), 1-6 (Hung.). (*Chem. Abstr.* **112**, 210690y).
4. Masuda, H. et al *Chem. Pharm. Bull.* 1990, **39**(6), 1382-1384

H15 heptachlor



$C_{10}H_5Cl_7$ **Mol. Wt.** 373.32 **CAS Registry No.** 76-44-8

Synonyms 1,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-*endo*-methanoindene; 3-chlorochlordene; 1,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-indene; 3,4,5,6,7,8,8a-hepta-chlorodicyclopentadiene

EINECS No. 200-962-3 **RTECS No.** PC 0700000

Uses Non-systemic insecticide for the control of termites, ants, soil insects, and also household insects.

Physical properties

M. Pt. 95-96°C **Specific gravity** 1.66 at 25°C **Partition coefficient** log P_{ow} 7.248 (1)

Volatility v.p. 3.0×10^{-4} mmHg at 25°C

Solubility Water: 0.056 mg l^{-1} at 25-29°C. Organic solvents: acetone, benzene, carbon tetrachloride, cyclohexanone, ethanol, xylene

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable fraction of aerosol)

FR-VME 0.03 ppm (0.5 mg m^{-3})

US-TWA 0.05 mg m^{-3}

Supply classification toxic, dangerous for the environment

Risk phrases Toxic in contact with skin and if swallowed – Danger of cumulative effects – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R33, R40, R50/53)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show

label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) Indian catfish 0.22 mg l^{-1} (2).
LC_{50} (14 days) guppy, zebra fish 0.6-0.8 μg l^{-1} (3).
LC_{50} (96 hr) rainbow trout, American eel, guppy, bluegill sunfish, fathead minnow 7-150 μg l^{-1} (4-6).

Invertebrate toxicity

EC_{50} (96 hr) *Gammarus lacustris, Gammarus fasciatus, Palaemonetes kadiakensis,* and *Orconectes nais* 1.8-40 μg l^{-1} (7,8).

Bioaccumulation

Bioconcentration factor for fathead minnow, sheepshead minnow, mosquito fish, snail, alga and oyster 3600-37,000 (9-11).

Environmental fate

Degradation studies

$t_{1/2}$ for hydrolysis to 1-hydroxychlordene 3 days. This undergoes microbial epoxidation to 1-hydroxy-2,3-epoxychlordene (4,12).
Metabolised in soil by the white rot fungus *Phanerochaete chrysosporium* and *Pseudomonas* species (13,14).
Microbial degradation products in soils include chlordene, 1-*exo*-hydroxychlordene and heptachlor epoxide (13,15).
95.3% degradation occurred in 4 wk in aerobic acclimated microbial cultures (16).
Anaerobic incubation of 10 ppm in thick sludge at 53°C resulted in 100% degradation in ~1 day (17).

Abiotic removal

In solution undergoes photodegradation to photoheptachlor, which is reported to have increased toxicity to aquatic species (18).
Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in the atmosphere ~6 hr (19).
Effectively removed from water by combined treatment with UV irradiation and hydrogen peroxide (20).
Estimated $t_{1/2}$ for volatilisation from streams, rivers and lakes 3.4 hr, 6.3 hr and 282 days, respectively (21).

Adsorption and retention

Estimated log K_{oc} for soils 4.48 indicates strong adsorption to soil and sediments (22).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, hamster, guinea pig, rat 68, 100, 116, 147-220 mg kg^{-1}, respectively (4,23-25).
LD_{50} dermal rat, rabbit 120, 500 mg kg^{-1}, respectively (4,25,26).
LD_{50} intravenous mouse 20 mg kg^{-1} (27).
LD_{50} intraperitoneal rat, mouse 27, 130 mg kg^{-1}, respectively (28,29).

Sub-acute and sub-chronic data

LC_{50} (5 day) oral bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck 92-480 mg kg^{-1} diet (30).

Carcinogenicity and chronic effects

Inadequate evidence of carcinogenicity of heptachlor and chlordane to humans and limited evidence of carcinogenicity to animals, IARC classification group 3 (31).
National Toxicology Program tested rats and mice via feed. Negative results were reported for ♂ rats, equivocal results for ♀ rats, positive results for ♂ and ♀ mice (32).
Oral mouse (2 yr) 10 mg kg^{-1} diet. Survival was not significantly different from controls. A significant excess of liver carcinomas was found in treated animals compared with controls (33).

Teratogenicity and reproductive effects

Oral rat, 5 doses of 10 or 20 mg kg^{-1} from days 7-17 of gestation, caused a decrease in maternal body weight gain. No foetotoxic or teratogenic effects were observed (34).

Subcutaneously injected ♂ rats (2 wk) 0-25 mg kg^{-1} body weight. Plasma luteinising hormone (LH) and cortisol levels were significantly elevated. LH and testosterone levels showed strong correlation. Testes showed some pathological changes in animals treated with 25 mg kg^{-1} (35).

Injection of 1.5 mg egg^{-1} resulted in 12% reduction in hatchability but no abnormal chicks (36).

Metabolism and toxicokinetics

Following intraperitoneal administration of ^{14}C-heptachlor to lambs, 35% of radioactivity was eliminated via the excreta in 21 days, of which 67% appeared in the urine and 33% in faeces. $t_{1/2}$ for clearance from the blood was 14 days (37).

Following intravenous administration of ^{14}C-heptachlor, the epoxide was found in the tissues, faeces and urine. Another urinary metabolite identified was the hydrophilic 4,5,6,7,8,8-heptachloro-1-*exo*-hydroxy-6,7- *exo*-epoxy-1,2,3a,4,7,7a-hexahydro-1,4-*endo*-methyleneindene (1,2,3,4,8,8-hexachloro-5-*exo*- hydroxy-6,7-*exo*-epoxy-1,4,4a,7a,5,6-hexahydro-1,4- *endo*-methyleneindene). In rabbits the radioactive label was found mainly in the urine (20% epoxide, 80% hydrophilic metabolites (38).

Rats fed 30 mg kg^{-1} diet heptachlor had maximum concentrations of heptachlor epoxide in fat within 2-4 wk. 12 wk after exposure was discontinued, heptachlor epoxide was completely removed from adipose tissue (39).

Transplacental transfer and excretion in milk have been identified in humans (40).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation marginally positive (41).

Drosophila melanogaster sex-linked recessive lethal assay negative (42).

In vitro mouse lymphoma L5178Y tk^+/tk^- forward mutation assay without metabolic activation positive (43).

CASE predicted *in vitro* Chinese hamster ovary cells, chromosomal aberrations negative, sister chromatid exchanges positive (44).

In vivo mouse, dominant lethal assay negative (45).

Induced somatic chromosomal anomalies in the root tip of *Pisum* species (46).

In vitro primary rat hepatocytes, unscheduled DNA synthesis negative (47).

Other effects

Other adverse effects (human)

Case reports have indicated a relationship between exposure to heptachlor and blood dyscrasias and acute leukaemia (48,49).

Any other adverse effects

Inhibits oxidative phosphorylation and electron transport in rat liver mitochondria (50).

Legislation

EEC maximum residue levels: cereals, fruit and vegetables 0.01 ppm; meat, meat preparations and animal fats, 0.2 ppm; raw and whole cream cow's milk 0.004 ppm; all feedstuffs except fats 0.01 ppm (fats 0.2 ppm) (4).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (51).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (52).

The log P_{ow} exceeds the European Community recommended value 3.0 (6th and 7th amendments) (53).

WHO Toxicity Class II (54).

EPA Toxicity Class II (formulation) (4).

WHO ADI 0.0001 mg kg^{-1} day^{-1} (55).

EPA cancelled all uses of heptachlor in the US in 1988.

WHO guide level for total of heptachlor and heptochlor epoxide in drinking water 0.03 μg l^{-1} (56).

Other comments

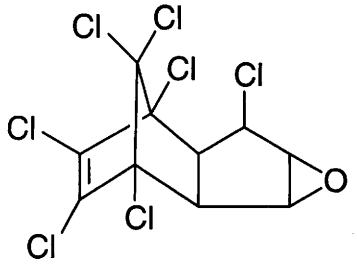
Residues have been detected in air, water, sediments, soil crops and in animal tissues. Present in technical grade chlordane (57,58).
Physical properties, use, occurrence, mammalian toxicity, metabolism, mutagenicity and carcinogenicity of heptachlor and heptochlor epoxide reviewed (57,5,59).
Environmental fate reviewed (58).

References

1. McCoy, G. D. et al *Carcinogenesis (London)* 1990, **11**(7), 1111-1117.
2. Srivastava, A. K. et al *Acta Hydrobiol.* 1988, **29**(4), 489-495.
3. Vittazzi, L. et al *Rapp. ISTISAN* 1988, **ISTISAN 88/10**.
4. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
5. *IPCS Environmental Health Criteria 38: Heptachlor* 1984, WHO, Geneva, Switzerland.
6. Henderson, C. et al *Trans. Am. Fish Soc.* 1959, **88**, 23-32.
7. Sanders, H. O. *Toxicity of Pesticides to the Crustacean, Gammarus lacustris* 1969, Bureau of Sport Fisheries and Wildlife. Technical Paper No. 25, Govt. Printing Office, Washington, DC, USA.
8. Sanders, H. O. *Toxicity of Some Insecticides to Four Species of Malocostracan Crustacea* 1972, Fish Pesticide Res. Lab. Colombia, MO, USA.
9. Biddinger, G. R. et al *Residue. Rev.* 1984, **91**, 103-145.
10. Callahan, M. A. et al *Water-Related Environmental Fate of 129 Priority Pollutants* 1979, USEPA-440/4-79-029a.
11. Zaroogian, G. E. et al *Environ. Toxicol. Contam.* 1985, **4**, 3-12.
12. Pirbazari, M. et al *J. Environ. Eng. (N. Y.)* 1991, **117**(1), 80-100.
13. Bowguin, A. W. et al *Dev. Ind. Microbiol.* 1972, **13**, 264-276.
14. Kennedy, D. W. et al *Appl. Environ. Microbiol.* 1990, **56**(8), 2347-2353.
15. Miles, J. R. W. et al *J. Econ. Entomol.* 1971, **64**, 839-841.
16. Leigh, G. M. *J. Water Pollut. Control Fed.* 1969, **41**, R450-460.
17. Hill, D. W. et al *J. Water Pollut. Control Fed.* 1967, **39**, 1259-1277.
18. Podowski, A. A. et al *Arch. Environ. Contam. Toxicol.* 1979, **8**, 509-518.
19. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
20. Thiemann, W. et al *DVGW-Schriftenr., Wasser* 1988, **107**, 129-146. (Ger.) (*Chem. Abstr.*, **110**, 101421h).
21. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
22. Kenaga, E. E. *Ecotoxicol. Environ. Saf.* 1980, **4**, 26-30.
23. Gaines, T. B. *Toxicol. Appl. Pharmacol.* 1969, **14**, 515-534.
24. *Eur. J. Toxicol. Environ. Hyg.* 1974, **7**, 159.
25. *Spec. Publ. – Entomol. Soc. Am.* 1978, **78-1**, 12.
26. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure* 1982, CIP, Moscow, USSR.
27. Radomski, J. L. et al *J. Pharmacol. Exp. Ther.* 1953, **107**, 266-272.
28. *Food Cosmet. Toxicol.* 1973, **11**, 63.
29. *Sov. Genet. (Engl. Transl.)* B1966, **2**, 80.
30. Hill, E. F. et al *Lethal Dietary Toxicities of Environmental Pollutants to Birds* 1975, US Fish and Wildlife Service, Report Wildlife No.191, Washington, DC, USA.
31. *IARC Monograph* 1987, **Suppl.7**, 146-148.
32. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-009, NIEHS, Research Triangle Park, NC, USA.
33. Epstein, S. S. *Sci. Total Environ.* 1976, **6**, 103-154.
34. Yamaguchi, M. et al *Eisei Shikensho Hokoku* 1987, (105), 33-36 (Japan.) (*Chem. Abstr.* **108**, 145181t).
35. Wango, E. O. et al *Comp. Biochem. Physiol., C: Pharmacol., Toxicol. Endocrinol.* 1997, **118C**(3), 381-386.
36. Smith, S. I. et al *Toxicol. Appl. Pharmacol.* 1970, **16**, 179-185.
37. Smith, G. S. et al *J. Anim. Sci.* 1989, **67**(1), 187-195.
38. Klein, W. et al *Qual. Plant Mater. Veg.* 1968, **15**, 225-238 (Ger.) (*IARC Monograph* 1979, **20**, 144).
39. Radomski, J. L. et al *J. Pharmacol. Exp. Ther.* 1953, **107**, 266-272.
40. Wassermann, M. et al *Environ. Physical. Biochem.* 1972, **2**, 59-67.
41. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
42. Benes, V. et al *Ind. Med. Surg.* 1969, **38**, 50-52.
43. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **12**(1), 85-154.
44. Rosenkranz, H. S. et al *Mutagenesis* 1990, **5**(6), 559-571.

45. Epstein, S. S. et al *Toxicol. Appl. Pharmacol.* 1972, **23**, 288-325.
46. Jain, A. K. et al *Cytologia* 1987, **52**(1), 47-53.
47. Probst, G. S. et al *Environ. Mol. Mutagen.* 1981, **3**, 11-32.
48. Infante, P. F. et al *Scand. J. Work Environ. Health* 1978, **4**, 137-150.
49. Blair, A. et al *J. Natl. Cancer Inst.* 1983, **71**, 31-37.
50. Meguro, T. et al *Ind. Health* 1990, **28**(4), 151-157.
51. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
52. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
53. *1967 Directive on the Classification Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
54. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
55. Lu, F.C. *Toxicol. Pharmacol.* 1995, **21**, 351-364.
56. *Guidelines for Drinking Water Quality* 2nd ed. 1993, **1**, WHO, Geneva, Switzerland.
57. *IARC Monograph* 1979, **20**, 129-154.
58. Howard, P. H. (Ed.) *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, **3**, 385-401, Lewis Publishers, Chelsea, MI, USA.
59. Reuber, M. D. *J. Environ. Pathol. Toxicol. Oncol.* 1987, **7**(3), 85-114

H16 heptachlor epoxide



$C_{10}H_5Cl_7O$ **Mol. Wt.** 389.32 **CAS Registry No.** 1024-57-3

Synonyms epoxyheptachlor; HCE; 2,3,4,5,6,7,7-heptachloro-1a,1b,5,5a,6,6a-hexahydro-2,5-methano-2*H*-indeno[1,2-*b*]oxirene; 1,4,5,6,7,8,8-heptachloro-2,3-epoxy-3a,4,7,7a-tetrahydro-4,7-methanoindan

EINECS No. 213-831-0 **RTECS No.** PB 9450000

Physical properties

M. Pt. 160-161.5°C **Partition coefficient** log P_{ow} 5.40 (calc.) (1) **Volatility** v.p. 2.6×10^{-6} mmHg at 20°C
Solubility Water: ~0.3 mg l^{-1} at 25°C

Occupational exposure

US-TWA 0.05 mg m^{-3}
Supply classification toxic, dangerous for the environment
Risk phrases Toxic if swallowed – Danger of cumulative effects – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R25, R33, R40, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S36/37, S45, S60, S61)

Ecotoxicity

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 25 ppm, Microtox test (2).

Bioaccumulation

Bioconcentration factor for freshwater clam, mussel, snail, oyster, algae, fathead minnow, sheepshead minnow and pinfish 1600-66,000 (3-6).

Environmental fate

Degradation studies

Degraded to 1-*exo*-hydroxychlordene by soil microflora at 28°C with mean conversion rates of 2.8, 5.8 and 12.0% after 4, 8 and 12 wk, respectively (7).

$t_{1/2}$ for degradation in thick digester sludge under aerobic conditions at 35°C ~25 days. However, no significant degradation occurred at 20°C under aerobic or anaerobic conditions in 60 days (8).

Abiotic removal

45% degradation occurred when a thin film of heptachlor epoxide was exposed to sunlight for 250 hr. However, photodegradation may be more rapid in the presence of photosensitisers, including the pesticide rotenone, and acetone (9,10).

$t_{1/2}$ for volatilisation from model river water 60 hr (11).

Adsorption and retention

K_{oc} for Certamite clay 100, and for river water suspended solids 10,000-20,000 (8,12).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 39, 62 mg kg^{-1}, respectively (13,14).

LD_{Lo} intravenous mouse 10 mg kg^{-1} (15).

Carcinogenicity and chronic effects

Oral mouse, (2 yr) 10 mg kg^{-1} diet. 19/200 treated mice survived at 2 yr compared to 62/200 controls. A significant excess of liver carcinomas occurred in treated animals compared with controls (16).

Metabolism and toxicokinetics

A dehydrogenated derivative of 1-hydroxy-2,3-epoxychlordene was a faecal metabolite in rats fed 10 mg kg^{-1} diet for 30 days (17).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation marginally positive (18).

Aspergillus nidulans induction of forward mutations and mitotic segregation negative (19).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (20).

WHO guide level for the total of heptachlor and heptachlor epoxide in drinking water 0.03 μg l^{-1} (21).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (22).

The log P_{ow} exceeds the European Community recommended value 3.0 (6th and 7th Amendments) (23).

Other comments

Metabolite of the pesticide heptachlor. Residues have been identified in air, water, sediments, soil, crops and animal tissues (24,1).

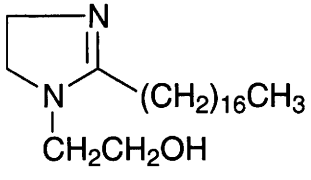
Environmental fate reviewed (1).

Physical properties, occurrence, mammalian toxicity, metabolism, mutagenicity and carcinogenicity of heptachlor and heptachlor epoxide reviewed (24,25).

References

1. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1991, **3**, 402-427, Lewis Publishers, Chelsea, MI, USA.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Lu, P. Y. et al *J. Agric. Food Chem.* 1975, **23**, 967-973.
4. Zaroogian, G. E. et al *Environ. Toxicol. Chem.* 1985, **4**, 3-12.
5. Hartley, D. M. et al *Bull. Environ. Contam. Toxicol.* 1983, **31**, 33-40.
6. Veith, G. D. et al *J. Fish. Res. Board Can.* 1979, **36**, 1040-1048.
7. Miles, J. R. W. et al *J. Econ. Entomol.* 1971, **64**, 839-841.
8. Hill, D. W. et al *J. Water Pollut. Control Fed.* 1967, **39**, 1259-1277.
9. Benson, W. R. et al *J. Agric. Food Chem.* 1971, **19**, 857-862.
10. Ivie, G. W. et al *Bull. Environ. Contam. Toxicol.* 1972, **7**, 376-382.
11. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
12. Frank, R. *J. Great Lakes Res.* 1981, **7**, 440-454.
13. Sperling, F. et al *Toxicol. Appl. Pharmacol.* 1969, **14**, 622.
14. *USDA Information Memorandum* 1966, **20**, 27, Agricultural Research Service, Bettsville, MD, USA.
15. *J. Pharmacol. Exp. Ther.* 1953, **107**, 266.
16. Epstein, S. S. *Sci. Total Environ.* 1976, **6**, 103-154.
17. Matsumuna, F. et al *Bull. Environ. Contam. Toxicol.* 1971, **5**, 489-492.
18. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
19. Crebelli, R. et al *Mutat. Res.* 1986, **172**(2), 139-149.
20. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
21. *Guidelines for Drinking Water Quality* 2nd ed. 1993, **1**, WHO, Geneva, Switzerland.
22. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
23. *1967 Directive on the Classification, Packaging and Labelling of Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
24. *IARC Monograph* 1979, **20**, 129-154.
25. Reuber, M. D. *J. Environ. Pathol. Toxicol. Oncol.* 1987, **7**(3), 85-114

H17 2-heptadecyl-2-imidazoline-1-ethanol



$C_{22}H_{46}N_2O$ **Mol. Wt.** 354.62 **CAS Registry No.** 95-19-2

Synonyms 1-hydroxyethyl-2-heptadecylglyoxalidine

EINECS No. 202-397-8 **RTECS No.** NJ 2985000

Physical properties

M. Pt. 63-65°C **B. Pt.** 260°C at 3 mmHg.

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3800 mg kg^{-1} (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (2).

References

1. *Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 494.
2. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109

H18 heptafluorobutyric anhydride

$$CF_3(CF_2)_2C(O)OC(O)(CF_2)_2CF_3$$

$C_8F_{14}O_3$ **Mol. Wt.** 410.06 **CAS Registry No.** 336-59-4

Synonyms heptafluorobutanoic acid anhydride

EINECS No. 206-410-8

Uses Organic synthesis. Derivatisation agent in GLC analyses of amino acids.

Physical properties

B. Pt. 108-110°C **Specific gravity** 1.653 at 25°C with respect to water at 4°C

Other effects

Other adverse effects (human)

Extremely destrutive to tissues of the mucous membranes and upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of bronchial spasm. Inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (1).

References

1. Lenga, R. E. (Ed.) *The Sigma Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1819, Sigma-Aldrich, Milwaukee, WI, USA

H19 heptanal

$$CH_3(CH_2)_5CHO$$

$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 111-71-7

Synonyms aldehyde C7; heptaldehyde; enanthal; enanthaldehyde; oenanthaldehyde; oenanthole

EINECS No. 203-898-4 **RTECS No.** MI 6900000

Uses Organic synthesis. Flavouring and fragrance agent.

Occurrence Aroma component of plants, cooked meat and fish.

Physical properties

M. Pt. –43°C **B. Pt.** 153°C **Flash point** 35°C **Specific gravity** 0.8216 at 15°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.99 (1) **Volatility** v.p. 3 mmHg at 25°C ; v.den. 3.9
Solubility Water: slightly soluble. Organic solvents: diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

UN No. 3056 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy 11 mg l^{-1} (1).

Environmental fate

Degradation studies
Reduction of ThOD in wastewater by activated sludge 5% after 6 hr; 7% after 12 hr; 15% after 24 hr (2).
BOD_5 28% of ThOD; COD 73% of ThOD (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 14,000, 20,000 mg kg^{-1}, respectively (4,5).

Irritancy
Vapour or mist irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).

References

1. Deneer, J. W. et al *Aquat. Toxicol.* 1988, **12**(2), 185-192.
2. Gerhold, R. M. et al *J. Water Poll. Control. Fed.* 1960, **32**, 1173.
3. Dove, M. et al *Trib. CEBEDEAU* 1975, **28**(374), 3-11.
4. *Biochem. J.* 1940, **34**, 1196.
5. Food & Drug Research Lab. *Report* 1976, 123, Waverly, New York, NY, USA.
6. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1820, Sigma-Aldrich, Milwaukee, WI, USA.
7. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141

H20 heptane

$$CH_3(CH_2)_5CH_3$$

C_7H_{16} **Mol. Wt.** 100.20 **CAS Registry No.** 142-82-5
Synonyms *n*-heptane; dipropylmethane; Gettysolve-C; heptyl hydride
EINECS No. 205-563-8 **RTECS No.** MI 7700000

Uses Solvent.
Occurrence Aroma component of plants and cooked meats. Major component of petroleum spirit. Present in fossil fuels. Residues have been isolated from natural and drinking water, soil and urban air samples (1).

Physical properties

M. Pt. –91°C **B. Pt.** 98°C **Flash point** –4°C **Specific gravity** 0.684 at 20°C **Partition coefficient** log P_{ow} 4.66 **Volatility** v.p. 40 mmHg at 22.3°C ; v.den. 3.5
Solubility Water: 2.93 mg l^{-1} at 25°C. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 500 ppm (2100 mg m^{-3})
FR-VME 400 ppm (1600 mg m^{-3})
JP-OEL 200 ppm (820 mg m^{-3})
SE-LEVL 200 ppm (800 mg m^{-3}) **SE-STEL** 300 ppm (1200 mg m^{-3})
US-TWA 400 ppm (1640 mg m^{-3}) **US-STEL** 500 ppm (2050 mg m^{-3})

UN No. 1206 (heptanes) **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not breathe vapour – Do not empty into drains – Take precautionary measures against static discharges (S2, S9, S16, S23, S29, S33)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) ciclid fish 375 mg l^{-1} (2).
LC_{50} (24 hr) goldfish 4 mg l^{-1} (3).
LC_{50} (24 hr) mosquito fish 4900 mg l^{-1} (4,5).

Invertebrate toxicity
LC_{50} (96 hr) *Branchiura sowerbyi* 2500 mg l^{-1} (2).

Bioaccumulation
Calculated bioconcentration factors of 340-2000 indicate that environmental accumulation is likely (6).

Environmental fate

Degradation studies
BOD_5 1.92 mg $l^{-1}O_2$; COD 0.06 mg $l^{-1}O_2$ (3).
Oxidised to the corresponding fatty acid, which is oxidised further by β-oxidation yielding shorter fatty acids by *Pseudomonas aleovorans* (7).

Abiotic removal
Calculated $t_{1/2}$ for volatilisation from model river water 2.9 hr and from model pond water 13 days (6,8).
Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in the atmosphere 2.2 days (9).

Adsorption and retention
Calc. K_{oc} values of 2400-8100 indicate that heptane may be moderately adsorbed by soil and sediments (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >15,000 mg kg^{-1} (10).
LC_{Lo} (6 min) inhalation human 1000 ppm (central nervous system effects) (11).
LD_{50} intravenous mouse 220 mg kg^{-1} (12).

Sub-acute and sub-chronic data
Inhalation rat (26 wk) 400-3000 ppm 6 hr day^{-1} for 26 wk caused no neurological disturbances or organ toxicity. Except for increased serum alkaline phosphatase activity in ♀ rats at the high dose, blood chemistry showed no haematological, renal or liver disorders (10).

Metabolism and toxicokinetics

Metabolised in mammals to hydroxy derivatives by a cytochrome P_{450} containing mixed function oxidase system before being converted into the corresponding keto forms (13).

Irritancy

Irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (14).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (15).

Escherichia coli WP2, WP2*uvrA* with and without metabolic activation negative (15).

Saccharomyces cerevisiae mitotic gene conversion assay with and without metabolic activation negative (15).

In vitro rat liver cell line RL_4 chromosome assay without metabolic activation negative (15).

Other effects

Other adverse effects (human)

Humans exposed to 0.1% heptane showed slight vertigo in 6 min, at 0.2% in 4 min, and at 0.5% marked inability to maintain equilibrium and coordination in 7 min (16).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (17).

Other comments

Physical properties, environmental fate, toxicity and hazards reviewed (1,18-20).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (21).

References

1. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1993, **4**, 326-336, Lewis Publishers, Chelsea, MI, USA.
2. Ghatak, D. B. et al *Environ. Ecol.* 1988, **6**(4), 943-947.
3. Shell Chemie *Shell Industrie Chemicalien Gids* 1 Jan 1975, 's-Gravenhage, Netherlands.
4. Wallen, I. E. et al *Sewage Ind. Wastes* 1957, **29**(6), 695-711.
5. Merrick, F. et al *Les Eaux Residuaires Industrielles* 1970.
6. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
7. *EXAMS II Computer Simulation* 1987, USEPA, Athens, GA, USA.
8. Lagevern, R. G. et al *Appl. Environ. Microbiol.* 1988, **54**(12), 2924-2932.
9. Atkinson, R. *Chem. Rev.* 1985, **85**, 69-201.
10. American Petroleum Institute *A 26-Week Inhalation Toxicity Study of Heptane in the Rat* 1980, API Contract No. PS-29. Biodynamics Inc. East Millstone, NJ, USA.
11. *US Bureau of Mines Report of Investigation No. 2979* 1929, 2879.
12. *J. Pharm. Sci.* 1978, **68**, 566.
13. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, **2B**, 3188-3189, John Wiley & Sons, New York, NY, USA.
14. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1821, Sigma-Aldrich, Milwaukee, WI, USA.
15. Brooks, T. M. et al *Mutagenesis* 1988, **3**(3), 227-232.
16. Patty, F. A. et al *Odor Intensity and Symptoms Produced by Commercial Propane, Butane, Hexane and Heptane Vapour* 1929, US Bureau of Mines Report of Investigation No. 2979.
17. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
18. *Cah. Notes Doc.* 1988, 133, 787-790.
19. *Ethel Browning's Toxicity and Metabolism of Industrial Solvents* 2nd ed., 1987, **1**, 297-306, Elsevier, New York, NY, USA.
20. *Chemical Safety Data Sheets* 1989, **1**, 178-180, The Royal Society of Chemistry, London, UK.
21. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H21 1-heptanethiol

$$CH_3(CH_2)_5CH_2SH$$

$C_7H_{16}S$ **Mol. Wt.** 132.27 **CAS Registry No.** 1639-09-4

Synonyms heptyl mercaptan; USAF EK-2122

EINECS No. 216-678-8 **RTECS No.** MJ 1400000

Uses Organic synthesis.

Occurrence Present in fossil fuels.

Physical properties

M. Pt. –43.4°C **B. Pt.** 173-176°C at 765 mmHg **Flash point** 46°C **Specific gravity** 0.839 at 25°C with respect to water at 4°C

Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1228

Environmental fate

Abiotic removal

99% removal from flue gases by incorporation of permangate in wet scrubber at pH 8.5 (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (2).

Other effects

Other adverse effects (human)

May be harmful by inhalation, ingestion or absorption. Exposure in humans may cause irritation of the eyes and skin, nausea, headache and vomiting (3).

References

1. Possett, H. S. et al *Ind. Eng. Chem. Prod. Res. Developm.* 1965, **4**, 48.
2. *NTIS Report AD277-689* Natl. Tech. Inf. Serv., Springfield, VA, USA.
3. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1828, Sigma-Aldrich, Milwaukee, WI, USA

H22 heptanoic acid

$$CH_3(CH_2)_5CO_2H$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 111-14-8

Synonyms *n*-heptanoic acid; enanthic acid; hepthlic acid; *n*-heptylic acid; hexacid C-7; oenanthic acid

EINECS No. 203-838-7 **RTECS No.** MJ 1575000

Uses Organic synthesis. Manufacture of lubricants.

Occurrence Aroma component of plants, cooked meats and fish and dairy products.

Physical properties

M. Pt. –8.9 to -8.7°C **B. Pt.** 223°C **Flash point** >110°C **Specific gravity** 0.9345 at 0°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.72 (calc.) (1) **Volatility** v.p. 1.0 mmHg at 78°C
Solubility Water: 2.4 g l^{-1} at 15°C. Organic solvents: acetone, diethyl ether, dimethylformamide, dimethyl sulfoxide, ethanol

Occupational exposure

Supply classification corrosive
Risk phrases Causes burns (R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S28, S36/37/39, S45)

Environmental fate

Anaerobic effects
Degraded to methane and carbon dioxide by methanogenic bacteria (2).

Degradation studies
Removal from waste water by activated sludge 13% of ThOD after 6 hr; 25% of ThOD after 12 hr; 43% of ThOD after 24 hr (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 6400, 7000 mg kg^{-1}, respectively (4,5).
LD_{50} intravenous mouse 1200 mg kg^{-1} (6).

Metabolism and toxicokinetics
In mammals, metabolism occurs by β-oxidation, resulting in the appearance of ketone bodies. Metabolism of the remaining propionic acid moiety results in glucose and glycogen formation (7).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (8).

Other effects

Other adverse effects (human)
Extremely destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema. Symptoms of exposure include burning sensation, coughing, wheezing, laryngitis, shortness of breath, headache, nausea and vomiting (9).

References

1. Verschueren, N. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, 603, Van Nostrand Reinhold, New York, NY, USA.
2. Kalyuzhnyi, S. V. et al *Dokl. Akad. Nauk SSR* 1989, **309**(1), 244-247 (Russ.) (*Chem. Abstr.* **112**, 73555a).
3. Maloney, G. W. et al *J. Water Pollut. Control Fed.* 1969, **41**(2), R18-R33.
4. *Biochem. J.* 1940, **34**, 1196.
5. Food & Drug Research Labs. *Report* 1976, 123, Waverly, New York, NY, USA.

6. Oroe, L. et al *Acta Pharmacol. Toxicol.* 1961, **18**, 141.
7. *Patty's Industrial Hygiene and Toxicology* 3rd ed. 1982, **2c**, 4923, John Wiley, New York, NY, USA.
8. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141.
9. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed. 1988, **1**, 1823, Sigma-Aldrich, Milwaukee, WI, USA

H23 2-heptanone

$$CH_3C(O)(CH_2)_4CH_3$$

$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 110-43-0

Synonyms heptan-2-one; amyl methyl ketone; methyl amyl ketone; methyl *n*-amyl ketone; methyl pentyl ketone; *n*-pentyl methyl ketone

EINECS No. 203-767-1 **RTECS No.** MJ 5075000

Uses Organic synthesis. As a perfume and flavouring agent. Solvent.
Occurrence Aroma component of plants, dairy products, cooked meat and fish. Bee alarm pheromone.

Physical properties

M. Pt. –35°C **B. Pt.** 149-150°C **Flash point** 47°C **Specific gravity** 0.8197 at 15°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.98 **Volatility** v.p. 2.6 mmHg at 20°C ; v.den. 3.94
Solubility Water: 4.3 g l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 50 ppm (235 mg m^{-3})
SE-LEVL 25 ppm (120 mg m^{-3}) **SE-STEL** 50 ppm (250 mg m^{-3})
UK-LTEL 50 ppm (237 mg m^{-3}) **UK-STEL** 100 ppm (475 mg m^{-3})
US-TWA 50 ppm (233 mg m^{-3})

UN No. 1110 **HAZCHEM Code** 3[illegible] **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful if swallowed (R10, R22)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Environmental fate

Degradation studies
BOD_{10} 0.50 mg l^{-1} O_2 in standard dilute sewage (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1670 mg kg^{-1} (2).
LD_{50} oral mouse 730 mg kg^{-1} (3).
LC_{Lo} (4 hr) inhalation rat 4000 ppm (2).
LD_{50} dermal rabbit 12,600 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse, rat 400, 800 mg kg^{-1}, respectively (4).

Sub-acute and sub-chronic data
Inhalation rat, monkey (9 month) 1000 ppm caused no significant pulmonary, electrocardiogram or clinical effects (4).

Metabolism and toxicokinetics
Following oral administration to rabbits, 40% was excreted in the urine as heptyl-2-glucuronide with traces of unchanged ketone (5).

Irritancy
Dermal rabbit (24 hr) 14 mg caused mild irritation (2).

Sensitisation
Negative in skin sensistisation studies on 26 human volunteers (4).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).
Autoignition temperature 485°C.

References

1. Mills, E. J. et al *Proc. 8th Purdue Ind. Waste Conf.* 1953, 492.
2. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
3. *Acta Pharm. Jugosl.* 1962, **12**, 79.
4. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, **2**, 4758, John Wiley & Sons, New York, NY, USA.
5. Opdyke, D. L. J. (Ed.) *Monographs on Fragrance Raw Materials* 1979, 532, Pergamon Press, New York, NY, USA.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H24 3-heptanone

$$CH_3(CH_2)_3COCH_2CH_3$$

$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 106-35-4

Synonyms butyl ethyl ketone; *n*-butyl ethyl ketone; ethyl butyl ketone; heptan-3-one

EINECS No. 203-388-1 **RTECS No.** MJ 5250000

Uses Used in solvent mixtures for air dried and baked finishes. Polyvinyl and nitrocellulose resins.

Physical properties

M. Pt. –36.7°C **B. Pt.** 148°C **Flash point** 46.1°C (open cup) **Specific gravity** 0.8198 at 20°C with respect to water at 20°C **Volatility** v.p. 1.4 mmHg at 25°C ; v.den. 3.93
Solubility Water: 14.3 g l^{-1} at 20°C. Organic solvents: ethanol

Occupational exposure

FR-VME 50 ppm (230 mg m^{-3})
SE-LEVL 25 ppm (120 mg m^{-3})
UK-LTEL 50 ppm (237 mg m^{-3})
US-TWA 50 ppm (234 mg m^{-3})
Supply classification harmful

SE-STEL 50 ppm (250 mg m^{-3})
UK-STEL 100 ppm (475 mg m^{-3})
US-STEL 75 ppm

Risk phrases Flammable – Harmful by inhalation – Irritating to the eyes (R10, R20, R36)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin (S2, S24)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2760 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (1).

Sub-acute and sub-chronic data
Inhalation rat (24 wk) 700 ppm 72 hr wk^{-1}, no clinical signs of systemic toxicity or neurotoxicity (2).

Metabolism and toxicokinetics
Metabolites in rats are 6-hydroxy-3-heptanone and 2,5-heptanedione (2).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation (3).
Dermal rabbit (24 hr) 500 mg caused moderate irritation and 100 mg instilled into rabbit eye caused mild irritation (4).

Sensitisation
Non-sensitiser (5).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

Other comments

Health and safety standards discussed (7).
Toxicity, including irritations sensitisation and metabolism in invertebrates and microorganisms reviewed (4).
Reviews on experimental toxicology and human health effects listed (8).

References

1. *J. Ind. Hyg. Toxicol.* 1949, **31**, 60, 343.
2. Katz, G. V. *Toxicol. Appl. Pharmacol.* 1980, **52**(1), 153-158.
3. *Union Carbide Data Sheet* 1969 (12 Mar), Union Carbide Corp., New York, NY, USA.
4. Opdyke, D. L. J. *Food Cosmet. Toxicol.* 1978, **16**(Suppl. 1), 731-732.
5. Sharp, D. W. *Toxicology* 1978, **9**, 261-271.
6. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. Clack, G. *Job Saf. Health* 1975, **3**(6), 5-10.
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H25 4-heptanone

$$CH_3CH_2CH_2COCH_2CH_2CH_3$$

$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 123-19-3
Synonyms dipropyl ketone; di-*n*-propyl ketone; propyl ketone
EINECS No. 204-608-9 **RTECS No.** MJ 5600000
Uses Organic synthesis. Solvent.

Occurrence Aroma component of plants and cooked meat and fish.

Physical properties

M. Pt. –33°C **B. Pt.** 145°C **Flash point** 48°C **Specific gravity** 0.8174 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.98 (1) **Volatility** v.p. 5.2 mmHg at 20°C ; v.den. 3.93
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 50 ppm (235 mg m^{-3})
US-TWA 50 ppm (233 mg m^{-3})

UN No. 2710 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Risk phrases Flammable (R10)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Ecotoxicity

Invertebrate toxicity
IC_{50} (48 hr) *Tetrahymena pyriformis* 20 mg l^{-1} (1).

Environmental fate

Degradation studies
Degradation by activated sludge 1.4% of ThOD after 6 hr; 2.2% of ThOD after 12 hr; 3.8% of ThOD after 24 hr (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3000 mg kg^{-1} (3).
LC_{Lo} (4 hr) inhalation rat 4000 ppm (3).
LD_{50} dermal rabbit 5660 mg kg^{-1} (3).
LD_{Lo} intravenous mouse 270 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Gavage rat (12 wk) 2000 mg kg^{-1} day^{-1} 5 days wk^{-1} produced severe central nervous system depression and reduced weight gain. Relative liver and kidney weights were increased and histological examination revealed hepatocyte hypertrophy. Hyperkeratosis in the stomach and chronic irritation of the non-glandular gastric epithelium were also reported (5).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation, 500 mg instilled into rabbit eye for 24 hr caused mild irritation (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

References

1. Schultz, T. W. et al *Bull. Environ. Contam. Toxicol.* 1990, **44**(1), 67-72.
2. Malaney, G. W. et al *J. Water Poll. Control Fed.* 1969, **41**(2), R18-R33.
3. Carpenter, C. P. et al *Toxicol. Appl. Pharmacol.* 1974, **28**, 313.
4. *Acta Pharmacol. Toxicol.* 1975, **37**, 56.

5. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, **2**, 4763-4764, John Wiley & Sons, New York, NY, USA.
6. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, 286, Prague, Czechoslovakia.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H26 1-heptene

$$CH_3(CH_2)_4CH{=}CH_2$$

C_7H_{14} **Mol. Wt.** 98.19 **CAS Registry No.** 592-76-7

Synonyms *n*-heptene; heptylene

EINECS No. 209-767-8 **RTECS No.** MJ 8840000

Uses Chemical intermediate.
Occurrence In coal-derived naphtha.

Physical properties

M. Pt. –119°C **B. Pt.** 94°C **Flash point** –8°C **Specific gravity** 0.6970 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.99 **Volatility** v.den. 0.7
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2278 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity
IC_{Lo} *Uronema parduczi* Chatton-Lwoff 1.8 mg l^{-1} (exposure unspecified) (1).

Environmental fate

Abiotic removal
Condensation products are formed by irradiation under simulated atmospheric conditions in the presence of nitrogen oxides or mixture of nitrogen oxides and sulphur dioxide (2).

Mammalian & avian toxicity

Irritancy
Causes skin irritation. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (3).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation negative (4).

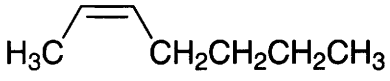
Other effects

Any other adverse effects
Hepatic microsomal cytochrome P_{450} from phenobarbital-pretreated rats is destroyed *in vitro* by *n*-heptene in the presence of NADPH (4).

References

1. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
2. Schwartz, W. E. et al *Chemical Characterisation of Mode Aerosols* 1976, US Natl. Tech. Info. Ser., Report PB-257512.
3. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1826, Sigma-Aldrich, Milwaukee, WI, USA.
4. Ortiz de Montellano, P. R. et al *Biochem. Biophys. Acta* 1978, **544**, 504

H27 (*Z*)-2-heptene



C_7H_{14} **Mol. Wt.** 98.19 **CAS Registry No.** 6443-92-1

Synonyms *cis*-2-heptene

EINECS No. 229-242-7

Uses Organic synthesis.

Occurrence Present in coal-derived naphtha.

Physical properties

B. Pt. 98-99°C **Flash point** –6°C **Specific gravity** 0.708 at 20°C with respect to water at 4°C

Solubility Organic solvents: acetone, benzene, carbon tetrachloride, chloroform, diethyl ether, ethanol, petroleum ether

Mammalian & avian toxicity

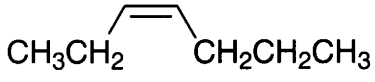
Irritancy

Causes skin irritation. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (1).

References

1. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1826, Sigma-Aldrich, Milwaukee, WI, USA

H28 (*Z*)-3-heptene



C_7H_{14} **Mol. Wt.** 98.19 **CAS Registry No.** 7642-10-6

Synonyms *cis*-3-heptene

Occurrence Present in coal-derived naphtha.

Physical properties

B. Pt. 95.7°C **Flash point** -7°C **Specific gravity** 0.7030 at 20°C with respect to water at 4°C
Volatility v.den. 3.4
Solubility Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, petroleum ether

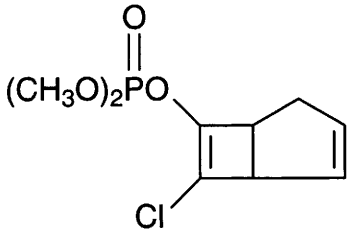
Mammalian & avian toxicity

Irritancy
Causes skin irritation. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (1).

References

1. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1827, Sigma-Aldrich, Milwaukee, WI, USA

H29 heptenophos



$C_9H_{12}ClO_4P$ **Mol. Wt.** 250.62 **CAS Registry No.** 23560-59-0
Synonyms dimethyl 7-chlorobicyclo[3.2.0]hepta-2,6-dien-6-yl dimethylphosphate; Hostaquick; Ragadan; XOE 2982
EINECS No. 245-737-0 **RTECS No.** TB 8545000
Uses Insecticide.

Physical properties

B. Pt. 94-95°C; 64°C at 0.075 mmHg **Specific gravity** 1.294 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.32 **Volatility** v.p. 7.5×10^4 mmHg at 20°C
Solubility Water: 2.2 g l^{-1} at 23°C. Organic solvents: acetone, methanol, hexane, xylene

Occupational exposure

Supply classification toxic
Risk phrases Toxic if swallowed (R25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – After contact with skin, wash immediately with plenty of water – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S28, S37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) trout, guppy, carp 0.056, 13.1, 24-41 mg l^{-1}, respectively (1,2).

Mammalian & avian toxicity

Acute data

LD_{50} oral Japanese quail, 17-55 mg kg^{-1} (2).
LD_{50} oral rat 96 mg kg^{-1} (3).
LC_{50} (4 hr) inhalation rat 400 mg m^{-3} (1).
LD_{50} dermal mouse, rat 2000, 2900 mg kg^{-1}, respectively (1,4).

Carcinogenicity and chronic effects

Oral rat and dog, (2 yr) no-adverse-effect level 12-15 mg kg^{-1} diet (1).

Metabolism and toxicokinetics

Following oral administration to rats, 90% was excreted in the urine and 6% in the faeces as metabolites within 6 days (1).

Genotoxicity

In vitro mouse bone marrow cells, chromosomal aberrations positive (5).

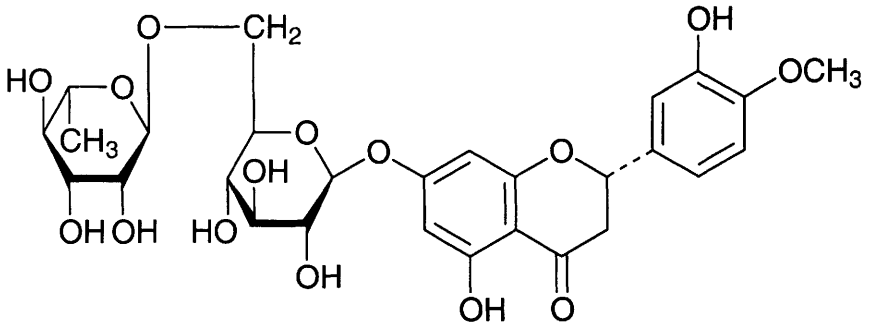
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
WHO Toxicity Class II (8).
EPA Toxicity Class II (2).
ADI 0.003 mg kg^{-1} body weight (2).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Thomson, W. T. et al *Agricultural Chemicals* 1977, **1**(1), 11, Thomson Publications, Fresno, CA, USA.
4. *Sanit. Hyg. (USSR)* 1984, **49**(4), 18.
5. German, I. V. *Gig. Sanit.* 1990, (5), 72-74 (Russ.) (*Chem. Abstr.* **113**, 93130g).
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

H30 hesperidine



$C_{28}H_{34}O_{15}$ **Mol. Wt.** 610.57 **CAS Registry No.** 520-26-3

Synonyms Cirantin; (*S*)-7-[[6-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy] hesperetin; hesperidin; hesperidoside; hesperitin-7-rhamnoglucoside; USAF CF-3

EINECS No. 208-288-1 **RTECS No.** MK 6650000

Uses Permitted food additive in USA.

Occurrence Flavonoid isolated from citrus fruit rind.

Physical properties

M. Pt. 258-262°C

Solubility Water: 200 mg l^{-1}. Organic solvents: pyridine, formamide, dimethylformamide

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >100 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 1000 mg kg^{-1} (2).

Genotoxicity

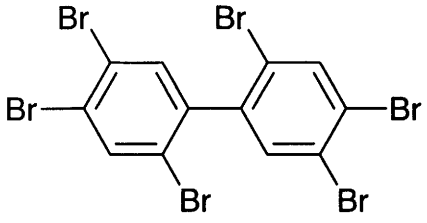
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (3).

Escherichia coli WP2 negative (3).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *NTIS Report* No. AD277-689 Natl. Tech. Inf. Ser., Springfield, VA, USA.
3. Prival, M. J. et al *Mutat. Res.* 1991, **260**(4), 321-329

H31 2,2′,4,4′,5,5′-hexabromobiphenyl



$C_{12}H_4Br_6$ **Mol. Wt.** 627.59 **CAS Registry No.** 59080-40-9

Synonyms 2,2′,4,4′,5,5′-hexabromo-1,1′-biphenyl; 2,4,5,2′,4′,5′-hexabromobiphenyl

RTECS No. DV 5341000

Uses Formerly used as a fire retardant.

Physical properties

M. Pt. 72 °C **Volatility** v.p. 7.6×10^{-5} mmHg at 90 °C

Solubility Water: 11 μg l^{-1}. Organic solvents: acetone, benzene

Ecotoxicity

Fish toxicity

No loss of equilibrium nor death to stickleback, steelhead and sockeye salmon at 10 mg l^{-1} for 24 hr. Test water: total hardness, 67-120 mg l^{-1}; methyl orange alkalinity, 151-183 mg l^{-1}; total dissolved solids, 160-175 mg l^{-1}; and pH 7.1 (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).

Oral rat (16 month) 10 ppm diet for 140 days, beginning 30 days after a single intraperitoneal dose of 10 mg kg^{-1} *N*-nitrosodiethylamine. One group was also co-administered a diet of 0.1 ppm 3,3′,4,4′,5,5′-hexabromobiphenyl. Development of hepatic nodules and altered hepatic foci was enhanced and a synergistic effect was observed when co-administered with 0.1 ppm 3,3′,4,4′,5,5′-hexabromobiphenyl (3).

Teratogenicity and reproductive effects

Oral mouse, lowest toxic dose 360 mg kg^{-1} day^{-1} on days 6-15 gestation (foetotoxic effects) (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (5,6).

In vitro Chinese hamster V79 cells with and without metabolic activation negative, inhibition of intercellular communication positive (7,8).

In vivo mouse micronucleus test without metabolic activation negative (6).

In vivo rat, mouse bone marrow cells, chromosomal aberrations without activation negative (9).

Other effects

Any other adverse effects

Enters, *in vitro*, mouse 3T3LI cell line adipocytes by passive diffusion and is sequestered in either cells or medium according to its relative solubility in these compartments. The quantity of triglyceride in the cells strongly influences the movement (10).

Removal from preloaded, *in vitro*, 3T3LI adipocytes was increased with addition of human lipoprotein. Depostion within the cells was reduced. Rate of removal was related to the concentrations of lipoprotein cholesterol, cholesterol ester and phospholipid (11).

Legislation

Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

Other comments

Physical properties, use, carcinogenicity and mutagenicity reviewed (13).

References

1. Mc Phee, C. et al *Lethal Effects of 2014 Chemicals to Fish* 1989, EPA 560/6-89-001, PB 89-156-715, Washington, DC, USA.
2. *IARC Monograph* 1987, **Suppl. 7**, 321-322.
3. Jensen, R. K. et al *Carcinogenesis (London)* 1986, **7**(10), 1771-1774.
4. *Toxicol. Appl. Pharmacol.* 1985, **81**, 431.
5. Haworth, S. et al *Environ. Mol. Mutagen.* 1983, **5**, (Suppl. 1), 3-142.
6. Millischer, R. et al *Toxicol. Eur. Res.* 1979, **2**, 155-161.
7. Kavanagh, T. J. et al *Toxicol. Appl. Pharmacol.* 1985, **79**, 91-98.
8. Williams, G. M. et al *Environ. Res.* 1984, **34**, 310-320.
9. Wertz, G. F. et al *Environ. Health Perspect.* 1978, **23**, 129-132.
10. Kraus, A. L. et al *J. Toxicol. Environ. Health* 1986, **19**(4), 541-554.
11. Krauns, A. L. et al *J. Toxicol. Environ. Health* 1989, **26**(2), 157-174.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
13. *IARC Monograph* 1986, **42**, 261-292

H32 hexachloroacetone

$$Cl_3CC(O)CCl_3$$

C_3Cl_6O **Mol. Wt.** 264.75 **CAS Registry No.** 116-16-5

Synonyms 1,1,1,3,3,3-hexachloro-2-propanone; hexachloro-2-propanone; GC 1106

EINECS No. 204-129-5 **RTECS No.** UC 2100000

Uses Organic synthesis. UV sensitiser. Analytical reagent. Herbicide.

Occurrence Occurs in the edible seaweed *Asparagopsis taxiformis* (1).

Physical properties

M. Pt. –30°C at 6 mmHg (99% purity) **B. Pt.** 66-70°C **Flash point** >110°C (99% purity)

Specific gravity 1.743 at 12°C with respect to water at 12°C **Partition coefficient** log P_{ow} 3.490 (2)

Volatility v.p. 0.376 mmHg at 20°C ; v.den. 9.2

Solubility Organic solvents: acetone, benzene; miscible with isopropanol, methanol, vegetable oils

Occupational exposure

UN No. 2661 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification harmful

Risk phrases Harmful if swallowed (R22)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 46 ppm, Microtox test (3).

Environmental fate

Abiotic removal

Estimated volatilisation $t_{1/2}$ 6.5 hr from model river water (4).

Adsorption and retention

Estimated K_{oc} of 1900 indicates that hexachloroacetone will have low mobility in soil (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral dog, rat 700, 1300 mg kg^{-1}, respectively (5,6).
LC_{50} (6 hr) inhalation rat 360 ppm (7).
LD_{50} dermal rat, rabbit 3000 mg kg^{-1} (7).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (species unspecified) (8).

Genotoxicity

Saccharomyces cerevisiae D7, XV185-14C with and without metabolic activation positive (9).
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (1).

Other effects

Any other adverse effects

Inhalation, dermal and oral exposure of rats caused central nervous system depression (7).
Inhalation exposure in rats caused pulmonory oedema, haemorrhage and congestion. Oral administration in rats caused hypertrophy of the liver and kidneys and slight growth depression (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).
Partition coefficient exceeds European Union recommended limit of 3.0.

Other comments

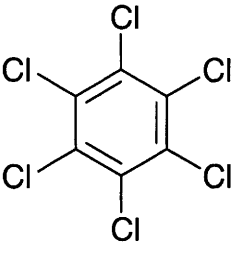
Residues have been identified in pulp mill effluents (1).

References

1. Zochlinski, H. et al *Mutat. Res.* 1981, **89**(2), 137-144.
2. *Graphical Exposure Modelling System* 1987, USEPA Office of Toxic Substances, Washington, DC, USA.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
5. *Residue Rev.* 1965, **10**, 97.
6. *Pesticide Chemicals Official Compendium* 1966, 580, Association of American Pesticide Control Officials, Topeka, KS, USA.
7. Borzelleca, J. F. et al *Toxicol. Appl. Pharmacol.* 1965, **7**(4), 592-597.

8. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1831, Sigma-Aldrich, Milwaukee, WI, USA.
9. Nestmann, E. R. et al *Mutat. Res.* 1985, **155**(1-2), 53-60.
10. Gosselin, R. E. et al *Chemical Toxicology of Commercial Products* 5th ed. 1984, Williams and Wilkins, Baltimore, MD, USA.
11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

H33 hexachlorobenzene



C_6Cl_6 **Mol. Wt.** 284.78 **CAS Registry No.** 118-74-1

Synonyms HCB; pentachlorophenyl chloride; perchlorobenzene

EINECS No. 204-273-9 **RTECS No.** DA 2975000

Uses Fungicidal fumigant. Organic synthesis.

Physical properties

M. Pt. 230°C **B. Pt.** 326°C **Flash point** 242°C **Specific gravity** 2.044 at 23°C
Partition coefficient log P_{ow} 6.44 (1) **Volatility** v.p. 1.09×10^{-5} mmHg at 20°C ; v.den. 9.8
Solubility Water: 6.21 μg l^{-1} at 25°C. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

FR-VME 0.5 mg m^{-3}
US-TWA 0.002 mg m^{-3}

UN No. 2729 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer – Toxic: danger of serious damage to health by prolonged exposure if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R48/25, R50/53)
Safety phrases Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet – Restricted to professional users (S53, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy >0.32 mg l^{-1} (2).

Invertebrate toxicity

EC_{50} (24 hr) *Daphnia magna* 60 μg l^{-1} (1).

LC_{50} (60 min) *Serratia liquifaciens* and *Pseudomonas aeruginosa* ~250-700 μg l^{-1} (3).

Fourteen-day, whole sediment toxicity tests using the amphipod *Hyalella azteca* and the midge *Chironomus tentans* were conducted on spiked sediment samples over a range of hexachlorobenzene concentrations. NOEC equalled the highest concentrations tested (42 mg kg^{-1}, normalised to 1% total organic carbon) (4).

Bioaccumulation

Log bioconcentration factors for trout, sunfish and fathead minnow 3.1-4.5, and for aquatic microorganisms 2.0-3.0 (5).

Bioaccumulation factor for tubificid sludgeworms *Tubifex tubifex* and *Limnodrilus hoffmeisteri* 7 (6).

Environmental fate

Nitrification inhibition

IC_{50} (25 days) *Nitrosomonas* 4.6 mg l^{-1} (7).

Carbonaceous inhibition

IC_{50} (5 day) aerobic heterotrophic bacteria isolated from activated sludge 350 mg l^{-1} (7).

Degradation studies

~50% removal from wastewater during anaerobic sewage sludge digestion after 32 days incubation (8).

Abiotic removal

Estimated $t_{1/2}$ ~2 yr for reaction with photochemically produced hydroxyl radicals in the atmosphere (9,10).

Degraded in water by treatment with UV irradiation and hydrogen peroxide (11).

Calculated $t_{1/2}$ for evaporation from water at 1 m depth ~ 8 hr (12).

Adsorption and retention

Measured log K_{oc} for soil and sediments range from 4-5 (9).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, mouse, rat 3500-10,000 mg kg^{-1}. Death in rats was due to neurotoxic effects (12,13).

LC_{50} inhalation rat, mouse 3600, 4000 mg m^{-3}, respectively (duration unspecified) (12).

LD_{50} subcutaneous mouse >10,000 mg kg^{-1} (14).

Sub-acute and sub-chronic data

Oral rat (4 month) 500 mg kg^{-1} 2 of 10 ♂ rats and 14 of 20 ♀ rats died (15).

Oral rat, 50 mg kg^{-1} day^{-1} 5 days wk^{-1} for 6 wk, or 100 mg kg^{-1} day^{-1} 5 days wk^{-1} for 3 wk. Hepatic porphyria occurred in ♀ rats treated for 6 wk (16).

Oral rat, mouse, hamster (90 day) 0, 100 or 200 mg kg^{-1} diet. Marked hepatosplenomegaly, enlarged thymuses and lymph nodes, or swollen and granular-looking renal cortices with depressions or nodulary areas were commonly observed (17).

Oral mouse, 170 mg kg^{-1} diet for 6 wk caused immunosuppression as indicated by decreased serum globulin levels and decreased response of spleen lymphocytes to sheep red blood cells (18).

LC_{50} (5 day) oral ring-necked pheasant 620 mg kg^{-1} diet (19).

Oral mallard (5 day) 700 mg kg^{-1} diet caused no mortality, 5000 mg kg^{-1}diet caused 30% mortality (19).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (20).

Oral rat (2 yr) 0, 75, 150 mg kg^{-1} diet. Progressive liver lesions started as hyperaemia and degeneration within 4 wk, and developed into toxic hepatitis, cirrhosis, bile-duct adenomas and hepatocellular carcinomas in very high incidences in ♀ rats and renal adenomas in ♂ rats (18).

Oral mouse, hamster (120 wk) 50, 100, 200 mg kg^{-1} diet, caused an increased incidence of liver tumours in both species. A significant increase in the incidence of thyroid tumours and liver haemangioendotheliomas was observed in hamsters (21).

Intraperitoneal mouse (24 wk) 0, 8, 20 or 40 mg kg^{-1} 3 × wk^{-1} for 8 wk did not cause a significant increase in the incidence of lung tumours compared with controls (22).

Teratogenicity and reproductive effects

Oral Japanese quail, 20 mg kg^{-1} diet for 90 days decreased chick survival (23).

Oral Japanese quail, 80 mg kg^{-1} diet from 90 days reduced egg production and hatchability (24). Mice were treated with 10 or 50 mg kg^{-1} day^{-1} on days 6-16 of pregnancy (route unspecified). Enlarged kidneys and hydronephrosis were observed on day-15 postpartum. Rats were treated with 10 mg kg^{-1} day^{-1} on days 15-20 of gestation (route unspecified). Enlarged kidneys were observed on day-5 postpartum but not on days 10 or 20 (25).

Oral mouse, 0, 0.5 or 5.0 mg kg^{-1} day^{-1} throughout gestation affected the development or maturation of the immune response which was assessed at 45 days of age. The study suggested an effect at the T-cell level (26).

Oral rat, 0, 10, 20, 40, 80, 160, 320 or 640 mg kg^{-1} diet over four generations. Suckling pups in the F1 generation were particularly sensitive, and many died prior to weaning when the mothers were fed 320 or 640 mg kg^{-1} diet. No gross abnormalities were found (27).

Metabolism and toxicokinetics

Adult ♀ rats were administered 100 mg kg^{-1} by gavage. Hexachlorobenzene accumulated in the brain and liver. Residues in the fat tissues were mobilised to the plasma and then redistributed (28).

Metabolism by rat liver microsomes involves dechlorination and hydroxylation by the mixed function oxidase system. ^{14}C-hexachlorobenzene was bound to microsomal protein (29).

Following oral administration to rats and monkeys of ^{14}C-hexachlorobenzene, more ^{14}C was recovered from the faeces than in urine. The major urinary metabolites were pentachlorophenol, tetrachlorohydroquinone and pentachlorothiophenol. Other urinary metabolites included tetrachlorobenzene, pentachlorobenzene and tri- and tetrachlorophenols. These metabolites were excreted as conjugates or in the free form. Unchanged hexachlorobenzene was found in the faeces and in fat (30-34).

Transplacental transfer has been reported in rats and mice (35).

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (36).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (37).

Escherichia coil WP2, WP2*uvra* with and without metabolic activation negative (37).

Saccharomyces cerevisiae 632/4, reversion to histidine and methionine auxotrophy without metabolic activation negative (38).

In vitro human lymphocytes, mitotic index and chromosomal aberrations negative (37).

In vitro Chinese hamster V79 lung fibroblasts, chromosomal aberrations positive (39).

In vivo rat, dominant lethal assay negative (40).

Other effects

Other adverse effects (human)

A case study of hepatocellular carcinoma in exposed workers is reported. The latency period from first exposure was ~18 yr (41).

Any other adverse effects

In vivo administration of hexachlorobenzene 1000 mg kg^{-1} to ♀ Wistar rats resulted in significant alterations of hepatic microsomal membrane function (42).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1}(43).

Included in Schedule 5 (Release into Water: Prescribed Substances) and Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (44).

Quality objective under EC Directives 86/280/EEC and 88/347/EEC 0.03 μg l^{-1} (annual mean) in all waters. A 'standstill' provision applies to concentrations in sediments, molluscs, shellfish and/or fish. Limit values under EC Directives 86/280/EEC and 88/347/EEC 1 mg l^{-1} HCB or 10 g HCB per tonne of HCB production capacity (monthly average) for HCB processing and production plant; 1.5 mg l^{-1} HCB or 1.5 g HCB per tonne of perchloroethylene and carbon tetrachloride total production capacity (monthly average) for perchloroethylene and carbon tetrachloride production plant by perchlorination (45).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (46).
WHO Guideline value for drinking water 1 μg l^{-1} (47).
UK Advisory value for drinking water 0.2 μg l^{-1} (48).
WHO Toxicity Class Ia (49).

Other comments

Metabolite of lindane. Occurs as a contaminant in some pesticides. Residues have been detected in natural waters, soil, sediments, meat, fish, dairy products and in animal and human tissues (5,50).
Physical properties, use, occurrence, environmental fate, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (5,50,51-53).
Toxicity and hazards comprehensively reviewed (54,55).
Environmental health criteria reviewed (56).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (57).

References

1. Vighi, M. et al *Chemosphere* 1987, **16**(5), 1043-1051.
2. Koenemann, W. H. *Quantitative Structure-Activity Relationships for Kinetics and Toxicity of Aquatic Pollutants and their Mixtures in Fish* 1979, Utrecht, Netherlands.
3. Hamdy, M. K. *Bull. Environ. Contam. Toxicol.* 1988, **41**(6), 936-942.
4. Barber, T. R. et al *Environ. Toxicol. Chem.* 1997, **16**(8), 1716-1720.
5. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1989, **1**, 351-359, Lewis Publishers, Chelsea, MI, USA.
6. Egeler, P. et al *Chemosphere* 1997, **35**(4), 835-852.
7. Blum, D. J. W. et al *Res. J. Water Pollut. Control Fed.* 1991, **63**(3), 198-207.
8. Kirk, P. W. W. et al *Chemosphere* 1989, **18**(9-10), 1771-1784.
9. Atkinson, R. A. *Chem. Rev.* 1985, **85**, 69-201.
10. Callahan, M. A. et al *Water-Related Environmental Fate of 129 Priority Pollutants* 1979, USEPA-440/4-79-029b.
11. Bandemer, T. et al *BBR, Brunnenbau, Bau von Wasserwerken, Rohrleitungsbau* 1986, **37**(11), 413-417 (Ger.) (*Chem. Abstr.* **106**, 89857n).
12. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
13. Booth, N. H. et al *J. Am. Vet. Med. Assoc.* 1975, **166**, 591-595.
14. *Sci. Rep. Res. Inst., Tohoku Univ., Ser. C* 1989, **36**(1-4), 10.
15. Kinbrough, R. D. et al *Res. Commun. Chem. Pathol. Pharmacol.* 1974, **8**, 653-664.
16. Krishnan, K. et al *Fundam. Appl. Toxicol.* 1991, **17**(3), 433-441.
17. Erturk, E. et al *IARC Sci. Publ.* 1986, **77** 417-423.
18. Loose, L. D. et al *J. Reticuloendothel. Soc.* 1977, **22**, 253-271.
19. Hill, E. F. et al *Lethal Dietary Toxicities of Environmental Pollutants to Birds* 1975, US Fish and Wildlife Service, Report Wildlife No. 191, Washington DC, USA.
20. *IARC Monograph* 1987, **Suppl. 7**, 219-220.
21. Cabral, J. R. P. et al *IARC Sci. Publ.* 1986, **77** 411-416.
22. Theiss, J. C. et al *Power Res.* 1977, **37**, 2717-2720.
23. Schwetz, B. A. et al *Toxicol. Appl. Pharmacol.* 1974, **30**, 255-265.
24. Vos, J. G. et al *Toxicol. Appl. Pharmacol.* 1971, **18**, 944-957.
25. Andrews, J. E. et al *IARC Sci. Publ.* 1986, **77** 381-391.
26. Barnett, J. B. et al *Toxicol. Lett.* 1987, **39**(2-3), 263-274.
27. Grant, D. L. et al *Arch. Environ. Contam. Toxicol.* 1977, **5**, 207-216.
28. Corbella, J. et al *IARC Sci. Publ.* 1987, **77**, 289-295.
29. Stewart, F. P. et al *IARC Sci. Publ.* 1987, **77**, 325-327.

30. Engst, R. et al *Bull. Environ. Contam. Toxicol.* 1978, **16**, 248-252.
31. Koss, G. et al *Arch. Toxicol.* 1976, **35**, 107-114.
32. Mehendale, H. M. et al *J. Agric. Food Chem.* 1975, **23**, 261-265.
33. Renner, G. et al *Toxicol. Appl. Pharmacol.* 1977, **39**, 355-356.
34. Rozman, K. et al *Chemosphere* 1977, **6**, 81-84.
35. Andrews, J. E. et al *Toxicol. Appl. Pharmacol.* 1976, **37**, 128.
36. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1831, Sigma-Aldrich, Milwaukee, WI, USA.
37. Siekel, P. et al *Teratog., Carcinog., Mutagen.* 1991, **11**(1), 55-60.
38. Guerzoni, M. E. et al *Riv. Sci. Technol. Alimenti Nutr. Um.* 1976, **6**, 161-165.
39. Kurodo, Y. *Basic Life Sci.* 1986, **39**, 359-375.
40. Khera, K. S. *Food Cosmet. Toxicol.* 1974, **12**, 471-477.
41. Selden, A. et al *Br. J. Ind. Med.* 1989, **46**(2), 138-140.
42. Randi, A. S. et al *Toxicology* 1998, **125**(2,3), 83-94.
43. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
44. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
45. *DoE Circular 7/89: Water and the environment. The implementation of EC directives on pollution caused by certain dangerous substances discharged into the aquatic environment* 1989, HMSO, London, UK.
46. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
47. *Guidelines for Drinking Water Quality* 2nd ed., 1993, **1**, WHO, Geneva, Switzerland.
48. *Guidance on Safeguarding the Quality of Public Water Supplies* 1989, HMSO, London, UK.
49. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
50. *IARC Monograph* 1979, **20**, 155-178.
51. De Matteis, F. *IARC Sci. Publ.* 1986, **77**, 427-431.
52. Vos, J. G. *IARC Sci. Publ.* 1986, **77**, 347-356.
53. Renner, G. *Toxicol. Environ. Chem.* 1988, **18**(1), 51-78.
54. *Scientific Reviews of Soviet Literature on Toxicity and Hazards of Chemicals* 1992, No. 134, UNEP, CIP, Moscow, USSR.
55. *Reviews of scientific literature in Russian on selected hazardous chemicals: Hexachlorobenzene, 134* 1993, UNEP/IRPTC, CIP, Moscow, USSR.
56. *Environmental Health Criteria No. 195: Hexachlorobenzene* 1997, WHO/IPCS, Geneva, Switzerland.
57. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H34 hexachlorobutadiene

$$Cl_2C{=}CClCCl{=}CCl_2$$

C_4Cl_6 **Mol. Wt.** 260.76 **CAS Registry No.** 87-68-3

Synonyms 1,1,2,3,4,4-hexachloro-1,3-butadiene; hexachloro-1,3-butadiene; HCBD; perchlorobutadiene; C46; Dolen-pur

EINECS No. 201-765-5 **RTECS No.** EJ 0700000

Uses Adsorbent for drying of chlorine gas. Solvent. Chemical intermediate. Fluid for gyroscopes. Soil fumigant.

Physical properties

M. Pt. –22 to –19°C **B. Pt.** 210-220°C **Specific gravity** 1.665 at 15.5°C with respect to water at 15.5°C
Partition coefficient log P_{ow} 4.90 (1) **Volatility** v.p. 22 mmHg at 100°C ; v.den. 9.0
Solubility Water: 2 mg l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

US-TWA 0.02 ppm (0.21 mg m^{-3})

UN No. 2279 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) goldfish 0.09 mg l^{-1} – flow-through bioassay (2).
LC_{50} (14 day) guppy 0.4 mg l^{-1} (3).

Bioaccumulation

Bioconcentration factor for rainbow trout 5800-17000 (4,5).

Environmental fate

Anaerobic effects

28% inhibition of anaerobic digestion at 50 mg l^{-1}, 41% inhibition at 100 mg l^{-1} (5 hr) (4).

Degradation studies

No biodegradation occurred in an anaerobic batch culture incubated at 37°C for 48 hr. Under aerobic conditions with a domestic waste water innoculum, 100% was removed after 7 days at 25°C (4,6).

Abiotic removal

Estimated tropospheric $t_{1/2}$ 1.6 yr in the northern hemisphere and 0.6 yr in the southern hemisphere (7).

Adsorption and retention

Calculated K_{oc} of 5200 indicates that hexachlorobutadiene will adsorb strongly to organic materials in soil (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, guinea pig 65-270 mg kg^{-1} (9-11).
LC_{Lo} (4 hr) inhalation mouse 240 ppm (11).
LD_{50} dermal rabbit 1200 mg kg^{-1} (12).
LD_{50} intraperitoneal mouse, rat 75, 215 mg kg^{-1}, respectively (9).

Sub-acute and sub-chronic data

Oral rat (30 day) 30-100 mg kg^{-1} day^{-1} caused renal tubular degeneration, necrosis and regeneration (13).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (14).
Oral rat (2 yr) 0, 0.2, 2.0 or 20 mg kg^{-1} day^{-1}. A statistically significant increase in kidney tumours was observed in the high-dose group (adenomas and adenocarcinomas). The total incidences of tumours in ♂ rats were 39/90 controls, 24/40 low dose, 13/40 mid dose and 15/39 high-dose, and in ♀ rats 82/90 controls, 35/40 low dose, 37/40 mid dose and 39/40 high dose. Doses of 2 and 20 mg kg^{-1} day^{-1} caused renal tubular hyperplasia. Urinary excretion of cuproporphyrin was increased in ♂ and ♀ rats receiving the high dose and in ♀ rats receiving 2 mg kg^{-1} day^{-1} (15).
Intraperitoneal mouse (24 wk) 0, 4 or 8 mg kg^{-1} 3 × wk^{-1} for a total of 12-13 injections. The incidence of lung tumours was not increased compared with controls (16).

Teratogenicity and reproductive effects

Oral ♂ and ♀ Japanese quail 0.3, 3, 10 or 30 mg kg^{-1} diet for 90 days. These dose levels had no effect on body weight, demeanour, food consumption, egg production, egg fertility and hatchability, eggshell thickness or survival of chicks (17).
Oral ♂ and ♀ rat, 20 mg kg^{-1} day^{-1} for 90 days prior to mating caused no observable effects on fertility or in the health of the pups (13).
Subcutaneous ♀ rat, single dose of 20 mg kg^{-1} before mating. All newborn rats died within 3 months compared with 21% among controls (18).

Inhalation rat, 0, 2, 5, 10 or 15 ppm for 6 hr day^{-1} on days 6-20 of gestation. A significant reduction in maternal weight gain and foetal weight occurred at 15 ppm. No embryotoxic or teratogenic effects were observed (19).

Metabolism and toxicokinetics

Metabolism in the rat kidney involves conjugation with glutathione followed by the formation of the cysteine conjugate *S*-(pentachloro-1,3-butadienyl)cysteine and then the mercapturic acid *N*-acetyl-*S*-pentachloro-1,3-butadienylcysteine which becomes covalently bound to cytosolic protein (20).

Following a single injection, hexachlorobutadiene was found in the lung, blood, liver, brain, kidney, spleen and mesentary, and was excreted in the urine for 7 days. In the kidney the higher concentration was observed in the proximal section of the nephron (21,22).

Irritancy

Dermal rabbit (24 hr) 810 mg caused moderate irritation. 160 mg instilled into rabbit eye caused mild irritation (duration unspecified) (23).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (24).

Salmonella typhimurium Ara mutagenicity assay with and without metabolic activation positive (25).

Drosophila melanogaster sex-linked recessive lethal assay negative (26).

In vitro hamster embryo fibroblasts, morphological transformation and unscheduled DNA synthesis with and without metabolic activation positive (27).

In vitro human peripheral blood lymphocytes, chromosomal aberrations negative (28).

In vitro Chinese hamster ovary cells with and without metabolic activation, sister chromatid exchanges positive, chromosomal aberrations negative (29).

In vivo mouse bone marrow cells, chromosomal aberration positive (28,30).

Other effects

Other adverse effects (human)

A group of 250 vineyard workers exposed seasonally to hexachlorobutadiene and polychlorobutane-80 showed multiple toxic effects contributing to the development of hypotension, nervous disorders, cardiac disease, chronic bronchitis and chronic hepatitis (31).

Any other adverse effects

Hexachlorobutadiene has moderate acute toxicity. Effects of chronic exposure indicate a cumulative effect. It affects the central nervous system and causes hepatic disorders in mice (9).

Inhalation mouse (4 hr) 210 ppm caused a 50% reduction in respiratory rate. Reflex bradypnoea occurred indicating irritation of the nasal cavity. Histological examination demonstrated kidney injury (32).

Legislation

Included in Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (33).

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (33).

Quality objective under EC Directives 86/280/EEC and 88/347/EEC 0.1 $\mu g\ l^{-1}$ (annual mean) in all waters. A 'standstill' provision applies to concentrations in sediments, molluscs, shellfish and/or fish. Limit value under EC Directives 86/280/EEC and 88/347/EEC 1.5 mg l^{-1} HCBD or 1.5 g HCBD per tonne of total production capacity of perchloroethylene and carbon tetrachloride (monthly average) for perchloroethylene and carbon tetrachloride production plant by perchlorination (34).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (35).

Other comments

Residues have been found in water, soil, sediments, in various foods and drink and in marine animals (36,37).

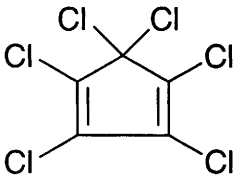
Disinfectant by-product in some chlorinated water supplies (38).

Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity and mutagenicity reviewed (36,37,39,40).
Autoignition temperature 610°C.

References

1. Chiou, C. T. *Environ. Sci. Technol.* 1983, **19**, 57-62.
2. Leeuwangh, P. et al in *Sublethal Effects of Toxic Chemicals in Aquatic Animals* 1975, 167, Elsevier, New York, NY, USA.
3. Koenemann, W. H. *Quantitative Structure-Activity Relationships for Kinetics and Toxicity of Aquatic Pollutants and their Mixtures in Fish* 1979, Utrecht, Netherlands.
4. Johnson, L. D. et al *J. Water Pollut. Control Fed.* 1983, **55**, 1441-1449.
5. Laska, A. L. et al *Bull. Environ. Contam. Toxicol.* 1976, **15**, 535-542.
6. Tabak, H. H. et al *J. Water Pollut. Control Fed.* 1981, **18**, 73-81.
7. Class, T. et al *Fresenius Z. Anal. Chem.* 1987, **327**, 198-204.
8. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
9. Gradiski, D. et al *Eur. J. Toxicol.* 1975, **8**(3), 180-187.
10. *Hyg. Sanit. (USSR)* 1963, **28**, 9.
11. Shell Chemical Co. *Report* 1961, 5, San Romon, CA, USA.
12. *Acta Pharmacol. Toxicol.* 1978, **43**, 346.
13. Schwetz, B. A. et al *Toxicol. Appl. Pharmacol.* 1977, **42**, 387-398.
14. *IARC Monograph* 1987, **Suppl. 7**, 65.
15. Kociba, R. J. et al *Am. Ind. Hyg. Assoc. J.* 1977, **38**, 589-602.
16. Theiss, J. C. et al *Cancer Res.* 1977, **37**, 2717-2720.
17. Schwetz, B. A. et al *Toxicol. Appl. Pharmacol.* 1974, **30**, 255-265.
18. Potergaera, G. E. *Gig. Sanit.* 1966, **31**, 33-36.
19. Saillenfait, A. M. et al *Toxicol. Lett.* 1989, **47**(3), 235-240.
20. Prath, I. S. et al *Arch. Toxicol.* 1988, **62**(5), 341-345.
21. Gul'ko, A. G. et al *Aktual. Vopr. Gig. Epidemiol.* 1972, 58-60. (Russ.) (*Chem. Abstr.* **81**, 346q).
22. Shroit, I. G. et al *Aktual. Vopr. Gig. Epidemiol.* 1972, 73-75 (Russ.) (*Chem. Abstr.* **81**, 73128e).
23. *J. Eur. Toxicol.* 1976, **9**, 171.
24. Wild, D. et al *Carcinogenesis* 1986, **7**(3), 431-434.
25. Roldan-Arjora, T. et al *Mutagenesis* 1991, **6**(3), 199-205.
26. Woodruff, R. C. et al *Environ. Mutagen.* 1985, **4**, 677-702.
27. Schiffman, D. et al *Cancer Lett. (Shannon, Irel.* 1984, **23**(3), 297-305.
28. German, I. V. *Tsitol. Genet.* 1988, **22**(4), 40-42. (Russ.) (*Chem Abstr.* **109**, 144410a).
29. Galloway, S. M. et al *Environ. Mol. Mutagen.* 1987, **10** (Suppl. 10), 1-175.
30. German, I. V. *Gig. Sanit.* 1990, (5), 72-74, (Russ.) (*Chem. Abstr.* **113**, 93130g).
31. Kransiuk, E. P. et al *Vrach. Delo* 1969, **7**, 111-115.
32. De Ceawriz, J. et al *J. Appl. Toxicol.* 1988, **8**(6), 417-422.
33. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
34. *DoE Circular 7/89: Water and the environment. The implementation of EC directives on pollution caused by certain dangerous substances discharged into the aquatic environment* 1989, HMSO, London, UK.
35. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
36. *IARC Monograph* 1979, **20**, 179-193.
37. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1989, **1**, 360-369, Lewis Publishers, Chelsea, MI, USA.
38. Tardiff, R. G. et al *Halogenated Organics in Tap Water: A Toxicological Evaluation* in *The Environmental Impact of Water Chlorination* 1976, 213-227, NTIS, Springfield VA, USA.
39. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
40. Yeng, R. S. H. *Rev. Environ. Contam. Toxicol.* 1988, **101**, 121-137

H35 hexachlorocyclopentadiene



C_5Cl_6 **Mol. Wt.** 272.77 **CAS Registry No.** 77-47-4

Synonyms 1,2,3,4,5,5-hexachloro-1,3-cyclopentadiene; perchlorocyclopentadiene

EINECS No. 201-029-3 **RTECS No.** GY 1225000

Uses Flame retardant. Manufacture of pesticides.

Physical properties

M. Pt. –10°C **B. Pt.** 239°C at 753 mmHg **Specific gravity** 1.715 at 15.5°C with respect to water at 15.5°C
Volatility v.p. 0.08 mmHg at 25°C ; v.den. 9.42
Solubility Water: 0.8 mg l^{-1}. Organic solvents: acetone, carbon tetrachloride, hexane, methanol

Occupational exposure

FR-VME 0.01 ppm (0.1 mg m^{-3})
US-TWA 0.01 ppm (0.11 mg m^{-3})

UN No. 2646 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification very toxic
Supply classification dangerous for the environment
Risk phrases Harmful if swallowed – Toxic in contact with skin – Very toxic by inhalation – Causes burns – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R24, R26, R34, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the eyes – Wear eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid exposure – obtain special instruction before use – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S25, S39, S45, S53, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 7 μg l^{-1} (flowthrough bioassay) (1).

Bioaccumulation
Bioaccumulation factor for *Chlorella fusea*, *Physa* and *Culex* species, fathead minnow, golden orfe and mosquito fish 450-1250 (2-5).

Environmental fate

Degradation studies
100% loss was observed after 7 days incubation of 10 mg l^{-1} in the dark with settled domestic wastewater innoculum. Volatilisation was reported to be insignificant (6).

Abiotic removal
Hydrolysis $t_{1/2}$ 16.1 days at 22°C. Hydrolysis is reported to be independent over the pH range 5-9 (7-9).
$t_{1/2}$ for photodegradation in sunlight <4 min. The primary degradation products included 2,3,4,4,5-pentachloro-2-

cyclopentanone; hexachloro-2-cyclopentanone and hexachloro-3-cyclopentanone, Pentachloro-*cis*-2,4-pentadienoic acid, *Z*- and *E*-pentachlorobutadiene were secondary degradation products (10).
Estimated volatilisation $t_{1/2}$ 5, 58 hr in model river, pond water, respectively (11,12).

Adsorption and retention
Average K_{oc} for 15 different soils 4265 (13).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 505 mg kg^{-1} (14).
LD_{50} oral rat 1300 mg kg^{-1} (15).
LC_{50} (4 hr) inhalation rat 1.6 ppm (16).
LD_{50} dermal rabbit 430 mg kg^{-1} (17).

Sub-acute and sub-chronic data
Inhalation rat (216 day) 0.15 ppm for 7 hr day^{-1} caused mild liver and kidney injury (18).

Teratogenicity and reproductive effects
Oral rabbit, TD_{Lo} 975 mg kg^{-1} day^{-1} on days 6-18 of gestation, teratogenic effects (musculoskeletal system) (19).

Metabolism and toxicokinetics
Rats administered 6 mg kg^{-1} orally excreted 33% in the urine and 10% in faeces within 7 days (20).
Following inhalation exposure of rats for 1 hr periods, 84% of the administered dose was retained, principally in the lungs. Excretion was mainly in the unchanged form, primarily in the urine (21).

Irritancy
Dermal rabbit (4 hr) 500 mg caused severe irritation (22).
20 mg instilled into rabbit eye for 24 hr caused moderate irritation (23).

Genotoxicity

Bacillus subtilis microsome rec-assay, DNA damage positive (24).
Escherichia coli K12 with and without metabolic activation negative (25).
In vitro primary rat hepatocytes, DNA repair assay negative (26).

Other effects

Other adverse effects (human)
Extremely destructive to tissue of the mucous membranes and upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema. Symptoms of exposure include burning sensation, coughing, wheezing, laryngitis, shortness of breath, headache, nausea and vomiting (27).

Legislation

Proposed maximum level in U.S. drinking water 0.05 mg l^{-1} (28).

Other comments

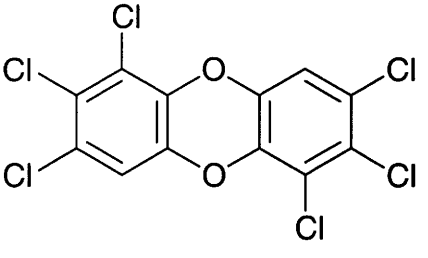
Disinfection by-product detected in some chlorinated drinking water and in wastewater from paper pulp mills (29,24).
Physical properties, use, occurrence and toxicity reviewed (30,31).

References

1. Spehar, R. L. et al *Bull. Environ. Contam. Toxicol.* 1979, **21**, 576-583.
2. Lu, P. Y. et al *J. Agric. Food Chem.* 1975, **5**, 967-973.
3. Geyer, H. et al *Chemosphere* 1981, **10**, 1307-1313.

4. Podowski, A. A. et al *Arch. Environ. Contam. Toxicol.* 1989, **13**, 471-482.
5. Freitig, D. et al *Ecotoxicol. Environ. Saf.* 1982, **6**, 60-81.
6. *Health Assessment for Hexachlorocyclopentadiene* 1984, US EPA-600/8-84-001A, 5-16.
7. Pallaham, M. A. et al *Water Related Environmental Fate of 129 Priority Pollutants* 1979, **2**, 57-63, EPA-440/4-79-029B.
8. Wolfe, N. L. et al *Chemosphere* 1982, **11**, 91-101.
9. Chou, S. F. J. et al *Aqueous Chemistry and Adsorption of Hexachlorocyclopentadiene by Earth Materials* 1981, NTIS PB81-173882.
10. Chou, S. F. J. et al *Environ. Toxicol. Chem.* 1987, **6**(5), 371-376.
11. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
12. *EXAMS II Computer Model Simulation* 1987, USEPA, Athens, GA, USA.
13. Chou, S. F. J. et al *Soil, Clay and Caustic Soda Effects on Solubility, Sorption and Mobility of Hexachlorocyclopentadiene* 1983, NTIS PB-84-116060.
14. *J. Agric. Food Chem.* 1975, **23**, 967.
15. USEPA Office of Toxic Substances *Report* 1986, OTS 0513386.
16. *J. Toxicol. Environ. Health* 1982, **9**, 743.
17. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, 308, Academic Press, New York, NY, USA.
18. Deichmann, W. B. et al *Am. Ind. Hyg. Assoc. J.* 1976, **34**, 495.
19. *Toxicol. Appl. Pharmacol.* 1980, **53**, 497.
20. Mehendale, H. M. *Environ. Health Perspect.* 1977, **21**, 275-278.
21. Lawrence, L. J. *Bull. Environ. Contam. Toxicol.* 1981, **26**(5), 663-668.
22. Velsicol Chemical Corp. *Product Bulletin* 1976, 50101-50102, Chicago, IL, USA.
23. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
24. Matsui, S. et al *Water Sci. Technol.* 1989, **21**(8-9), 875-887.
25. Goggleman, W. et al *Biochem. Pharmacol.* 1978, **27**, 2927-2929.
26. Naylor Dara Institute *Hepatocyte Primary Culture/DNA Repair Assay on Compound Hexachlorocyclopentadiene* 1983, US EPA Document No. 878213752.
27. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, 1833, Sigma-Aldrich, Milwaukee, WI, USA.
28. *Fed. Regist.* 25 July 1990, **55**(143), 30370-30448.
29. Garden, S. et al *Chemosphere* 1990, **20**(10-12), 1695-1700.
30. *IPCS Environmental Health Criteria No. 120* 1991, WHO, Geneva, Switzerland.
31. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H36 1,2,3,6,7,8-hexachlorodibenzo-*p*-dioxin



$C_{12}H_2Cl_6O_2$ **Mol. Wt.** 390.86 **CAS Registry No.** 57653-85-7

Synonyms 1,2,3,6,7,8-hexachlorodibenzodioxin; **RTECS No.** HP 3280100

Physical properties

M. Pt. 285-286°C **Partition coefficient** log P_{ow} 7.8 (1) **Volatility** v.p. 3.6×10^{-11} mmHg at 25°C

Environmental fate

Abiotic removal

Photolytic $t_{1/2}$ 380 min (2).

Removal from flue gases by catalytic degradation or by adsorption onto activated carbon (3,4).

Degraded by ozone at pH 10 following a 2nd order reaction. No significant degradation occurs at pH 5 (5).

Adsorption and retention

Estimated log K_{oc} 5.6-7.6 (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig 73 μg kg^{-1} (7).

LD_{50} oral mouse 825 μg kg^{-1} (7).

Sub-acute and sub-chronic data

Oral monkey (6 month) 5 μg kg^{-1} diet. After 3 months, swelling of the eye lids and loss of eye lashes occurred and after 6 months the animals had difficulty seeing. There was also loss of hair over the entire body. Intermittent periods of vomiting and diarrhoea from the 4th-6th month were observed. Anaemia and leucopenia were apparent after 6 months (8).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (9).

National Toxicology Program tested rats and mice via gavage. Designated positive in ♂ and ♀ mice and in ♀ rats. Equivocal results were reported in ♂ rats (10).

National Toxicology Program tested mice via dermal administration. Designated non-carcinogen in ♂ and ♀ mice (11).

A CASE control study reported carcinogenic potential for hexachlorodibenzodioxin in humans (12).

Teratogenicity and reproductive effects

Oral rat, 0-100 μg kg^{-1} day^{-1} (total exposure not specified) caused a dose-related decrease in maternal weight gain. 10 or 100 μg kg^{-1} day^{-1} was lethal to foetuses during late gestation. The high-dose level caused a significant increase in the incidence of foetal soft tissue and skeletal abnormalities (13).

Metabolism and toxicokinetics

Crosses the placenta to foetuses and present in milk of marmosets following subcutaneous administration (14).

Sensitisation

Acnegenic response was observed in the rabbit ear bioassay (13).

Genotoxicity

Salmonella typhimurium mutagenicity assay positive (no details given) (12).

In vitro morphological transformation of C3H/10T1/2 cells positive (15).

Other effects

Any other adverse effects

Oral chick, 10 or 100 μg kg^{-1} day^{-1} (duration not specified) produced chick oedema disease, characterised by hydropericardium, subcutaneous oedema, liver necrosis and death (13).

The immunoglobulin M antibody response to sheep red blood cells was suppressed in ♀ mice sub-chronically exposed (14 days) (16).

Legislation

Polychlorinated dibenzo-*p*-dioxins are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (17).

Partition coefficient exceeds European Union recommended limit of 3.0.

Other comments

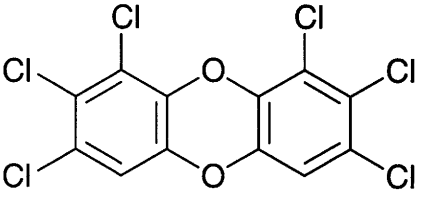
Occurs in commercial 2,4,5-T. Detected in fly ash from municipal waste incinerators, sediments and in fish and animal tissues (18-22).

Physical properties, use, occurrence, environmental fate, analysis, carcinogenicity and toxicity of polychlorinated dibenzo-*p*-dioxins reviewed (18,23).

References

1. Burkhard, L. P. et al *Chemosphere* 1986, **15**, 163-167.
2. Mamantov, A. *Environ. Sci. Technol.* 1984, **18**, 808-810.
3. Hagenmaier, H. et al *VGB Kraftwerkstech.* 1990, **70**(6), 491-493 (Ger.) (*Chem. Abstr.* **113**, 157801m).
4. Hoffman, J. E. et al *Proc. Annu. Conf., Am. Water Works Assoc.* 1990, **183**(2), 90/25.2.
5. Von der Mark, D. et al *Proc. Ind. Waste Conf.* 1987, **42nd**, 499-507.
6. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
7. *Toxicol. Appl. Pharmacol.* 1978, **44**, 335.
8. Allen, J. R. et al *Toxicol. Appl. Pharmacol.* 1979, **48**(1), 7179.
9. *IARC Monograph* 1987, **Suppl. 7**, 59.
10. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-198, NIEHS, Research Triangle Park, NC, USA.
11. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-202, NIEHS, Research Triangle Park, NC, USA.
12. Rosenkranz, H. S. et al *Mutat. Res.* 1990, **228**(2), 105-124.
13. Schwetz, B. A. et al *Environ. Health Perspect.* 1973, **5**, 87-99.
14. Krowke, R. et al *Chemosphere* 1990, **20**(7-9), 1065-1070.
15. Abernethy, D. J. et al *Carcinogenesis (London)* 1987, **8**(10), 1485-1490.
16. Holsapple, M. C. et al *J. Pharmacol. Exp. Ther.* 1984, **231**(3), 518-526.
17. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
18. *IARC Monograph* 1977, **15**, 41-102.
19. Kuehl, D. W. et al *Chemosphere* 1987, **16**, 657-666.
20. Ballschmitter, K. et al *Chemosphere* 1986, **15**, 901-915.
21. Van den Berg, M. et al *Arch. Environ. Contam. Toxicol.* 1987, **16**, 149-158.
22. Schecter, A. et al *Chemosphere* 1987, **16**, 2003-2016.
23. Huff, J. E. et al *Cell Biol.* 1991, **7**(1), 67-94

H37 1,2,3,7,8,9-hexachlorodibenzo-*p*-dioxin



$C_{12}H_2Cl_6O_2$ **Mol. Wt.** 390.86 **CAS Registry No.** 19408-74-3

Synonyms HCDD mixture 1,2,3,7,8,9 isomer; 1,2,3,7,8,9-hexachlorodibenzo[*b*,*e*][1,4]dioxin; D70; dibenzo-*p*-dioxin, 1,2,3,7,8,9-hexachloro-

RTECS No. HP 3310000

Physical properties

M. Pt. 243°C **Volatility** v.p. 6.5×10^{-6} mmHg at 25°C
Solubility Organic solvents: chloroform

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig 60 μg kg^{-1} (1).

Carcinogenicity and chronic effects
No adequate data for evalution of carcinogenicity of chlorinated dibenyodioxins (other than 2,3,7, 8-tetrachloro-*p*-dioxin) to humans, and insufficient evidence of carcinogenicity to animals. IARC classification group 3 (2).

Teratogenicity and reproductive effects
A mixture of unspecified isomers of hexachlorodibenzo-*p*-dioxin was administered to rats on days 6-15 of gestation. Doses of 100 μg kg^{-1} day^{-1} induced cleft palate and skeletal abnormalities. Doses of 1-10 μg kg^{-1} day^{-1} produced only subcutaneous oedema of the foetuses. A dose of 0.1 μg kg^{-1} day^{-1} produced no embryotoxic effects (3).

Sensitisation
Reported to be acnegenic in the rabbit ear bioassay (3).

Genotoxicity

In vitro C3H/1OT1/2 cells, morphological transformation after induction with *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine positive (4).
In vitro Chinese hamster ovary cells chromosomal aberrations positive, sister chromatid exchanges negative (5).

Other effects

Any other adverse effects
Daily doses of 10 or 100 μg kg^{-1} (duration unspecified) produced a positive response in the chick oedema bioassay, characterised by hydropericardium, subcutaneous oedema, liver necrosis and possibly death (3).

Other comments

May occur in commercial preparations of the herbicide pentachlorophenol and as a contaminant in batches of commercial fatty acids (6,7).
Occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity of substituted dibenzo-*p*-dioxins reviewed (6,8).
Carcinogenicity studies reviewed (9,10).

References

1. *Toxicol. Appl. Pharmacol.* 1978, **44**, 335.
2. *IARC Monograph* 1987, **Suppl. 7**, 59.
3. Schwetz, B. A. et al *Environ. Health Perspect.* 1973, **5**, 87-99.
4. Abernethy, D. J. et al *Carcinogenesis (London)* 1987, **8**(10), 1485-1490.
5. Rosenkranz, H. S. et al *Mutagenesis* 1990, **5**(6), 559-571.
6. Johnson, R. L. et al *Environ. Health Perspect.* 1973, **5**, 171-175.
7. Firestone, D. *Environ. Health Perspect.* 1973, **5**, 59-66.
8. *IARC Monograph* 1977, **15**, 41-102.
9. Huff, J. E. et al *Cell Biol. Toxicol.* 1991, **7**(1), 67-94.
10. Zeise, L. et al *Adv. Mod. Environ. Toxicol.* 1990, **17**, 293-342

H38 hexachloroethane

Cl_3CCCl_3

C_2Cl_6 **Mol. Wt.** 236.74 **CAS Registry No.** 67-72-1

Synonyms carbon hexachloride; Distopan; Egitol; Fasciolin; Phenohep

EINECS No. 200-666-4 **RTECS No.** KI 4025000

Uses Polymerisation catalyst. Component of fluxes. Lubricating oil additive. Solvent. Moth repellent, anthelmintic and fungicide. To generate smoke from candles and grenades. Degassing agent for magnesium.

Physical properties

M. Pt. 190-195°C (sublimes) (99% purity) **Specific gravity** 2.091 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 4.19 (1) **Volatility** v.p. 1.0 mmHg at 32.7°C
Solubility Water: 50 mg l^{-1} at 22.3°C. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 1 ppm (9.8 mg m^{-3})
FR-VME 1 ppm **FR-VLE** 10 ppm
UK-LTEL 5 ppm (49 mg m^{-3}) (vapour); 10 mg m^{-3} (total inhalable dust); 4 mg m^{-3} (respirable dust)
US-TWA 1 ppm (9.7 mg m^{-3})

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 1.4 mg l^{-1} flow-through bioassay (2).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 0.21-0.34 ppm, Microtox test (3).

Bioaccumulation
Bioconcentration factor for bluegill sunfish and rainbow trout 140-510 (4,5).

Environmental fate

Nitrification inhibition
IC_{50} (25 day) *Nitrosomonas* 32 mg l^{-1} (2).

Anaerobic effects
IC_{50} (50 day) methanogenic bacterial culture 22 mg l^{-1} (2).
27% inhibition of anaerobic digestion at 10 mg l^{-1}, 86% inhibition at 50 mg l^{-1} (5 hr) (6).

Degradation studies
<30% biodegradation after 2 wk incubation at 100 mg l^{-1} in activated sludge under aerobic conditions (7).

Abiotic removal
$t_{1/2}$ for volatilisation from model river water 15 hr (8).

Adsorption and retention
Calculated K_{oc} 173-960 indicate that hexachloroethane is likely to adsorb moderately to soil and sediments (8,9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, guinea pig 4450, 5000 mg kg^{-1}, respectively (10).
LD_{50} dermal rabbit 32000 mg kg^{-1} (10).
LD_{50} intraperitoneal rat, mouse 2900-4500 mg kg^{-1}, respectively (10,11).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence of carcinogenicity to animals, IARC classification group 3 (12).

National Toxicology Program tested rats via gavage. Clear evidence of carcinogenicity in ♂ and ♀ rats (increased incidence of malignant neoplasms, increased combination of malignant and benign neoplasms, or marked increase of benign neoplasms with indication of progress to malignancy) (13).

National Toxicology Program tested rats and mice via gavage. Positive results reported in ♂ and ♀ mice, negative results in ♂ and ♀ rats (14).

Metabolism and toxicokinetics

Following oral administration to mammals, hexachloroethane is absorbed and appears rapidly in the systemic circulation. It is widely distributed throughout the body, the highest concentrations being found in the fat, the lowest in muscle (15).

In sheep a small proportion of the dose was excreted in the bile. Pentachloroethane and tetrachloroethylene were formed in sheep liver *in vitro* (15).

When 500 mg kg^{-1} ^{14}C-hexachloroethane was fed to rabbits only 5% of the radioactivity was excreted in the urine after 3 days. Urinary metabolites were di- and trichloroethanol, mono-, di- and trichloroacetic acid and oxalic acid. 14-24% of the dose was exhaled unchanged, as carbon dioxide, tetrachloroethylene, or 1,1,2,2-tetrachloroethane. The remainder was retained in the carcass (16).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (17).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (18).

Aspergillus nidulans gene mutation, mitotic crossing over, chromosome malsegregation and aneuploidy negative (19).

In vitro Chinese hamster ovary cells, sister chromatid exchanges with metabolic activation positive, chromosome aberrations with and without metabolic activation negative (20).

Other effects

Other adverse effects (human)

Eye irritation and photophobia have been reported as a result of industrial exposure to the vapour (21).

Any other adverse effects

Hexachloroethane depresses the central nervous system and causes hepatic dysfunction and damage (15,22).

Oral rat, single dose of 2500 mg kg^{-1} reduced the activity of hepatic microsomal mono-oxygenase activity by 50% (23).

Legislation

Organic solvents and pesticides are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (24).

Partition coefficient exceeds European Union recommended limit of 3.0.

Other comments

Residues have been detected in trade effluents, river water, drinking water and in fishes (25,26).

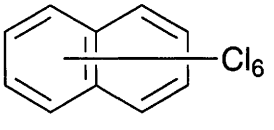
Physical properties, use, occurrence, environmental fate, analysis, carcinogenicity and mammalian toxicity reviewed (25,26,27,28).

References

1. McCoy, G. D. et al *Carcinogenesis (London)* 1990, **11**(7), 1111-1117.

2. Blum, D. J. W. et al *Res. J. Water Pollut. Control Fed.* 1991, **63**(3), 198-207.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Oliver, B. G. et al *Environ. Sci. Technol.* 1983, **17**, 287-291.
5. Barrows, M. E. et al *Dyn. Exp. Hazard Assess. Toxic Chem.* 1980, 379-392, Ann Arbor Science, MI, USA.
6. Johnson, L. D. et al *J. Water Pollut. Control Fed.* 1983, **55**, 1441-1449.
7. Kawasaki, M. *Ecotoxicol. Environ. Saf.* 1980, **4**, 444-454.
8. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
9. Sabhjic, A. *J. Agric. Food. Chem.* 1984, **32**, 243-246.
10. *Am. Ind. Hyg. Assoc. J.* 1979, **40**, 187.
11. Baganz, H. et al *Arzneim.-Forsch.* 1961, **11**, 902-905.
12. *IARC Monographs* 1987, **Suppl. 7**, 64.
13. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-361, NIEHS, Research Triangle Park, NC, USA.
14. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-068, NIEHS, Research Triangle Park, NC, USA.
15. Fowler, J. S. K. *Br. J. Pharmacol.* 1969, **35**, 530-542.
16. Jorndoff, W. R. et al *Biochem. J.* 1957, **65**, 14-15P.
17. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1834, Sigma-Aldrich, Milwaukee, WI, USA.
18. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
19. Crebelli, R. et al *Proc. ICMR Semin.* 1988, **8**, 437-442.
20. Galloway, S. M. et al *Environ. Mol. Mutagen.* 1987, **10**(Suppl. 10), 1-175.
21. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
22. Bywater, H. E. *Vet. Rec.* 1955, **67**, 382.
23. Vainio, H. et al *Xenobiotica* 1976, **6**, 599-604.
24. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
25. *IARC Monograph* 1979, **20**, 467-476.
26. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1989, **1**, 370-376, Lewis Publishers, Chelsea, MI, USA.
27. USEPA *Report* 1987, EPA/600/8-88/043.
28. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H39 hexachloronaphthalene



$C_{10}H_2Cl_6$ **Mol. Wt.** 334.84 **CAS Registry No.** 1335-87-1

Synonyms Halowax

EINECS No. 215-641-3 **RTECS No.** QJ 7350000

Uses Lubricant. Electrical insulating material. Surface coating.

Physical properties

M. Pt. 137°C **B. Pt.** 344-388°C **Specific gravity** 1.78 at 20°C **Volatility** v.p. <1.0 mmHg at 20°C ; v.den. 11.6
Solubility Organic solvents: diethyl ether

Occupational exposure

FR-VME 0.2 mg m^{-3}
SE-LEVL 0.2 mg m^{-3} **SE-STEL** 0.6 mg m^{-3}
US-TWA 0.2 mg m^{-3}

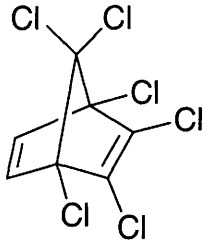
Other comments

Residues have been detected in sediments and in fish (1,2).
Reviews no human health effects, experimental toxicology, physico-chemical properties listed (3).

References

1. Jaena, K. et al *Chemosphere* 1990, **21**(12), 1371-1379.
2. Koistinan, J. et al *Chemosphere* 1988, **19**(1-6), 527-530.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H40 1,2,3,4,7,7′-hexachloronorbornadiene



$C_7H_2Cl_6$ **Mol. Wt.** 298.81 **CAS Registry No.** 3389-71-7

Synonyms 1,2,3,4,7,7′-hexachlorobicyçlo[2.2.1]hepta-2,5-diene; C601

EINECS No. 222-220-8

Uses In preparation of endrin and isodrin.

Physical properties

Partition coefficient log P_{ow} 5.28 (1)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 188 μg l^{-1} flow-through bioassay (2).

Bioaccumulation
Bioaccumulation factor for fathead minnow 6400 (2).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (3).

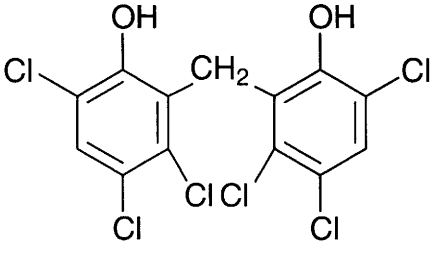
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

References

1. Schrurmann, G. et al *Chemosphere* 1988, **17**(8), 1551-1574.
2. Spehar, R. L. et al *Bull. Environ. Contam. Toxicol.* 1979, **21**, 576-583.
3. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H41 hexachlorophene



$C_{13}H_6Cl_6O_2$ **Mol. Wt.** 406.91 **CAS Registry No.** 70-30-4

Synonyms 2,2′-methylenebis(3,4,6-trichlorophenol); HCP; 3,3′,4,4′,6,6′-hexachloro-2,2′-methylenediphenol; bis(2-hydroxy-3,5,6-trichlorophenyl)methane; 2,2′-dihydroxy-3,3′,5,5′,6,6′-hexachlorophenylmethane; hexachlorophane; hexophene; trichlorophene; Dermadex; Gamophene; Turgex; Nabac

EINECS No. 200-733-8 **RTECS No.** SM 0700000

Uses Antiseptic, used in manufacture of germicidal soaps. Veterinary anthelminthic.

Physical properties

M. Pt. 163-165°C **Partition coefficient** log P_{ow} 7.54 (1)
Solubility Organic solvents: acetone, benzene, chloroform, cotton seed oil, diethyl ether, ethanol, olive oil, polypropylene glycol

Occupational exposure

UN No. 2875 **HAZCHEM Code** 1Z **Conveyance classification** toxic substance
Supply classification toxic, dangerous for the environment
Risk phrases Toxic in contact with skin and if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – When using do not eat or drink – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S20, S37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 100 μg l^{-1} (2).

Bioaccumulation
Estimated bioaccumulation factor of 317,000 indicates that environmental accumulation would be significant (3). Bioconcentration factor for mosquito fish 280, and for *Physa* species 970 (4).

Environmental fate

Degradation studies

~70% removal from wastewater containing up to 30 μg l^{-1} by sewage treatment plant (5).

Abiotic removal

Reaction with photochemically produced hydroxyl radicals in the atmosphere estimated $t_{1/2}$ 2.47 days (6).
73-95% removal from waste waters by coagulation with bentonite clays at doses of 100-400 mg l^{-1} (7).

Adsorption and retention

Estimated K_{oc} of 300,000 indicates that hexachlorophene will adsorb strongly to soil and sediments (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 56, 67 mg kg^{-1}, respectively (9-11).
LC_{50} inhalation mouse, rat 290, 340 mg m^{-3}, respectively (exposure not specified) (12).
LD_{50} dermal rat, mouse 270, 1840 mg kg^{-1}, respectively (12).
LD_{50} intraperitoneal rat, mouse, 20-22 mg kg^{-1} (13,14).
LD_{50} intravenous rat 7.5 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Gavage mouse, 60 mg day^{-1} for 7 days caused an increase in the concentration of free amino acids and a reduction in the activity of alanine aminotranferase. The study indicated that this may be due to hydrolysis of muscle protein and the failure of the liver and muscle to utilise free amino acids (15).
Oral rat 400 mg kg^{-1} diet induced neurotoxic symptoms which were characterised initially by a weakness of the hind legs. This effect was reported to be partially reversible when the hexachlorophene containing diet was replaced (16,17).

Carcinogenicity and chronic effects

National Toxicology Program tested rats via feed. Designated non-carcinogenic in ♂ and ♀ rats (18).
Inhalation rat (12 month) 30 mg m^{-3} caused an increased incidence of lung tumours. These were not typical of spontaneous neoplasms in rats (19).
Dermal mouse, 1, 5 or 10 mg 2 × wk^{-1} for life. Treatment caused skin ulceration, necrosis and inflammation, and neurological symptoms. ~25% of all treated animals died within 40 wk compared with 5% of the controls. 50-65% of all treated animals died within 60 wk compared to 10% of the controls. In the treated groups lymphomas, lung adenomas, liver haemangiomas and other tumours developed in 10/50 (15 tumours), 14/50 (17 tumours), and 15/50 (19 tumours), respectively. 20/50 controls developed a total of 29 tumours. Among treated animals only 1 skin papilloma developed (20).

Teratogenicity and reproductive effects

Dermal ♂ rat, 3% solution caused reduced fertility due to inability to ejaculate (21).
Gavage rat, 500 mg kg^{-1} diet or 20-30 mg kg^{-1} day^{-1} caused some angulated ribs, cleft palate, micro- and anophthalmia and a reduction in litter size (22-24).
Subcutaneous mouse 25 mg kg^{-1} day^{-1} on days 3-8, 7-12 or 11-17 of gestation caused foetal resorptions but no malformations (25).

Metabolism and toxicokinetics

Transplacental transfer and excretion in the milk of rats occurs (22).
80-90% of oral administration to rats was recovered unchanged in the faeces within 10 days (26).
Following intraperitoneal administration 31-47% biliary excretion occurred within 24 hr and enterohepatic circulation occurred. The principal biliary metabolite was the monoglucuronide (27,28).

Irritancy

Dermal human (24 hr) 50 μg caused mild irritation (29).

Genotoxicity

Salmonella typhimurium G46 host mediated assay negative (30).
In vitro human peripheral blood lymphocytes chromosomal aberrations negative, suppression of mitosis positive (31).
In vivo mouse, dominant lethal assay negative (32).

Other effects

Other adverse effects (human)

Therapeutic use, particularly in children and in burns patients, has led to circulatory failure, body temperature fluctuations and central nervous system symptoms, including headache, twitching, convulsions and death (16).
Spongiform brain changes were observed in infants who died from over exposure (33).
Severe malformations in children of women hospital personnel exposed to hexachlorophene soap during pregnancy have been reported. Four severe and six slight malformations were observed in 82 babies born to the exposed group, compared to one slight malformation in 46 babies born to unexposed mothers. In another report, 25 severe malformations, such as eye and central nervous system defects, were reported among 460 live births among exposed mothers, compared with no severe malformations among 233 live births to unexposed mothers. Minor malformations were more frequent among the exposed group (34,35).
Asthma developed in a 43-year-old nurse after long-term exposure to hexachlorophene powder (36).

Any other adverse effects

IC_{50} sheep brain acetylcholinesterase activity 160 mg (route unspecified) (37).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (38).

Other comments

Residues have been detected in natural and waste waters. Residues have also been detected in body tissues and in human milk after use of soaps containing hexachlorophene (39).
Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (39,40).

References

1. Hansch, C. et al *Report* 1985, Medchem Project, Pomona College, Claremont, CA, USA.
2. Protic, M. et al *Aquat. Toxicol.* 1989, **14**(1), 47-64.
3. Lee, R. F. et al *Microbial Degradation of Organochlorine Compounds in Estuarine Waters and Sediments* 1979, USEPA-600/9-79-012.
4. Sanborn, J. R. *The Fate of Selected Pesticides in the Aquatic Environment* 1974, USEPA-660/3-74-025.
5. Buhler, D. R. et al *Environ. Sci. Technol.* 1973, **7**(10), 929-934.
6. *GEMS: Graphical Exposure Modeling System: Fate of Atmospheric Pollutants* 1986, USEPA Office of Toxic Substances, Washington DC, USA.
7. Gandwina, L. V. et al *Tekst. Promst. (Moscow)* 1988 (10), 50-52, (Russ.) (*Chem Abstr.* **110**, 81888k).
8. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
9. Nieminen, L. et al *Food Cosmet. Toxicol.* 1973, **11**, 635-639.
10. Gaines, T. B. et al *Toxicol. Appl. Pharmacol.* 1973, **25**, 332-343.
11. *Chin. Med. J. (Peking, 1932-1966)* 1963, **82**, 691.
12. *Gig. Sanit.* 1984, **49**(8), 25.
13. *Toxicol. Appl. Pharmacol.* 1973, **24**, 239.
14. *Zentralbl. Bakteriol. Parasitenkd. Infektionskrankh. Hyg., Abt. 1: Orig., Reihe A* 1976, **234**, 110.
15. Prasad, G. et al *Bull. Environ. Contam. Toxicol.* 1987, **38**(3), 442-448.
16. Kimbrough, R. D. *Essays Toxicol.* 1976, **7**, 99-120.
17. de Jesus, P. V. et al *Arch. Neurol.* 1973, **29**, 180-182.
18. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-040, NIEHS, Research Triangle Park, NC, USA.

19. Portyani, A. A. et al *Vopr. Onkol.* 1987, **33**(1), 62-64, (Russ.) (*Chem. Abstr.* **106**, 207337t).
20. Stenbaeck, F. *Arch. Environ. Health* 1975, **30**, 32-35.
21. Gellert, R. J. et al *Toxicol. Appl. Pharmacol.* 1978, **43**, 339-349.
22. Kennedy, G. L. et al *Toxicol. Appl. Pharmacol.* 1977, **40**, 571-576.
23. Kennedy, G. L. et al *Teratology* 1975, **12**, 83-88.
24. Oakley, G. P. et al *Teratology* 1972, **5**, 264.
25. Majumdar, S. K. et al *Proc. Pennsylvania Acad. Sci.* 1975, **49**, 110-112.
26. Bjondahl, K. et al *Food Cosmet. Toxicol.* 1976, **14**, 179-182.
27. Edelson, J. et al *Arch. Int. Pharmacodyn. Ther.* 1976, **220**, 140-147.
28. Gonlalfi, A. J. et al *Xenobiotica* 1974, 693-704.
29. *J. Soc. Cosmet. Chem.* 1974, **25**, 113.
30. Arnold, D. W. et al *Toxicol. Appl. Pharmacol.* 1975, **33**, 185.
31. Vig, B. K. et al *EMS Newslett.* 1972, **6**, 5-6.
32. Kennedy, G. L. et al *Toxicology* 1975, **5**, 159-162.
33. Powell, H. et al *J. Pediatr.* 1973, **82**, 976-981.
34. *FDA Consumer* 1978, July-August, 16.
35. Hay, A. *Nature (London)* 1978, **274**, 533-534.
36. Nagy, L. et al *Thorax* 1984, **39**, 630.
37. Prasad, G. et al *Bull. Environ. Contam. Toxicol.* 1987, **38**(1), 139-142.
38. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
39. *IARC Monograph* 1979, **20**, 241-257.
40. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H42 hexachloropropene

$$CCl_3CClCCl_2$$

C_3Cl_6 **Mol. Wt.** 248.75 **CAS Registry No.** 1888-71-7

Synonyms 1,1,2,3,3,3-hexachloro-1-propene; hexachloropropylene

EINECS No. 217-560-9 **RTECS No.** UD 0175000

Uses Solvent. Plasticiser. Hydraulic fluid.

Physical properties

B. Pt. 209-210°C **Specific gravity** 1.765 at 20°C with respect to water at 4°C
Solubility Organic solvents: carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

UN No. 2810

Ecotoxicity

Fish toxicity
5 mg l^{-1} fatal to yellow perch in 2 hr, fatal to brown trout in 24 hr. 5 mg l^{-1} caused no adverse effects to bluegill sunfish or goldfish in 24 hr (1).

Mammalian & avian toxicity

Acute data

LC_{50} (30 min) inhalation rat 425 ppm (2).

LD_{50} intraperitoneal rat 400 mg kg^{-1} (2).

Irritancy

Irritating to skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (3).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (4).

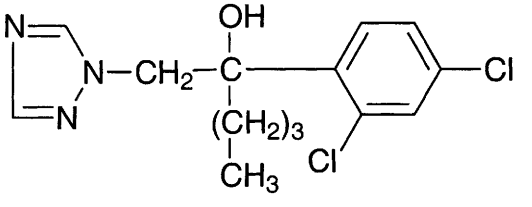
Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1984, EPA 560/6-87-002; PB 87-200-275.
2. U.S. Atomic Energy Commission *Res. Dev. Rep.* MDDC-1715, University of Rochester, New York, NY, USA.
3. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 1836, Sigma-Aldrich, Milwaukee, WI, USA.
4. Neudecker, T. et al *Mutat. Res.* 1986, **170**(1), 1-9.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.

H43 hexaconazole



$C_{14}H_{17}Cl_2N_3O$ **Mol. Wt.** 314.21 **CAS Registry No.** 79983-71-4

Synonyms (*RS*)-2-(2,4-dichlorophenyl)-1-(1*H*-1,2,4-triazol-1-yl)hexan-2-ol; (±)-α-butyl-α-(2,4-dichlorophenyl)-1*H*-1,2,4-triazole-1-ethanol; Anvil; Planete; Contaf; Recif

RTECS No. XZ 4803200

Uses Fungicide.

Physical properties

M. Pt. 111°C **Specific gravity** 1.29 at 25°C **Partition coefficient** $\log P_{ow}$ 3.9 **Volatility** v.p. 7.52×10^{-8} mmHg at 20°C

Solubility Water: 17 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, hexane, methanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, mirror carp 3.4, 5.94 mg l^{-1}, respectively (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia* sp. 2.9 mg l^{-1} (1).

LD_{50} oral, contact honey bee >0.1 mg bee^{-1} (1).

Environmental fate

Degradation studies

Rapidly degraded in soil (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >4000 mg kg^{-1} (1).

LD_{50} oral rat ♂ 2190 and ♀ 6070 mg kg^{-1} (1).

LD_{50} dermal rat >2000 mg kg^{-1} (1).

Teratogenicity and reproductive effects

In a 29-day range-finding study ♀ mice dosed at 225 mg kg^{-1} day^{-1} suffered decreased numbers of corpora lutea and decreased uterine weight (2).

♀ Mice administered 26.3 mg kg^{-} day^{-1} (the highest dose level tested) in a carcinogenicity study suffered nominally decreased numbers of cystic glands in uteri and increased numbers of hemorrhagic ovaries (3).

Metabolism and toxicokinetics

Readily excreted by mammals, with no significant retention in organs or tissues (1).

Irritancy

Dermal rabbit non-irritating and instilled into rabbit eye caused mild irritation (doses and durations unspecified) (1).

Legislation

Limited Under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maxiumum admissible concentration 0.1 μg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No.472, 1991 (5).

WHO Class Table 5 (6).

EPA Toxicity Class IV (1).

ADI 0.005 mg kg^{-1} body weight (1).

Other comments

Considered an endocrine disruptor in the female (7).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *US Environmental Protection Agency, Office of Pesticide Programs* OPP database files MRID#41142801, HED Doc#007917.
3. *US Environmental Protection Agency, Office of Pesticide Programs* OPP database files MRID#40944809, HED Doc#007917.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S.I. 1991, No.472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
7. *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* 1997, EPA/630/R-96/012, Risk Assessment Forum, US Environmental Agency, Washington, DC 20460, USA

H44 hexaethyl tetraphosphate

$$CH_3CH_2[OP(O)(OCH_2CH_3)]_3OP(=O)(OCH_2CH_3)_2$$

$C_{12}H_{30}O_{13}P_4$ **Mol. Wt.** 506.26 **CAS Registry No.** 757-58-4

Synonyms ethyl tetraphosphate; HET; HETP; tetraphosphoric acid, hexaethyl ester

EINECS No. 212-057-0 **RTECS No.** XF 1575000

Physical properties

M. Pt. –40°C **B. Pt.** 150°C (decomp.)

Occupational exposure

UN No. 1611 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, rabbit 7-56 mg kg^{-1} (1).

LD_{Lo} dermal rat 15 mg kg^{-1} (2).

LD_{50} intraperitoneal rat, mouse 2500, 6100 μg kg^{-1}, respectively (3,4).

LD_{50} intravenous rabbit, dog 690, 1300 μg kg^{-1}, respectively (1,4).

LD_{50} subcutaneous guinea pig 1500 μg kg^{-1} (2).

References

1. *Fed. Proc., Fed. Am. Soc. Exp. Biol.* 1947, **6**, 335.
2. *Acta. Pharmacol. Toxicol.* 1948, **4**, 143.
3. *JAMA, J. Am. Med. Assoc.* 1950, **144**, 104.
4. *J. Pharmacol. Exp. Ther.* 1948, **92**, 173

H45 hexafluoroacetone

$$F_3CC(O)CF_3$$

C_3F_6O **Mol. Wt.** 166.02 **CAS Registry No.** 684-16-2

Synonyms 6FK; NCI-C56440; GC 7887; 1,1,1,3,3,3-hexafluoro-2-propanone; perfluoro-2-propanone; perfluoroacetone

EINECS No. 211-676-3 **RTECS No.** UC 2450000

Physical properties

M. Pt. –129°C **B. Pt.** –26°C **Specific gravity** 1.65 at 25°C

Occupational exposure

FR-VME 0.1 ppm (0.7 mg m^{-3})

US-TWA 0.1 ppm (0.68 mg m^{-3})

UN No. 2420 **HAZCHEM Code** 4WE **Conveyance classification** toxic gas, corrosive

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 190 mg kg^{-1} (1,2).
LC_{50} (3 hr) inhalation rat 275 ppm (1,2).
TD_{Lo} dermal rat 55-100 mg kg^{-1} (3,4).

Teratogenicity and reproductive effects

Inhalation rat 0, 0.1, 1 and 12 ppm for 6 h day^{-1}, 5 day wk^{-1} for 30 or 90 days and 28 or 84 days post-exposure. At the highest concentration lower body weight gain, testicular atrophy and little or no sperm in the epididymal tubules. Regeneration of the testes was incomplete and spermatogenesis only partly restored post-exposure (5). Reproductive and teratogenic effects have been reported for rats (3,4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Reviews on experimental toxicology, human health effects and environmental fate listed (7).
Toxicology reviewed (8).

References

1. *Toxicol. Appl. Pharmacol.* 1964, **6**, 341.
2. Kennedy, G. L. et al *Toxicol. Lett.* 1991, **56**(3), 317-326.
3. *Fundam. Appl. Toxicol.* 1982, **2**, 73.
4. *Toxicol. Appl. Pharmacol.* 1977, **41**, 195.
5. Lee, K. P. et al *Toxicology* 1991, **67**(3), 249-265.
6. *S.I. 1991 No.472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
8. Kennedy, G. L. *CRC Crit. Rev. Toxicol.* 1990, **21**(2), 149-170

H46 hexafluoroethane

$$CF_3CF_3$$

C_2F_6 **Mol. Wt.** 138.01 **CAS Registry No.** 76-16-4

Synonyms F-116; R116; Freon 116; perfluoroethane

EINECS No. 200-939-8 **RTECS No.** KI 4110000

Uses Refrigerant. Aerosol propellant.

Occurrence Discharged into atmosphere from electrolytic aluminium reduction processes. Global emission rate 3.2×10^3 ton yr^{-1} (1).

Physical properties

M. Pt. –100°C **B. Pt.** –78°C

Occupational exposure

UN No. 2193 **HAZCHEM Code** 2RE **Conveyance classification** non-flammable non-toxic gas

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Change in atmospheric concentration, effect on atmospheric temperature and destruction of atmospheric ozone discussed (3).

References

1. Fabian, P. et al *J. Geophys. Res., [Atmos.]* 1987, **92**(D8), 9831-9835.
2. *S.I. 1991 No.472 The Environment Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. Yamamoto, S. *Kogai* 1988, **23**(1), 1-16, (Japan.) (*Chem. Abstr.* **109**, 134188v)

H47 1,1,1,3,3,3-hexafluoro-2-propanol

$$CF_3CH(OH)CF_3$$

$C_3H_2F_6O$ **Mol. Wt.** 168.04 **CAS Registry No.** 920-66-1

Synonyms hexafluoroisopropanol; HFIP; 2,2,2-trifluoro-1-(trifluoromethyl)ethanol; bis(trifluoromethyl)methanol

EINECS No. 213-059-4 **RTECS No.** UB 6450000

Uses Esterification reagent for the determination of aromatic acids by GLC.

Physical properties

M. Pt. –4°C **B. Pt.** 59°C **Specific gravity** 1.596

Ecotoxicity

Bioaccumulation
Confirmed to be non-accumulative or low accumulative (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 600 mg kg^{-1} (2).
LC_{Lo} (4 hr) inhalation rat 3200 ppm (3).
LD_{50} intravenous mouse 180 mg kg^{-1} (4).

Irritancy
100 mg instilled into rabbit eye caused severed erythema to slight eschar formation and severe oedema (3).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

References

1. *Bioaccumulation in Fish* 1987, Chemicals Inspection and Testing Institute, Japan.
2. *J. Med. Chem.* 1970, **13**, 1215.
3. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
4. U.S. Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Chemicals, No.03172.
5. *S.I. 1991 No.472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

H48 hexafluoropropene

$$CF_3CF{=}CF_2$$

C_3F_6 **Mol. Wt.** 150.02 **CAS Registry No.** 116-15-4

Synonyms hexafluoropropylene; perfluoropropene; perfluoropropylene; 1,1,2,3,3,3-hexafluoropropene

EINECS No. 204-127-4 **RTECS No.** UD 0350000

Physical properties

M. Pt. –156°C **B. Pt.** –29°C **Specific gravity** 1.583 at –40°C with respect to water at 4°C

Occupational exposure

UN No. 1858 **HAZCHEM Code** 2XE **Conveyance classification** non-flammable non-toxic gas

Supply classification harmful

Risk phrases Harmful by inhalation – Irritating to the respiratory system (R20, R37)

Safety phrases Keep out of reach of children (if sold to general public) – In case of fire and/or explosion do not breathe fumes (S2, S41)

Mammalian & avian toxicity

Acute data

LC_{50} (4 hr) inhalation rat 11200 mg m^{-3} (1).

LC_{50} (4 hr) inhalation mouse 750 ppm (2).

Metabolism and toxicokinetics

In vitro in presence of reduced glutathione metabolised to predominantly *S*-(1,2,3,3,3-pentafluoropropenyl)-glutathione in rat liver fraction and to *S*-(1,1,2,3,3,3-hexafluoropropyl)glutathione in rat kidney fraction. Inhalation rat (1 hr) 800 ppm resulted in biliary elimination of *S*-(1,2,3,3,3-pentafluoropropenyl)glutathione without detection of *S*-(1,1,2,3,3,3-hexafluoropropyl)glutathione. *N*-Acetyl-*S*-(1,1,2,3,3,3-hexafluoropropyl)-L-cysteine was the metabolite excreted exclusively in the urine. Metabolites formed in the liver and eliminated with bile were not translocated to the kidneys (3).

Other effects

Any other adverse effects

Nephrotoxicity may be caused by intrarenal bioactivation of the reduced glutathione-conjugate (3).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No.472, 1991 (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No.472, 1991 (4).
Regulated under US Federal Registry Toxic Substances Control Act (5).

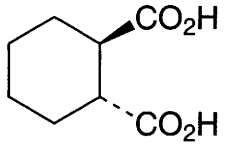
Other comments

Reviews on experimental toxicology, human health effects and physico-chemical properties listed (6). Toxicity tests for oncogenicity, chromosomal aberrations, inhalation toxicity and gene mutations given (7). Toxicology reviewed (8).

References

1. *Gig. Tr. Prof. Zabol.* 1971, **15**(2), 38.
2. *Arch. Mal. Prof. Med. Trav. Secur. Soc.* 1966, **27**, 66.
3. Koob, M. et al *Drug Metab. Dispos.* 1990, **18**(6), 911-916.
4. *S.I. 1991 No.472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *Fed. Regist.* 1989, **54**(124), 27352-27359, US EPA.
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
7. *Fed. Regist.* 1987, **52**(109), 21516-21532, US EPA.
8. Kennedy, G. L. *CRC Crit. Rev. Toxicol.* 1990, **21**(2), 149-170

H49 hexahydrophthalic acid



$C_8H_{12}O_4$ **Mol. Wt.** 172.18 **CAS Registry No.** 1687-30-5

Synonyms *trans*-1,2-cyclohexanedicarboxylic acid

EINECS No. 216-872-2

Uses Cross-linking agent.

Physical properties

M. Pt. 179-183°C

Solubility Organic solvents: benzene, diethyl ether, ethanol

Ecotoxicity

Bioaccumulation

No or low bioaccumulation level (testing based on MITI method) (1).

Other effects

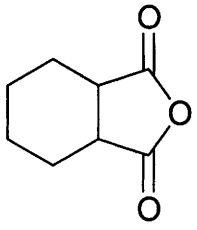
Any other adverse effects

The effect of hexahydrophthalic acid on the physical state of membrane proteins in human erythrocytes was investigated. Results produced highly significant alterations in the physical state of membrane proteins. Separate studies have shown the compound to be neurotoxic (2).

References

1. *JETOC Newsletter No. 5* 1987, 20-23, Japan Chemical Industry Ecology, Toxicology and Information Centre, Nanba Bldg. 2F, 19-4, 1-Chome, Nishishinbashi, Minato-ku, Tokyo, Japan.
2. Butterfield, D. A. et al *Biochem. Arch.* 1986, **2**(4), 245-252

H50 *cis*-hexahydrophthalic anhydride



$C_8H_{10}O_3$ **Mol. Wt.** 154.17 **CAS Registry No.** 13149-00-3

Synonyms *cis*-1,2-cyclohexanedicarboxylic anhydride; *cis*-1,3-isobenzofurandione, hydro-

EINECS No. 236-086-3

Uses Cross-linking agent. Epoxy hardener.

Physical properties

M. Pt. 32-34°C **B. Pt.** 157°C at 15 mmHg **Flash point** >110°C

Occupational exposure

Supply classification harmful

Risk phrases Risk of serious damage to eyes – May cause sensitisation by inhalation and skin contact (R41, R42/43)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour – Avoid contact with the skin – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves and eye/face protection (S2, S23, S24, S26, S37/39)

Ecotoxicity

Bioaccumulation

No or low bioaccumulation (testing based on MITI method) (1).

Mammalian & avian toxicity

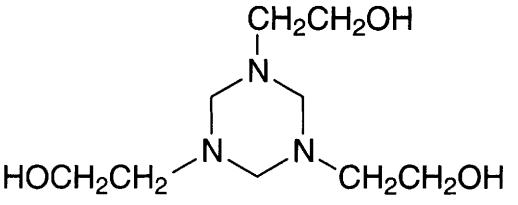
Sensitisation

Sensitising to humans at low exposure levels. Exposed workers had post-shift and next-morning urine samples analysed. Exposure levels of *cis*-hexahydrophthalic anhydride of 30-270 μg m^{-3} corresponded to urinary concentrations of 155-480 μg 1,2-cyclohexanedicarboxylic acid mmol $creatine^{-1}$, suggesting that 1,2-cyclohexanedicarboxylic acid in urine is suitable for biological monitoring of *cis*-hexahydrophthalic anhydride (2).

References

1. *JETOC Newsletter No. 5* 1987, 20-23, Japan Chemical Industry Ecology, Toxicology of Information Centre, Nanba Bldg. 2F, 19-4, 1-Chome, Nishishinbashi, Minatu-ku, Tokyo, Japan.
2. Joensson, B. et al *Int. Arch. Occup. Environ. Health* 1991, **63**(1), 77-79

H51 hexahydro-1,3,5-tris(2-hydroxyethyl)-*s*-triazine



$C_9H_{21}N_3O_3$ **Mol. Wt.** 219.28 **CAS Registry No.** 4719-04-4

Synonyms 1,3,5-triazine-1,3,5(2*H*,4*H*,6*H*)-triethanol; 1,3,5-tris(2-hydroxyethyl)hexahydro-1,3,5-triazine; Actane; Busan 1060; Grotan; Kalpur TE; Roksol T1-7; Bioban GK; Canguard 454; Triadine 3; Onyxide 200

EINECS No. 225-208-0 **RTECS No.** XZ 1600000

Uses Cutting-fluid biocide (formaldehyde releaser).

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – May cause sensitisation by skin contact (R22, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin – Wear suitable gloves (S2, S24, S37)

Ecotoxicity

Invertebrate toxicity
EC_{50} (15 min) *Photobacterium phosphoreum* 28.9 ppm Microtox test (1).

Environmental fate

Degradation studies
Closed-bottle test at 2-5 mg l^{-1} ThOD 96%. Oxygen consumption inhibition test 360 mg l^{-1} (2).

Mammalian & avian toxicity

Sensitisation
174 patients with 6 month-5 yr history of cutting-fluid dermatitis were studied. 43% showed allergic reactions which were considered to be relevant to their dermatitis. Irritant contact dermatitis occurred in 63%, but only in 21% was it thought to be the sole diagnosis. The commonest cause of allergic reactions were biocides, especially formaldehyde releasers, in a cutting fluid patch-test series (3).
In a study of 501 consecutive suspected contact dermatitis patients, three individuals (0.6%) showed a positive reaction to 1% aqueous solution in patch testing (4).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Gerike, P. et al *Chemosphere* 1990, **21**(6), 799-812.
3. Grattan, C. E. H. et al *Contact Dermatitis* 1989, **20**, 372-376.
4. de Groot, A. C. et al *Contact Dermatitis* 1986, **15**, 218-222

H52 hexamethyldisilazane

$$(H_3C)_3SiNHSi(CH_3)_3$$

$C_6H_{19}NSi_2$ **Mol. Wt.** 161.39 **CAS Registry No.** 999-97-3

Synonyms bis(trimethylsilyl)amine; hexamethylsilazane; HMDS; OAP; 1,1,1-trimethyl-*N*-(trimethylsilyl)silanamine; hexamethylsilylamine

EINECS No. 213-668-5 **RTECS No.** JM 9230000

Physical properties

B. Pt. 126°C **Specific gravity** 0.765 **Partition coefficient** 8°C

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 650 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Intraperitoneal mouse, two injections of 200-1000 mg kg^{-1} (total dose) did not cause any increase in the incidence of lung tumours (period of exposure unspecified) (1).

Other comments

Selected for general toxicology study by NTP (2).

References

1. Stoner, G. D. et al *J. Natl. Cancer Inst.* 1975, **54**(2), 495-497.
2. *Management Studies Report* 4 Feb 1992, National Toxicology Program Division of Toxicology Research and Testing, Research Triangle Park, NC, USA

H53 hexamethyldisiloxane

$$(H_3C)_3SiOSi(CH_3)_3$$

$C_6H_{18}OSi_2$ **Mol. Wt.** 162.38 **CAS Registry No.** 107-46-0

Synonyms oxybis(trimethylsilane); Dow Corning 200

EINECS No. 203-492-7 **RTECS No.** JM 9237000

Uses Reagent for the synthesis of benzoyl chlorides; to prepare silyl ethers from alcohols; as a high temperature NMR internal standard.

Physical properties

B. Pt. 101°C **Flash point** -2°C **Specific gravity** 0.764 **Volatility** v.den. 5.5

Mammalian & avian toxicity

Acute data

LD_{Lo} oral guinea pig 50 g kg^{-1} (1).

LD_{50} intraperitoneal mouse 4500 mg kg^{-1} (2).

Irritancy
500 mg applied to rabbit skin for 24 hr caused mild irritation (3).

References

1. *J. Ind. Hyg. Toxicol.* 1948, **30**, 332.
2. *Russ. Chem. Rev. (Engl. Transl.)* 1969, **38**, 975.
3. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia

H54 hexamethylenediamine

$$H_2N(CH_2)_6NH_2$$

$C_6H_{16}N_2$ **Mol. Wt.** 116.21 **CAS Registry No.** 124-09-4

Synonyms 1,6-hexanediamine; 1,6-diaminohexane; HMDA; NCI-C61405; Diamine H Extra

EINECS No. 204-679-6 **RTECS No.** MO 1180000

Uses Intermediate in nylon manufacture.

Physical properties

M. Pt. 42°C **B. Pt.** 205°C **Flash point** 81°C
Solubility Water: soluble. Organic solvents: benzene, ethanol

Occupational exposure

US-TWA 0.5 ppm (2.3 mg m^{-3})

UN No. 2280 (solid); 1783 (solution) **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Harmful in contact with skin and if swallowed – Causes burns – Irritating to the respiratory system (R21/22, R34, R37)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S26, S36/37/39, S45)

Environmental fate

Degradation studies
Degraded enzymatically by aminooxidases in *Bacillus subtilis* to non-toxic metabolites (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 750 mg kg^{-1} (2).
LC_{Lo} (10 min) inhalation mouse 750 mg m^{-3} (3).
LD_{50} dermal rabbit 1110 mg kg^{-1} (2).
LD_{50} intravenous, intraperitoneal and subcutaneous mouse 180, 320 and 1300 mg kg^{-1}, respectively (4-6).

Sub-acute and sub-chronic data
♂ and ♀ rats were exposed to 0, 12.8 or 51 mg m^{-3}, 6 hr day^{-1}, 5 days wk^{-1} for 13 wk. Exposure to 215 mg m^{-3} was terminated at 7 wk because of high mortality. Significantly reduced weight gain and slight haemopoietic

stimulation of peripheral blood parameters occurred at 215 mg m^{-3}, in addition to microscopic lesions of the respiratory tract. The no-effect level was 12.8 mg m^{-3} (7).
Modest retardation in weight gain was the only observed effect of dietary administration of 150 or 500 mg kg^{-1} for 3 months (8).

Teratogenicity and reproductive effects
Administration by gavage to rats on days 6-15 of pregnancy at 0, 112, 184 and 300 mg kg^{-1} day^{-1} did not indicate teratogenicity. Maternal toxicity occurred at 300 mg kg^{-1}, embryotoxicity at 184 and 300 mg kg^{-1}, but no treatment-related effects were reported at 112 mg kg^{-1} (8).
Slightly reduced litter size and weight gain of pups and dams reported in a two generation study on rats fed 500 mg kg^{-1} day^{-1} (9).

Metabolism and toxicokinetics
Hexamethylenediamine and 1,6-diaminohexanoic acid were identified in the urine of human volunteers after oral administration. Excretion was rapid and completed within 10 hr (10).
Metabolism to 1,6-diaminohexanoic acid is via 3,4, 5,6-tetrahydro-2*H*-azepine by mammalian liver aldehyde oxidase activity (11).

Irritancy
Respiratory and conjunctival irritation reported in rats exposed to 51 or 215 mg m^{-3}, 6 hr day^{-1}, 5 days wk^{-1} for 13 wk (7).

References

1. Gvozdyak, P. I. et al *Khim. Tekhnol. Vody* 1987, **9**(2), 172-173.
2. *Toxicol. Appl. Pharmacol.* 1977, **42**, 417.
3. Progress Report NDCrc-132, Sep 1942, Nat. Def. Res. Cttee., Off. Sci. Res. Dev.
4. *Hyg. Sanit. (USSR)* 1978, **43**(11), 110.
5. Izmerov, N. F. et al *Toxicometric Properties of Industrial Toxic Chemicals Under Single Exposure* 1982, CIP, Moscow, USSR.
6. NX 02313 U.S. Army Armament Res. Dev. Command, Chem. Sys. Lab., NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD 21010, USA.
7. Johannsen, F. R. et al *Fundam. Appl. Toxicol.* 1987, **9**(3), 504-511.
8. Johannsen, F. R. et al *J. Appl. Toxicol.* 1987, **7**(4), 259-63.
9. Johannsen, F. R. et al *Fundam. Appl. Toxicol.* 1991, **16**(3), 490-494.
10. Brorson, T. et al *Int. Arch. Occup. Environ. Health* 1990, **62**(1), 79-84.
11. Subramanyam, B. et al *Xenobiotica* 1989, **19**(1), 33-42

H55 hexamethylene diisocyanate

$$OCN(CH_2)_6NCO$$

$C_8H_{12}N_2O_2$ **Mol. Wt.** 168.20 **CAS Registry No.** 822-06-0

Synonyms 1,6-diisocyanatohexane; hexane 1,6-diisocyanate; HMDI; isocyanic acid, hexamethylene ester; Tolonate

EINECS No. 212-485-8 **RTECS No.** MO 1740000

Uses Cross-linking agent or hardener in production of polyurethane materials.

Physical properties

B. Pt. 255°C **Flash point** 140°C **Specific gravity** 1.05 at 25°C **Volatility** v.p. 0.05 mmHg at 25°C ; v.den. 6.0

Occupational exposure

DE-MAK 0.005 ppm (0.035 mg m^{-3})
FR-VME 0.01 ppm (0.1 mg m^{-3}) **FR-VLE** 0.02 ppm (0.2 mg m^{-3})
JP-OEL 0.005 ppm (0.034 mg m^{-3})
SE-LEVL 0.005 ppm (0.03 mg m^{-3}) **SE-CEIL** 0.01 ppm (0.07 mg m^{-3})
UK-LTEL MEL 0.02 mg m^{-3} (as NCO) **UK-STEL** MEL 0.07 mg m^{-3} (as NCO)
US-TWA 0.005 ppm (0.034 mg m^{-3})

UN No. 2281 **HAZCHEM Code** 3X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by inhalation and skin contact (R23, R36/37/38, R42/43)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S28, S38, S45)

Ecotoxicity

Fish toxicity
Not expected to result in significant toxicity to aquatic species, owing to high reactivity with water (1).

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 15.7 ppm Microtox test (2).

Bioaccumulation
Unlikely to bioaccumulate in aquatic or terrestrial organisms, owing to high reactivity with water (1).

Environmental fate

Abiotic removal
Isocyanates typically have aqueous $t_{1/2}$ <10 min (1).
Estimated atmospheric $t_{1/2}$ for photoxidation 2 days (1).
Readily degrades by reaction with water when released onto soil or water, hence leaching from soil is not a concern (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 738 mg kg^{-1} (4).
LC_{Lo} (4 hr) inhalation rat 60 mg m^{-3} (5).
LC_{Lo} (10 min) inhalation mouse 1570 mg m^{-3} (6).
LD_{50} dermal rabbit 593 mg kg^{-1} (4).
LD_{50} intravenous mouse 5600 μg kg^{-1} (7).

Carcinogenicity and chronic effects
Not classifiable (group D) because of lack of human and animal data (8).
Increased incidence of tumours reported for other diisocyanates, which are currently under review by EPA (1).

Metabolism and toxicokinetics
Five ♂ humans were exposed to an average air concentration of 25 μg m^{-3} (inhaled dose 100 μg) for 7.5 hr in a test chamber. 11-21% of the dose was excreted as 1,6-hexamethylenediamine (HDA) during 28 hr. Urinary elimination was rapid; $t_{1/2}$ for HDA concentration was 1.2 hr. No specific IgE or IgG antibodies to hexamethylene diisocyanate were detected, nor were spirometry or bronchial activity changed (9).
Excretion, probably involving deamination, is via urine; urinary $t_{1/2}$ 1.2 hr (9).

Irritancy

Severe eye irritant and lachrymator in humans; conjunctivitis, glaucoma, keratitis and corneal damage reported (1).

Severe skin irritant in animal studies (species and dose unspecified) and dermatitis reported in humans (10). Reacts with skin proteins to produce a tanning effect, but dermal absorption appears to be low (1).

Sensitisation

High titres of hexamethylene diisocyanate-specific IgG antibodies found in serum of a car painter who experienced a hypersensitivity pneumonitis-like disease after exposure to two-component acrylic lacquers with hexamethylene diisocyanate as the curing agent (11).

No specific IgG or IgE antibodies reported in humans exposed to 25 μg m^{-3} for 7.5 hr (estimated total inhaled dose 100 μg) (9).

Genotoxicity

Salmonella typhimurium TA98, TA100 and TA1537 with and without metabolic activation negative (12).

Decreased induced mutation frequency in *Escherichia coli* (13).

Inhibited growth of Ehrlich ascites tumour cells in ♀ mice (14).

Other effects

Other adverse effects (human)

Spirometry in car painters did not differ from controls, but closing volume in relation to vital capacity was increased in painters, suggesting small-airway disease. The painters were exposed to hexamethylene diisocyanate and biuret-modified hexamethylene diisocyanate (8).

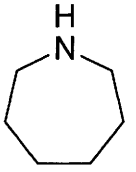
Productive cough, dyspnoea, impaired lung function and sensitisation reported in exposed workers (15).

Primarily affects the respiratory system, although acetylcholinesterase activity inhibition has been reported (16), and primary effects are local rather than systemic, owing to its reactivity with biological macromolecules (17).

References

1. *J. Appl. Toxicol.* 1993, **13**(6), 435-439.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Kirk Othmer *Encyclopedia of Chemical Technology* 3rd ed., New York, NY, USA.
4. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
5. *Hyg. Sanit. (USSR)* 1968, **12**(10), 40.
6. Progress Report NDCrc-132, Aug. 1942, Off. Sci. Res. Dev., Nat. Def. Res. Cttee.
7. NX07805 US Army Armament Res. Dev. Command, Chem. Sys. Lab. NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA.
8. Alexandersson, R. et al *Arch. Environ. Health* 1987, **42**(6), 367-373.
9. *IRIS, Integrated Risk Information Systems* 1993, EPA, Washington, DC, USA.
10. Brorson, T. et al *Int. Arch. Occup. Environ. Health* 1990, **62**(5), 385-389.
11. *Material Safety Data Sheet* 1991, Rhone-Poulenc, Princeton, NJ, USA.
12. Selden, A. et al *Scand. J. Work, Environ. Health* 1989, **15**(3), 234-237.
13. Anderson, M. et al *Scand. J. Work, Environ. Health* 1980, **6**, 221-226.
14. Kawazoe, Y. et al *Chem. Pharm. Bull.* 1981, **29**, 2631-2638.
15. Moos, G. E. et al *Cancer Res.* 1971, **31**, 937-941.
16. Cockcroft, D. W. et al *J. Can. Med. Assoc.* 1979, **121**, 602-604.
17. Dewair, M. *J. Occup. Med.* 1983, **25**, 279-282

H56 hexamethyleneimine



$C_6H_{13}N$ **Mol. Wt.** 99.18 **CAS Registry No.** 111-49-9

Synonyms azacycloheptane; cyclohexamethylenimine; hexahydroazepine; homopiperdine; perhydroazepine

EINECS No. 203-875-9 **RTECS No.** CM 3150000

Physical properties

B. Pt. 138°C at 749 mmHg **Flash point** 18°C **Specific gravity** 0.880 at 25°C
Solubility Water: soluble. Organic solvents: ethanol, ether

Occupational exposure

UN No. 2493 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, corrosive

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 410 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 4800 ppm (2).
LC_{50} (2 hr) inhalation mouse 10,800 mg m^{-3} (3).
LD_{Lo} dermal mouse 550 mg kg^{-1} (4).

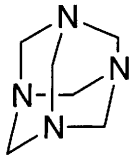
Other comments

Biodegradation reviewed (5).

References

1. *Gig. Tr. Prof. Zabol.* 1974, **18**(2), 29.
2. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
3. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure* 1982, CIP, Moscow, USSR.
4. *Arch. Exp. Pathol. Pharmakol.* 1903, **50**, 199.
5. Farago, C. et al *Rev. Chim. (Bucharest)* 1989, **40**(2), 166-170

H57 hexamethylenetetramine



$C_6H_{12}N_4$ **Mol. Wt.** 140.19 **CAS Registry No.** 100-97-0

Synonyms hexamine; ammonioformaldehyde; formamine; methenamine; HMT; hexamethylenamine; Aminoform

EINECS No. 202-905-8 **RTECS No.** MN 4725000

Uses As an antibacterial agent in treating human and veterinary urinary infections. In adhesives, coatings and sealing compounds. Used in preservation of hides and chemical detection of metals. Corrosion inhibitor in steel, dye fixative, oil stabiliser. Used as cross-linking agent for hardening phenol-formaldehyde resin and vulcanising rubber, in explosives manufacture and as fuel for camping stoves.

Physical properties

M. Pt. 280°C (sublimes) **Flash point** 250°C **Specific gravity** 1.33 at –5°C
Solubility Water: 0.66 g l^{-1}. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

SE-LEVL 3 mg m^{-3} **SE-STEL** 5 mg m^{-3}

UN No. 1328 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid
Supply classification highly flammable
Supply classification harmful
Risk phrases Highly flammable – May cause sensitisation by inhalation and skin contact (R11, R42/43)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Do not breathe dust – Avoid contact with the skin – Wear suitable gloves (S2, S16, S22, S24, S37)

Environmental fate

Nitrification inhibition
No inhibition of ammonia oxidation by *Pseudomonas* sp. at 100 mg l^{-1}(1).

Degradation studies
Completely degraded in the activated sludge process (2).
BOD_5 0.015 mg $l^{-1}O_2$;0.026 mg $l^{-1}O_2$ in normal sewage diluted by the standard technique (3).

Abiotic removal
Hydrolysed by acids to release formaldehyde.

Mammalian & avian toxicity

Acute data
LD_{Lo} oral mouse 512 mg kg^{-1} (4).
LD_{50} subcutaneous mouse 215 mg kg^{-1} (5).
LD_{50} intravenous rat 9200 mg kg^{-1} (6).

Sub-acute and sub-chronic data
Oral rat 400 mg day^{-1} for 90 or 333 days by gavage showed no adverse effects (7).

♀ cat fed 1250 mg kg^{-1} day^{-1} for 2 years died of pyogenic infection of the nasal cavity and paranasal sinuses in month 23. No effects were observed on weight gain, food consumption or tissue morphology (8).
Man 8 g day^{-1} for 3-4 wk caused bladder irritation, painful and frequent micturition, albuminuria and haematuria (9).

Carcinogenicity and chronic effects
CTM, C_3 Hf/Dp and SWR/Dp mice 19% in drinking water for 60 wk;CTM mice 0.5% for 60 wk and 5% for 30 wk; Wister rats 1% for 104 wk or 5% for 2 wk. No carcinogenic activity observed throughout remaining lifetime correlated to hexamine administration (10).
30 ♂ and 30 ♀ NHRI/Han albino mice 0 and 1% for 2 yr in feed. Benign and malignant tumours were found in 31 animals, 20 in treated and 11 in controls. All tumours occurred in ♀ except 1 control and 2 treated ♂. Malignant tumours were mainly subcutaneous carcinomas and adenocarcinomas (8).

Teratogenicity and reproductive effects
♂, ♀ rats 0, 400, 800, 1600 mg kg^{-1} for 2 yr in feed were mated at 20, 28 and 35 wk. No effects observed on body growth, survival, reproduction or viability of offspring (8).
2 ♂ and 4 ♀ mongrel dogs were fed 125-1875 mg kg^{-1} day^{-1} for 32 months. 3 ♂ and 2 ♀ from litters of the original dogs were fed 1250 mg kg^{-1} day^{-1}. After the test period, treated dogs were fed a normal diet. No effect was seen on food consumption, growth, reproduction or litter numbers and weights. 20/30 litters were unusual, containing stillborn, eaten and defective animals (8).

Metabolism and toxicokinetics
Hexamine is readily absorbed from the human gastro-intestinal tract and widely distributed in the body. 10-30% may be hydrolysed under acid conditions in the stomach to ammonia and formaldehyde, but is otherwise inactive in the body and is eliminated in the urine (11).

Sensitisation
32 ethylenediamine-sensitive patients tested for cross-sensitivity reacted positively to a 0.1% solution of hexamine (12).

Other effects

Any other adverse effects
Therapeutically important in eukaryotic cells as under acid conditions, hexamine inhibits the proliferation of L5178Y cells and decreases the cell volume and size of the nucleus (13).

References

1. Hockenbury, M. K. *J. Water Pollut. Control Fed.* 1977, May.
2. Smith, A et al *Chemosphere* 1987, **16**(7), 1555-1556.
3. Swope, H. G. *Sewage Ind. Waste Eng.* 1950, **21**, 467.
4. *NTIS Report* AD-A066-307, Natl. Tech. Inf. Ser., Springfield, VA, USA.
5. *Naunyn-Schmiedebergs Arch. Exp. Pathol. Pharmakol.* 1955, **225**, 428.
6. *Naunyn-Schmiedebergs Arch. Exp. Pathol. Pharmakol.* 1954, **221**, 166.
7. Brendal, R. *Arzneim.-Forsch.* 1964, **14**, 51.
8. Restani, P. et al *Crit. Rev. Toxicol.* 1991, **21**(5), 315-328.
9. Goodman, L. S. et al *The Pharmacological Basis of Therapeutics* 2nd ed., 1955, MacMillan, New York, NY, USA.
10. Della Porta, G. et al *Food Cosmet. Toxicol.* 1968, **6**, 707.
11. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
12. Balato, N. et al *Contact Dermatitis* 1986, **15**, 263-265.
13. Reitz, M. et al *Arzneim.-Forsch.* 1989, **39**(11), 1411-1412

H58 hexamethylphosphoramide

$$O=P[N(CH_3)_2]_3$$

$C_6H_{18}N_3OP$ **Mol. Wt.** 179.20 **CAS Registry No.** 680-31-9

Synonyms hexamethylphosphoric triamide; hexametapol; Hempa; HMPA; ENT 50882

EINECS No. 211-653-8 **RTECS No.** TD 0875000

Uses Solvent in organic synthesis, deicing additive for jet fuel, insect chemosterilant and chemical mutagen.

Physical properties

M. Pt. 7°C **B. Pt.** 230-232°C at 740 mmHg **Flash point** 105°C **Specific gravity** 1.024 at 25°C with respect to water at 25°C **Volatility** v.p. 0.03 mmHg at 20°C ; v.den. 6.18

Solubility Water: miscible

Occupational exposure

Supply classification toxic

Risk phrases May cause cancer – May cause heritable genetic damage (R45, R46)

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)

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, quail 100-1000 mg kg^{-1} (1).

LD_{50} oral ♂, ♀ rat 2650-3360 mg kg^{-1} (2).

LD_{50} oral guinea pig 1600 mg kg^{-1} (3).

LD_{50} dermal guinea pig, rabbit 1175, 2600 mg kg^{-1}, respectively (3,4).

LD_{50} intravenous, intraperitoneal mouse 800 1600 mg kg^{-1}, respectively (5,6).

Sub-acute and sub-chronic data

Oral rats (90 days) were administered 10-1000 ppm hexamethylphosphoramide (HMPA) day^{-1} in drinking water or 15-120 mg kg^{-1} day^{-1} by gavage or 40 mg kg^{-1} day^{-1} subcutaneously. Some rats receiving 10 ppm in their drinking water had tracheas lined with regenerated epithelium. No effects were observed in any other tissues. Increasingly severe nasal lesions were seen and tracheas showed regenerated epithelium and focal epithelial denudation of bronchi at dose levels of 100, 300 and 1000 ppm. An increase in the number of foamy alveolar macrophages was seen in the lungs at 300 and 1000 ppm. Rats dosed by gavage suffered nasal lesions that were identical to but slightly more severe than those seen in rats given HMPA in drinking water. Rats administered 40 mg kg^{-1} day^{-1} subcutaneously had slightly less severe nasal lesions than did rats given the same dose by gavage (7).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (8).

Rats exposed to 50, 100, 400 or 4000 ppb for 6-24 months developed nasal tumours and squamous metaplasia with inflammation in the nasal epithelium; no changes were observed at 10 ppb (9).

A low incidence of tumours, mainly reticulum-cell sarcomas or lymphosarcomas, observed in rats fed diets containing 0.78-6.25 mg kg^{-1} day^{-1} for 2 years (10).

Teratogenicity and reproductive effects

Rats receiving six consecutive oral daily doses of 500 mg kg^{-1} remained sterile for 23 wk (11).

No abnormalities reported in offspring of rats given daily doses of 200 mg kg^{-1} during days 7-20 of pregnancy (12).

Testicular atrophy occurred in rats receiving 1000 ppm in drinking water daily for 90 days and was present in rats receiving 120 mg kg^{-1} day^{-1} by gavage for 90 days (7).

Metabolism and toxicokinetics

Transformed to formaldehyde via oxidative metabolism *in vitro* and *in vivo* (13).

70% of an intraperitoneal dose to rats and mice was excreted within 20 hr (14).

Undergoes a sequence of *N*-demethylation reactions in rats and mice to pentamethylphosphoramide; *N*′,*N*′,*N*″,*N*″- tetramethylphosphoramide; and *N*′,*N*″,*N*‴- trimethylphosphoramide. *In vitro* studies with rat liver slices indicated oxidative demethylation, with simultaneous formation of formaldehyde (13).

Genotoxicity

Salmonella typhimurium (plate incorporation and preincubation assays) with and without metabolic activation negative (15).

Salmonella thyphimurium (suspension assay) with metabolic activation positive (15).

Induced aneuploidy and point mutation in *Saccharomyces cerevisiae* with or without metabolic activation (16).

Induced unscheduled DNA synthesis in HeLa cells with or without metabolic activation (17).

Induced chromosomal aberrations in human lymphocytes *in vitro* with or without metabolic activation. Increased incidence of polychromatic erythrocytes in mouse micronucleus assay (18).

References

1. Schafer, E.W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. Garnes, T. B. *Toxicol. Appl. Pharmacol.* 1969, **14**, 515.
3. Labrecque, G. C. et al (Eds.) *Principles of Insect Chemosterilization* 1968, Appleton-Century-Crofts, New York, NY, USA.
4. *Toxicol. Appl. Pharmacol.* 1971, **18**, 499.
5. *Chem. Ind. (London)* 1966, (36), 1529.
6. *Prog. Mutat. Res.* 1981, **1**, 682.
7. Keller, D. A. et al *Fundament. Appl. Toxicol.* 1997, **40**(1), 15-29.
8. *IARC Monograph* 1977, **15**, 211.
9. Lee, K. P. et al *Am. J. Pathol.* 1982, **106**(1), 8-19.
10. Kimbrough, R. D. et al *Bull. Environ. Contam. Toxicol.* 1973, **10**, 225-226.
11. Jackson, H. et al *J. Reprod. Fertil.* 1969, **20**, 263-269.
12. Shott, L. D. et al *Toxicol. Appl. Pharmacol.* 1971, **18**, 499-506.
13. Jones, A. R. et al *Biochem. Pharmacol.* 1968, **17**, 2247-2252.
14. Jackson, H. et al *Nature (London)* 1966, **212**, 86-87.
15. Sarrif, A. M. et al *Mutat. Res.* 1997, **380**(1,2), 167-177.
16. Parry, J. M. et al *Prog. Mutat. Res.* 1985, **5**, 285-295.
17. Martin, C. N. et al *Prog. Mutat. Res.* 1985, **5**, 375-379.
18. Ashby, J. et al *Mutat. Res.* 1985, **156**, 19-32

H59 hexanal

$$CH_3(CH_2)_4CHO$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 66-25-1

Synonyms caproic aldehyde; caproaldehyde; hexaldehyde

EINECS No. 200-624-5 **RTECS No.** MN 7175000

Occurrence Soil, water and air pollutant. In food aromas and flavours. Biomarker of diatoms and green algae (1).

Lipid peroxidation product of microsomal membranes (2).

Detected as contaminant in drinking water.

Physical properties

M. Pt. –56.3°C **B. Pt.** 128.7°C **Flash point** 32°C (open cup) **Specific gravity** 0.8335 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.78
Solubility Organic solvents: ethanol, propylene glycol, fixed oils

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 0.724 g l^{-1} (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4890 mg kg^{-1} (4).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (4).

Sub-acute and sub-chronic data
Up to 1000 mg ml^{-1} administered to rats via drinking water (duration unspecified) had no overt toxic effect and no changes in growth rate or haematological parameters were observed. Mild treatment-related morphologic changes (tissues unspecified) were observed in high-dose groups, but these could not be related to any functional changes. Reduced lactate dehydrogenase activity was noted in female rats (5).

Metabolism and toxicokinetics
Hexanal produced by lipid peroxidation of microsomal membranes was metabolised *in vitro* by purified Sprague-Dawley rat hepatic microsomal aldehyde dehydrogenase (2).
Metabolism of hexanal by cytosolic and microsomal fractions of rainbow trout liver with NAD^+ as a cofactor was indicated by high levels of aldehyde dehydrogenase activity (6).

Irritancy
Dermal rabbit (24 hr) 10 mg caused mild irritation (4).
100 mg instilled into rabbit eye (24 hr) caused mild irritation (7).

Genotoxicity

Salmonella typhimurium TA1531 with metabolic activation weakly positive (8).
In vitro Chinese hamster V79 lung cells were tested at the hypoxanthine-guanine phosphoribosyltransferase locus, as indicated by resistance to 6-thioguanine or at the Na/K ATPase locus as resistance to oubain. A dose-dependent increase in frequency of 6-thioguanine and oubain resistant mutants at 0.3-3 g l^{-1} concentrations was observed (9).
0.01 g hexanal incubated with human endothelial cells in Earl's solution caused no cytotoxicity (10).
Hexanal produced by lipid oxidation with linoleic acid at 37°C caused plasmid DNA damage (concentration unspecified) (11).

Other effects

Other adverse effects (human)
Humans exposed to a mixture of indoor air pollutants including hexanal for one day at concentrations up to 25 mg m^{-3} reported eye and nose irritation at 8 mg m^{-3} and significantly reduced well-being at 25 mg m^{-3} (12).

References

1. Jalliffier-Merlon, E. et al *Estuarine, Coastal Shelf Sci.* 1991, **32**(5), 463-482.
2. Mitchell, D .Y. et al *Arch. Biochem. Biophys.* 1989, **269**(1), 11-17.
3. Protic, M. et al *Aquat. Toxicol.* 1989, **14**, 47-64.
4. Smyth, H. F. et al *Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
5. Komsta, E. et al *Bull. Environ. Contam. Toxicol.* 1988, **41**(4), 515-522.
6. Parker, L. M. et al *Aquat. Toxicol.* 1990 **18**(1), 1-12.

7. *Food Cosmet. Toxicol.* 1973, **11**, 95.
8. Ono, Y. et al *Water Sci. Technol.* 1991, **23**, 329-338.
9. Brambilla, G. et al *Mutagenesis* 1989, **4**(4), 277-279.
10. Kaneko, T. et al *Chem.-Biol. Interact.* 1988, **67**(3-4), 295-304.
11. Kim, S.B. et al *Han'guk Susan Hakhoechi* 1987, **20**(5), 419-430 (Korean).
12. Molhave, L. et al *Atmos. Environ., Part A* 1991, **25A**(7), 1283-1293

H60 hexane

$$CH_3(CH_2)_4CH_3$$

C_6H_{14} **Mol. Wt.** 86.18 **CAS Registry No.** 110-54-3

Synonyms *n*-hexane

EINECS No. 203-777-6 **RTECS No.** MN 9275000

Uses Used with dye in thermometers and in determining refractive index of minerals. Industrial solvent.

Physical properties

M. Pt. −100 to −95°C **B. Pt.** 69°C **Flash point** −23 to −21°C **Specific gravity** 0.660 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 4.11 **Volatility** v.p. 100 mm Hg at 15.8°C ; v.den. 2.97
Solubility Water: 21 mg l^{-1}. Organic solvents: miscible with chloroform, ethanol, ether

Occupational exposure

DE-MAK 50 ppm (180 mg m^{-3})
FR-VME 50 ppm (170 mg m^{-3})
JP-OEL 40 ppm (140 mg m^{-3})
SE-LEVL 25 ppm (90 mg m^{-3}) **SE-STEL** 50 ppm (180 mg m^{-3})
UK-LTEL 20 ppm (72 mg m^{-3})
US-TWA 50 ppm

UN No. 1208 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful: danger of serious damage to health by prolonged exposure through inhalation (R11, R48/20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Avoid contact with skin and eyes – Do not empty into drains – Use only in well ventilated areas (S2, S9, S16, S24/25, S29, S51)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 4 mg l^{-1} (1).
LC_5, LC_{50}, LC_{95} cichlid 40-185.5 ppm at pH 7.1 and 27.8°C (duration unspecified). Exposed fish showed gill damage, respiratory distress and loss of balance (2).

Invertebrate toxicity
LC_{50} *Branchiura sowerbyi* 3290 ppm at pH 7.1 and 27.8°C (duration unspecified) (2).
LC_{50} (96 hr) *Chlorella vulgaris* 1079 mg l^{-1} (3).

Environmental fate

Degradation studies

Hydroxylated and oxidised to the corresponding alcohol, aldehyde, acid and ketone mixture by methane oxidising bacterium H-2 (type I) (4).

ThOD 3.52 mg $l^{-1}O_2$ (5).

Incubation with natural flora in groundwater in presence of other components of high octane gasoline (100 µl l^{-1}), biodegraded by 46% after 192 hr at 13°C, initial concentration 1.36 µl l^{-1} (6).

Catabolically degraded by gasoline-degrading bacteria *Pseudomonas* sp., *Nocardia* sp. and *Micrococcus* sp. (7).

Abiotic removal

Photooxidation by UV light in aqueous medium at 50°C, 50.51% degraded to carbon dioxide after 24 hr (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 28710 mg kg^{-1} (9).

LC_{Lo} inhalation mouse 120000 mg m^{-3} (10).

LD_{Lo} intraperitoneal rat 9100 mg kg^{-1} (11).

Sub-acute and sub-chronic data

$B6C3F_1$ mice 0, 500, 1000, 4000, 10,000 ppm 6 hr day^{-1}, 5 day wk^{-1} for 13 wk and at 1000 ppm for 22 hr day^{-1}, 5 day wk^{-1} for 13 wk. All mice survived. Mild exposure-related effects included weight gain depression, inflammatory, erosive and regenerative lesions in the olfactory and respiratory epithelium of the nasal cavity, decreased locomotor activity in females and paradonal axonal swelling in 10,000 ppm and 1000 ppm groups with sneezing in 10,000 ppm group and nasal lesions also in 4000 ppm group (12).

Intraperitoneal albino rats 1 ml kg^{-1} for 1, 2, 7, 45 days caused decreased hepatic protein content, increased lipid peroxidation after 24 hr, decreased hepatic drug-metabolising enzyme and glucose-6-phosphatase activity and increased phenobarbitone sleeping time (13).

Carcinogenicity and chronic effects

Calculated mean lifetime cancer risk in humans from indoor pollution levels of 1.8-51.0 µg m^{-3} was negligible (14).

Teratogenicity and reproductive effects

Inhalation pregnant rat and offspring 500, 800, 1000, 1500 ppm, 23 hr day^{-1} showed concentration-dependent intra-uterine mortality. Offspring exposed prenatally only showed reduced body growth at all concentrations and delayed cerebellar cortex maturation. In pre- and post-exposure cases, effects of malnutrition added to the solvent-induced retardation, causing delayed tissue maturation and cell maturation. Neurotoxicity was restricted to axonal damage in adults. No teratogenic effects were seen in dams or offspring (15).

Inhalation rat 5000 ppm for ≤ 6 wk caused testicular damage. The earliest lesions were observed after 24 hr continuous treatment, which involved primary spermatocytes and spermatids, while numerous exfoliated injured germ cells reached the epididymus. After interruption of treatment, testicular lesions became increasingly severe, suggesting an irreversible sterility of treated animals (16).

♂ dominant-lethal effects were evaluated in groups of 30 Swiss mice after exposure to 0, 200, 1000, 5000 ppm *n*-hexane 20 hr day^{-1} for 5 days. Ten ♂ in each group were sacrificed after cessation of exposure and their testes and epididymides removed for evaluation of the germinal epithelium. No evidence of toxicity was observed (17).

Inhalation ♀ Sprague-Dawley rat, inhalation 7 hr day^{-1} for 15 days prior to gestation and through to day-18 of gestation 0, 700, 2000, 10, 000 ppm. Litters exhibited no signs of neuropathy or differences in size, sex ratio, age of eye opening or growth rate. No significant *n*-hexane induced alterations were observed in latency or amplitude of visual and interhemispheric evoked responses on anaesthetised rats on post-natal days 11, 20, 60. Significant increases in amplitude of visual evoked response occurred in the 10,000 ppm group recorded under unanaesthetised conditions on day-45 (18).

Metabolism and toxicokinetics

Excreted in urine as 2,5-hexanedione (species unspecified) (19).

Rats exposed to 500 ppm for 2 hr, 94% was found in red blood cells. In *in vitro* studies on human blood, 66% of the added hexane was taken into the red blood cells. Hexane is probably taken up by hydrophobic sites of blood proteins, thus haemoglobin is a major carrier in blood (20).
Urine of male Wistar rats exposed to 2000 ppm *n*-hexane contained 4,5-dihydroxy-2-hexanone formed via 5-hydroxy-2-hexanone (21).
In rat, up to 300 ppm the metabolic rate was directly proportional to the atmospheric concentration. 17% exhaled unchanged. Above 300 ppm, body hexane concentrations rose with increasing atmospheric concentrations up to limiting value of 9.6, limited by transport to the enzyme system (22).
♂ Fischer 344 rats exposed to neat, 1/3 saturated, 2/3 saturated and saturated aqueous solutions of hexane on 3.1 cm^2 area of dorsal skin showed blood hexane concentrations directly related to exposure concentrations with a peak at 8.0 $\mu g\ ml^{-1}$ (23).

Irritancy
10 mg instilled into rabbit eye (72 hr) caused mild irritation (24).
Prolonged exposure to hexane liquid may cause dermal irritation. Hexane is a defatting agent and can cause dermatitis (25).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (26).

Other effects

Other adverse effects (human)
Of 56 offset printing workers exposed to *n*-hexane, 20 developed symptomatic peripheral neuropathy and 26 had sub-clinical neuropathy. Development of neuropathy bore no relationship to the duration of exposure (27).
Calculated whole body dermal permeability constants for humans were 2-4 × less than experimental permeability constants for rats exposed to 60,000 ppm, probably due to physiological differences in skin (28).
Solvent workers exposed to a mean concentration of 40 ppm showed elevated postural sway frequency (2-4 Hz) compared to controls (0-1 Hz) (29).

Other comments

Reviews on human health effects, experimental toxicity, environmental effects, ecotoxicity exposure levels, epidemiology and workplace experience are listed (30).
Constituent of petroleum ether or ligroin. Industrial air pollutant in paint and lacquer, printing, metal cutting, leather and shoe industries. Ground and surface water pollutant. Indoor air pollutant.

References

1. Shell Chemie. Shell Industrie Chemicalien Gids, Shell Nederland Chemie, Afd, Industrialchemicalien, Wassenaarseweg 80, 's-Gravenhage, Netherlands.
2. Ghatak, D. B. et al *Environ. Ecol.* 1988, **6**(4), 943-947.
3. Wardas, W. et al *Rocz. Panstw. Zakl. Hig.* 1987, **38**(6), 523-529 (Pol.).
4. Imai, T et al *Appl. Environ. Microbiol.* 1986, **52**(6), 1403-1406.
5. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **46**(5), 947-965.
6. Jamison, V. W. et al *Biodegradation of High Octane Gasoline*, 1976 Proceedings of the Third International Biodegradation Symposium, Applied Science Publishers.
7. Ridgway, H. F. et al *Appl. Environ. Microbiol.* 1990, **56**(11), 3565-3575.
8. Knoevenagel, K. et al *Arch. Environ. Contam. Toxicol.* 1976, **4**, 324-333.
9. Kimura, E. T. et al *Toxicol. Appl. Pharmacol.* 1971, **19**, 699.
10. Nikunen, E. et al *Environmental Properties of Chemicals* 1990, VAPK-Publishing, Helsinki, Finland.
11. *Toxicol. Appl. Pharmacol.* 1959, **1**, 156.
12. Dunnick, J. K. et al *Toxicology* 1989, **57**(2), 163-172.
13. Goel, S. K. et al *J. Appl. Toxicol.* 1988, **8**(2), 81-84.
14. Tancrede, M. et al *Atmos. Environ.* 1987, **21**(10), 2187-2205.
15. Stolterburg-Didinger, G. et al *Neurotoxicol. Teratol.* 1990, **12**(6), 585-589.

16. De Martino et al *Exp. Mol. Pathol.* 1987, **46**(2), 199-216.
17. Mast, T. J. *NTIS Report* 1988 Natl. Tech. Inf. Ser., PNL-6679, order no. DE8900271, Springfield, VA, USA.
18. Howell, W. E. et al *Toxicologist* 1981, **1**, 152.
19. Ahonen, I. et al *Br. J. Ind. Med.* 1988, **45**(2), 133-136.
20. Lam, C. W. et al *Toxicol. Appl. Pharmacol.* 1990, **104**(1), 117-129.
21. Fedtke, N. et al *Biomed. Environ. Mass. Spectrom.* 1987, **14**(10), 563-572.
22. Filser, J. G. et al *Arch. Toxicol.* 1987, **60**(1-3), 77-80.
23. Morgan, D. L. et al *Environ. Res.* 1991, **55**(1), 51-63.
24. *Toxicol. Appl. Pharmacol.* 1980, **55**, 501.
25. *NIOSH Publication No. 81-123*, U.S. Dept. Health and Human Services, Washington, DC, USA.
26. Houk, V. S. et al *Mutat. Res.* 1989, **223**(1), 49-64.
27. Chang, C. M. et al *J. Neurol., Neurosurg. Psychiatry* 1993, **56**(5), 538-542.
28. McDougal, J. N. et al *Fundam. Appl. Toxicol.* 1990, **14**(2), 299-308.
29. Yokoyama, K. et al *Environ. Res.* 1997, **74**(2), 110-115.
30. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H61 1,6-hexanediol diacrylate

$$H_2C{=}CHCO_2(CH_2)_6O_2CCH{=}CH_2$$

$C_{12}H_{18}O_4$ **Mol. Wt.** 226.27 **CAS Registry No.** 13048-33-4

Synonyms 2-propenoic acid, 1,6-hexanediyl ester; hexamethylene glycol diacrylate; Ageflex HDDA

EINECS No. 235-921-9 **RTECS No.** AT 1430000

Uses In cross-linking agents, photocurable coatings and adhesives.

Physical properties

B. Pt. 130°C at 1 mmHg **Flash point** above 110°C (closed cup) **Specific gravity** 1.010 at 25°C
Volatility v.p. 0.0005 mm Hg at 20°C

Occupational exposure

Supply classification irritant
Risk phrases Irritating to eyes and skin – May cause sensitisation by skin contact (R36/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Wear eye/face protection (S2, S39)

Mammalian & avian toxicity

Sensitisation
Potent skin sensitiser in the guinea pig maximisation test (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 and TA97 with or without metabolic activation negative (2).

Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (3).
Used as one of a series of acrylates for dermatological patch-testing (4).

References

1. Bjorkner, B. *Contact Dermatitis* 1984, **11**, 236-246.
2. Zeiger, E. et al *Environ. Mol. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
4. Kanerva, L. et al *Contact Dermatitis* 1988, **18**(1), 10-15

H62 2,5-hexanedione

$$CH_3C(O)CH_2CH_2C(O)CH_3$$

$C_6H_{10}O_2$ **Mol. Wt.** 114.14 **CAS Registry No.** 110-13-4

Synonyms acetonylacetone; α,β-diacetylethane; 1,2-diacetylethane; 2,5-diketohexane

EINECS No. 203-738-3 **RTECS No.** MO 3150000

Physical properties

M. Pt. –9°C **B. Pt.** 191°C **Flash point** 79°C **Specific gravity** 0.970 at 20°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2150 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (2).
LD_{50} dermal guinea pig 6422 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 1600 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Treatment of rats with 2,5-hexanedione (dose and duration unspecified) produced protein cross-linking in a dose-dependent manner and also decreased protein phosphorylation of neurofilament proteins as well as microtubule associated protein-2 (4).

Teratogenicity and reproductive effects

♂ F-344 rats 1% solution in drinking water for 1, 3 and 6 wk caused no functional change in central nervous system regulation of ♂ testicular homeostasis through gonadotropins. The significant changes in Sertoli cell-localised enzymes before the onset of azoospermia suggested a direct toxic effect on the testis (5).
A pathologic sequence for testicular injury in rats following 2,5-hexanedione intoxication is reported consisting of tubulin cross leading to microtubule assembly alteration, leading to shorter and more numerous microtubules, loss of Sertoli cell cytoskeletal integrity, and altered microtubule associated proteins leading to germ cell sloughing and necrosis following by irreversible germ cell loss (6).

Metabolism and toxicokinetics

Dermal hens 50 mg kg^{-1} [^{14}C]-2,5-hexanedione disappeared monoexponentially from the application site after 6 hr. After 48 hr, 35% of radioactivity was expired largely unchanged; 15% in urinary-faecal excreta and $^{14}CO_2$ for 11.9%. Highest concentrations of ^{14}C in bile, liver and kidney, most unchanged 2,5-hexanedione found in liver, lung and kidney, 5-hydroxy-2-hexanone most abundant in urinary-faecal excreta (7).
♂ Wister rats exposed intraperitoneal 200 mg kg^{-1}. Urine analysis revealed formation of 4,5-dihydroxy-2-hexanone (8).

Irritancy

19 mg instilled into rabbit eye (72 hr) caused irritation (9).

Other effects

Other adverse effects (human)

Dissociated dorsal root ganglion cells from human foetuses exposed to 0.319 g 2,5-hexanedione for 2 weeks showed disorganisation of neuronal and axonal neurofilaments responsible for focal enlargements and atrophic changes of unmyelinated fibres (10).

References

1. Clothier, R. H. et al *Mol. Toxicol.* 1987, **1**(4), 571-577.
2. *J. Ind. Hyg. Toxicol.* 1949, **31**, 343.
3. *J. Ind. Hyg. Toxicol.* 1944, **26**, 269.
4. Abou-Donia, M. B. et al *Toxicology* 1988, **49**(2-3), 469-477.
5. Chaplin, R. E. et al *Toxicol. Appl. Pharmacol.* 1982, **62**, 262-272.
6. Boekelheide, K. et al *Gov. Rep. Announce. Index (U. S.)* 1989, **89**(11), Abstr. No. 930, 610.
7. Suwita, E. et al *Drug Metab. Dispos.* 1987, **15**(6), 779-785.
8. Fedtke, N. et al *Biomed. Environ. Mass Spectrom.* 1987, **14**(10), 563-572.
9. *Am. J. Ophthalmol.* 1946, **29**, 1363.
10. Moretto, G. et al *Arch. Toxicol.* 1991, **65**(5), 409-413

H63 1-hexanethiol

$$CH_3(CH_2)_4CH_2SH$$

$C_6H_{14}S$ **Mol. Wt.** 118.24 **CAS Registry No.** 111-31-9

Synonyms hexyl mercaptan

EINECS No. 203-857-0 **RTECS No.** MO 4550000

Physical properties

M. Pt. –81°C **B. Pt.** 150-154°C **Flash point** 20°C **Specific gravity** 0.849 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1254 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat 1080 ppm (1).

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (2).

References

1. *Am. Ind. Hyg. Assoc. J.* 1958, **19**, 171.
2. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA

H64 hexanoic acid

$$CH_3(CH_2)_4CO_2H$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 142-62-1

Synonyms butylacetic acid; *n*-caproic acid; capronic acid; *n*-hexoic acid; pentiformic acid; pentylformic acid

EINECS No. 205-550-7 **RTECS No.** MO 5250000

Uses Manufacture of esters for artificial flavourings and hexyl derivatives.
Occurrence In milk fats, coconut and palm oils. In food aromas and flavours.

Physical properties

M. Pt. -3.4°C **B. Pt.** 202-203°C **Flash point** 104°C (open cup) **Specific gravity** 0.9265 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.88
Solubility Water: 11 g l^{-1}. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 88 mg l^{-1} (1).
LC_{50} (48 hr) red killifish 235 mg l^{-1} (seawater) (2).
LC_{50} (48 hr) scud 235 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (24 hr) *Daphnia magna* 22 mg l^{-1} (3).
Caused disorganisation of the mitochondrial membranes in *Penicillium crustosum* (duration and concentration unspecified) (4).

Environmental fate

Degradation studies
Degraded in serum bottle studies of coal conversion wastewaters (5).
BOD^{25}_2 1.77 mg $l^{-1}O_2$ with an inoculum of soil microorganisms. Substrate concentration 3.5 mg l^{-1} (6).
Cleavage of C-C bond (to methane and carbon dioxide) catalysed by methanogenic microbial association (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 6440 mg kg^{-1} (8).
LC_{50} (2 hr) inhalation mouse 4100 mg m^{-3} (9).
LD_{50} dermal rabbit, guinea pig 630, 4635 mg kg^{-1}, respectively (10,11).
LD_{50} intraperitoneal mouse 3180 mg kg^{-1} (12).

Irritancy
Dermal rabbit (24 hr) 10 mg caused mild irritation (10).
695 µg instilled into rabbit eye (72 hr) caused severe irritation (13).

References

1. Mattson, V. R. et al *Bull. Environ. Contam. Toxicol.* 1976, **27**(1).
2. Onitsuka, S. et al *Chemosphere* 1989, **18**(7-8), 1621-1631.
3. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold, New York, NY, USA.
4. Kinderlerer, J. L. et al *Food Addit. Contam.* 1990, **7**(5), 657-659.

5. Blum, D. J. W. et al *J. Water Pollut. Control Fed.* 1986, **58**(2), 122-131.
6. Hammond, M. W. et al *Environ. Sci. Technol.* 1972, **6**(8), 732-735.
7. Kalyuzhnyi, S. V. et al *Dokl. Akad. Nauk SSSR*, 1989, **309**(1), 244-247.
8. Patty, F. A. *Industrial Hygiene and Toxicology* 1967, **2**, Interscience Publishers, New York, NY, USA.
9. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
10. *Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
11. *J. Ind. Hyg. Toxicol.* 1944, **26**, 269.
12. *J. Pharm. Pharmacol.* 1969, **21**, 85.
13. *Am. J. Ophthalmol.* 1946, **29**, 1363

H65 1-hexanol

$$CH_3(CH_2)_4CH_2OH$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 111-27-3

Synonyms *n*-hexyl alcohol; amylcarbinol; pentylcarbinol; 1-hydroxyhexane; caproyl alcohol; Epal 6; Exxal 6; Nacol 6-98

EINECS No. 203-852-3 **RTECS No.** MQ 4025000

Uses Used in manufacture of antiseptics, hypnotics. Plasticiser. Intermediate for textile and leather finishing agents.

Occurrence Acetate in seeds and fruits of *Heracleum sphondylium, Heracleum giganteum* and Umbelliferae.

Physical properties

M. Pt. –51.6°C **B. Pt.** 157.2°C **Flash point** 60°C **Specific gravity** 0.8153 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.02
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 2282 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 0.11 g l^{-1} (1).
LC_{50} (48 hr) golden orfe 0.13 g l^{-1} (2).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 27.5 ppm Microtox test (3).
Cell multiplication inhibition test *Pseudomonas putida* 62 mg l^{-1}, *Scenedesmus quadricauda* 30 mg l^{-1}, *Uronema parduczi* 93 mg l^{-1} (4,5).
EC_{50} (48 hr) *Daphnia magna* 0.41 g l^{-1} (6).

Environmental fate

Degradation studies

Biodegraded in activated sludge process to carboxylic acids and ketones (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 720, 1950 mg kg^{-1}, respectively (8,9).

LD_{50} dermal rabbit 3100 mg kg^{-1} (10).

LD_{50} intravenous mouse 103 mg kg^{-1} (11).

Teratogenicity and reproductive effects

Inhalation rat 3500 mg m^{-3} on day-7 of gestation produced limited maternal toxicity but no teratogenic effect (12).

Irritancy

Dermal rabbit (24 hr) 10 mg caused mild irritation, 250 μg instilled into rabbit eye (72 hr) caused severe irritation (10).

Genotoxicity

Single intragastric administration of 0.2 LD_{50} caused chromosomal aberrations and polyploidy in rat bone marrow (13).

Other comments

Reviews on human health effects, experimental toxicity, physico-chemical properties, epidemiology, workplace experience and environmental effects listed (14).

References

1. Protic, M. et al *Aquat. Toxicol.* 1989, **14**(1), 47-64.
2. Kamlet, M. J. et al *Environ. Sci. Technol.*, 1987, **21**, 149-155.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
5. Bringmann, G. et al *Z. Wasser/Abwasser Forsch.* 1980, **1**, 26-31.
6. Vaishnav, D. D. et al *Arch. Environ. Contam. Toxicol.* 1990, **19**, 624-628.
7. Nutsuma, T. et al *Tohoku Gakuin Daigaku Kogakubu Kenkyu Hokoku* 1988, **23**(1), 57-60 (Japan).
8. *S. Afr. Med. J.* 1969, **43**, 795.
9. *Hyg. Sanit. (USSR)* 1966, **31**, 310.
10. *Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119.
11. *Arch. Int. Pharmacodyn. Ther.* 1962, **135**, 330.
12. Nelson, B. K. et al *J. Am. Coll. Toxicol.* 1989, **8**(2), 405-410.
13. Barllyak, I. R. et al *Tsitol. Genet.* 1988, **22**(2), 49-52 (Russ.) (*Chem. Abstr.* **109**, 68620b).
14. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H66 2-hexanol

$$CH_3(CH_2)_3CH(OH)CH_3$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 626-93-7

Synonyms butylmethylcarbinol

EINECS No. 210-971-4 **RTECS No.** MO 8470000

Physical properties

B. Pt. 136°C **Flash point** 41°C **Specific gravity** 0.809 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.76

Occupational exposure

UN No. 2282 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) zebra fish 340 mg l^{-1} (1).
LC_{50} (48 hr) ide 290-330 mg l^{-1} (1).

Invertebrate toxicity

Lowest observable effect concentration *Microcystis aeruginosa, Scenedesmus quadricauda* 32-72 mg l^{-1} (2,3).
Toxicity threshold *Pseudomonas putida, Entosiphon sulcatum, Uronema parduczi* Chatton-Lwoff 63, 116 and 335 mg l^{-1}, respectively (3,4).

Environmental fate

Degradation studies

Biodegradation by bench scale activated sludge 3.4% of ThOD after 6 hr, 2.9% after 12 hr and 3.7% after 24 hr (5).
Biodegraded to corresponding fatty acid in activated sludge process (6).

References

1. Wellens, H. Z. *Wasser Abwasser Forsch.* 1982, **15**, 49.
2. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9).
3. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
4. Bringmann, G. et al *Z. Wasser Abwasser Forsch.* 1980, **11**, 26-31.
5. Gerhold, R. M. et al *J. Water Pollut. Control Fed.* 1966, **38**(4), 562.
6. Niitsuma, T. et al *Tohoku Gakuin Daigaku Kogakubu Kenkyu Hokoku* 1988, **23**(1), 57-60 (Japan.) (*Chem. Abstr.* **110**, 140816k)

H67 2-hexanone

$$CH_3(CH_2)_3C(O)CH_3$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 591-78-6

Synonyms methyl butyl ketone; hexan-2-one; butyl methyl ketone; MBK; methyl *n*-butyl ketone

EINECS No. 209-731-1 **RTECS No.** MP 1400000

Uses Solvent.

Physical properties

M. Pt. –57°C **B. Pt.** 128°C **Flash point** 35°C (open cup) **Specific gravity** 0.83 at 0°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.38 **Volatility** v.p. 2 mmHg at 20°C ; v.den. 3.45
Solubility Water: 1.4 wt % at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (21 mg m^{-3})
FR-VME 5 ppm (20 mg m^{-3}) **FR-VLE** 8 ppm (35 mg m^{-3})
JP-OEL 5 ppm (20 mg m^{-3})
SE-LEVL 1 ppm (4 mg m^{-3}) **SE-STEL** 2 ppm (8 mg m^{-3})
UK-LTEL 5 ppm (21 mg m^{-3})
US-TWA 5 ppm **US-STEL** 10 ppm
Supply classification highly flammable, toxic
Risk phrases Highly flammable – Toxic: danger of serious damage to health by prolonged exposure through inhalation (R11, R48/23)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not empty into drains – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Use only in well ventilated areas (S1/2, S9, S16, S29, S45, S51)

Ecotoxicity

Fish toxicity
LC_{50} fathead minnow 430 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} mixed microbial culture 5.5 g l^{-1} (2).

Environmental fate

Anaerobic effects
IC_{50} (50 day) methanogenic bacterial culture 6100 mg l^{-1}; test conditions were 35°C, 50-day solids and hydraulic retention tissues, reactor fed acetate (50000 mg l^{-1}) as sole organic carbon source (3).

Degradation studies
BOD_5 65% of ThOD (1).

Abiotic removal
Activated carbon adsorbability 0.159 g g^{-1} carbon, 80.7% reduction, influent 1000 mg l^{-1}, effluent 191 mg l^{-1} (4).

Adsorption and retention
Activated carbon adsorbability 0.159 g g^{-1} carbon, 80.7% reduction, influent 1000 mg l^{-1}, effluent 191 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 2400, 2600 mg kg^{-1}, respectively (5,6).
LC_{50} (4 hr) inhalation rat 8000 ppm (7).
LD_{50} dermal rabbit 4800 mg kg^{-1} (7).

Teratogenicity and reproductive effects
Inhalation rat 500-2000 ppm 6 hr day^{-1} throughout pregnancy caused hyperactivity of offspring (8).

Irritancy
Mild skin and eye irritant in rabbits (9).
Vapours irritate mucous membranes (10).

Other effects

Other adverse effects (human)

Inhalation exposure to 1000 ppm caused eye, central nervous system and gastro-intestinal effects (7). Peripheral neuropathy reported after occupational exposure in a printing plant after replacement of methyl isobutyl ketone with 2-hexanone in a solvent mixture with methyl ethyl ketone (10).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

References

1. Blum, J. W. et al *Res. J. Water Pollut. Control Fed.* 1991, **63**(3), 198-207.
2. Vaishnav, D. D. et al *Toxic. Assess.* 1986, **1**(2), 227-240.
3. Vaishnav, D. D. et al *Chemosphere* 1987, **16**(4), 695-703.
4. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1974, **76**(5), 947-965.
5. *Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
6. *Toxicol. Lett.* 1986, **30**, 13.
7. *Raw Material Data Handbook* 1973, NAPIRI, Leigh Univ., Bethlehem, PA, USA.
8. Peters, M. A. et al *Ecotoxicol. Environ. Saf.* 1981, **5**, 291-306.
9. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, Prague, Czechoslovakia.
10. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H68 3-hexanone

$$CH_3CH_2C(O)CH_2CH_2CH_3$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 589-38-8

Synonyms ethyl propyl ketone

EINECS No. 209-645-4 **RTECS No.** MP 1575000

Physical properties

B. Pt. 123°C **Flash point** 35°C **Specific gravity** 0.813 at 22°C with respect to water at 4°C

Mammalian & avian toxicity

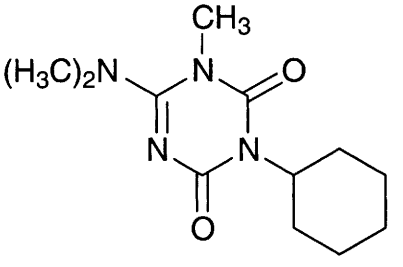
Acute data

LD_{50} oral rat 3360 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 400 ppm (1).
LD_{50} dermal rabbit 3170 mg kg^{-1} (1).
LD_{Lo} subcutaneous guinea pig 700 mg kg^{-1} (2).

References

1. *Toxicol. Appl. Pharmacol.* 1974, **28**, 313.
2. Bang, L. *Studien ueber die Pharmakologie des Pinakolins und einiger seiner Derivate mit besonderer Beruecksichtigung der Kreislaufwirkung (Dissertation)*, 1934, Pharmakologische Abteilung des Karolinischen Instituts, Stockholm, Sweden

H69 hexazinone



$C_{12}H_{20}N_4O_2$ **Mol. Wt.** 252.32 **CAS Registry No.** 51235-04-2

Synonyms 3-cyclohexyl-6-(dimethylamino)-1-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione; 3-cyclohexyl-6-(dimethylamino)-1-methyl-*s*-triazine-2,4(1*H*,3*H*)-dione; DPX 3674; Velpar; Ficsan; Forstgranulat

EINECS No. 257-074-4 **RTECS No.** XY 7850000

Uses Pre- and post-emergence herbicide against woody and herbaceous weeds.

Physical properties

M. Pt. 115-117°C **B. Pt.** decomp. on distillation **Specific gravity** 1.25 **Volatility** v.p. 0.23×10^{-6} mmHg **Solubility** Water: 33 g l^{-1} (25°C). Organic solvents: acetone, benzene, chloroform, dimethylformamide, hexane, methanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow, rainbow trout, juvenile chinook salmon, bluegill sunfish 270-420 mg l^{-1} (1,2).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia* sp. 442 mg l^{-1} (1).

EC_{50} (5 day) *Selenastrum capricornutum* 0.085 mg l^{-1} (3).

EC_{50} growth inhibition, green algae (two species) 0.01 mg l^{-1}, cyanobacteria (five species) 0.7 mg l^{-1}, diatoms (two species) 0.05 mg l^{-1} (4).

Not toxic to bees; LD_{50} 60 µg bee^{-1} (1).

Environmental fate

Degradation studies

Microbial degradation in soil and natural waters breaks triazine ring, liberating carbon dioxide. Soil $t_{1/2}$ ~1-6 month (1).

Plant $t_{1/2}$ 4-15 day; soil $t_{1/2}$ 11-180 day (5).

66% of hexazinone applied in a white spruce plantation at 4.3 kg hr^{-1} was degraded and dispersed after 104 days, decreasing from 7.12 µg g^{-1} on day-9 to 2.09 µg g^{-1} on day-104. The higher concentration of the metabolite 3-(4-hydroxycyclohexyl)-6-(dimethylamino)-1-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione (30-50% of hexazinone

detected) compared with 3-cyclohexyl-6-(methylamino)-1-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione indicated higher hydroxylation than demethylation activity in the silt loam soil (6).

Mammalian & avian toxicity

Acute data

LC_{50} oral guinea pig, rat 860, 1690 mg kg^{-1}, respectively (7,8).
LC_{50} (1 hr) inhalation rat >7.5 mg l^{-1} (1).
LD_{50} dermal rat 5278 mg kg^{-1} (9).
LD_{50} intraperitoneal rat, quail 530, 2258 mg kg^{-1}, respectively (10).

Sub-acute and sub-chronic data

LC_{50} (8 day) oral bobwhite quail, mallard duckling >10,000 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects

In 2-year feeding trial, rat and mouse, no-effect level 200 ppm in feed (11).
♂, ♀ rats 0, 200, 1000, 5000 ppm in diet for 3 months was not tumorigenic (10).

Teratogenicity and reproductive effects

Pregnant rats 0, 200, 1000, 5000 ppm in feed from day-6 of gestation to day-15. Rats sacrificed after 21 days showed no evidence of foetal malformations, variations or abnormalities in dams (11).
Pregnant rabbit 0, 20, 50, 125 mg kg^{-1} from days 6-19 of gestation. Rats sacrificed on day-29 showed no maternal toxicity, foetal viability was unaffected but offspring showed a slight decrease in body weight (11).

Metabolism and toxicokinetics

Major urinary metabolites in rats are 3-(4-hydroxycyclohexyl)-6-(dimethylamino)- 1-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione, 3-cyclohexyl-6-(methylamino)-1-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione, and 3-(4-hydroxycyclohexyl)-6-(methylamino)-1-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione (1).

Irritancy

48 mg instilled into rabbit eye (72 hr) caused moderate irritation (10).

Legislation

Limited Under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (12).
Included in schedule 6 (Release into land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).
WHO Toxicity Class III (14).
EPA Toxicity Class (formulation) II (1).

Other comments

EC_{50} growth inhibition duckweed 0.06 mg l^{-1} (4).
Effects on phytoplankton reviewed (15).
Effects on zooplankton reviewed (16).
Plant $t_{t/2}$ 4-15 day (5).
Detected as trace pollutant in drinking water.

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Wan, M. T. et al *Bull. Environ. Contam. Toxicol.* 1988, **41**, 609-616.
3. Abou-Waly, H. et al *Bull. Environ. Contam. Toxicol.* 1991, **46**, 223-229.
4. Peterson, H. G. et al *Aquat. Toxicol.* 1997, **39**(2), 111-134.
5. Michael, J. L. et al *J. Environ. Toxicol. Chem.* 1993, **12**, 405-410.
6. Feng, J. C. *J. Environ. Sci. Health, Part B* 1987, **B22**(2), 221-233.
7. *Pestic. Toxic. Chem. News* 1980, **9**, 21.
8. Neary, D. G. *South. J. Appl. For.* 1983, **7**, 217.

9. *Farm Chemicals Handbook* 1983, **C126**, Meister Publishing Co., Willoughby, OH, USA.
10. *Fundam. Appl. Toxicol.* 1984, **4**, 603.
11. Kennedy, G. L. et al *Fundam. Appl. Toxicol.* 1984, **4**, 960-971.
12. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
13. *S.I. 1991 No.472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
14. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
15. Thompson, D. G. et al *J. Environ. Toxicol. Chem.* 1993, **12**, 1695-1707.
16. Thompson, D. G. et al *J. Environ. Toxicol. Chem.* 1993, **12**, 1709-1717

H70 1-hexene

$$CH_3(CH_2)_3CH{=}CH_2$$

C_6H_{12} **Mol. Wt.** 84.16 **CAS Registry No.** 592-41-6

Synonyms butyl ethylene; hexylene

EINECS No. 209-753-1

Uses Synthesis of flavours, perfumes, dyes and resins. Fuels.

Physical properties

M. Pt. –139.9°C **B. Pt.** 64.5°C **Flash point** –9°C **Specific gravity** 0.6732 at 20°C with respect to water at 4°C
Volatility v.p. 310 mmHg at 38°C ; v.den. 3.0
Solubility Water: 50 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

US-TWA 30 ppm

UN No. 2370 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity
Quantitative structure-activity relationship research with a mixed microbial culture using acute static bioassay found 1-hexene had a toxic effect with a log EC_{10} of –0.49 mol l^{-1} (1).

Environmental fate

Degradation studies
Nocardia sp. strain H8 and *Pseudomonas* sp. strain H1 grew on and oxidised 1-hexene (2).
Resting cell suspensions of a thermophilic obligate methane-oxidising bacterium H2 (type 1) oxidised 1-hexene to its corresponding 1,2-epoxide (3).
Pseudomonas oleovorans grows on 1-hexene and oxidises it to corresponding fatty acids (4).
Waste water treatment with activated sludge; after 6 and 12 hr 0.5% of ThOD, 24 hr 0.7% of ThOD (5).

Abiotic removal
Rotating disk contact aerator: influent 189.3 mg l^{-1}; effluent 0.4 mg l^{-1} elimination; >99% (24 hr) or 4208 g m^{-3} (24 hr) (6).

Mammalian & avian toxicity

Acute data

LC_{Lo} (duration unspecified) inhalation mice 140.28 g m^{-3} (4.08% 40, 800 ppm) (7).
Minimal narcotic concentration in mice 99.96 g m^{-3} (2.9% 29,100 ppm) (7).

Irritancy

Low to moderate eye and skin irritant (species unspecified) (8).

Other effects

Other adverse effects (human)

Moderate aspiration hazard; inhalation of 0.1% causes narcosis, central nervous system effects, vertigo, cyanosis, vomiting and mucous membrane irritation in humans (8).

References

1. van Ginkel, C. G. et al *Appl. Environ. Microbiol.* 1987, **53**, 2903-2907.
2. Warne, M. S. J. et al *Ecotoxicol. Environ. Saf.* 1989, **17**(2), 133-148.
3. Imai, T. et al *Appl. Environ. Microbiol.* 1986, **52**(6), 1403-1406.
4. Lageveen, R. G. et al *Appl. Environ. Microbiol.* 1988, **54**(12), 2924-2932.
5. Gerhold, R. M. et al *J. Water Pollut. Control Fed.* 1966, **38**(4), 562.
6. Bringmann, G. et al *Concawe Doc.* 4797, 1970, Den Haag, Netherlands.
7. Lazarew, N. W. *Naunyn-Schmiedebergs Arch. Exp. Pathol. Pharmacol.* 1929, **143**, 223.
8. Clayton, G. D. et al *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, Interscience Publishers, New York, NY, USA

H71 1-hexen-3-ol

$$CH_3CH_2CH_2CH(OH)CH{=}CH_2$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 4798-44-1

Synonyms propylvinylcarbinol

EINECS No. 225-355-0

Uses Corrosion inhibitor.

Occurrence In *Cinnamomum platyphyllum* leaf oil, and *Acinos suaveolens* essential oil.

Physical properties

B. Pt. 134-135°C **Flash point** 35°C **Specific gravity** 0.884

Occupational exposure

UN No. 1987

Ecotoxicity

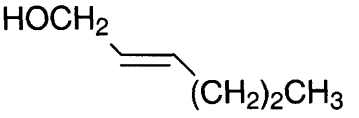
Fish toxicity

LC_{50} (96 hr) fathead minnow 30.4 mg l^{-1} (1).

References

1. Veith, G. et al *Xenobiotica* 1989, **19**(5), 555-565

H72 (*E*)-2-hexen-1-ol



$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 928-95-0

Synonyms *trans*-2-hexenol; 2-hexenol; FEMA No. 2562

EINECS No. 213-191-2 **RTECS No.** MP 8390000

Physical properties

B. Pt. 158-160°C **Flash point** 54°C **Specific gravity** 0.836-0.841

Solubility Organic solvents: ethanol, propylene glycol, fixed oils

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3500 mg kg^{-1} (1).

LD_{50} dermal rabbit 4500 mg kg^{-1} (1).

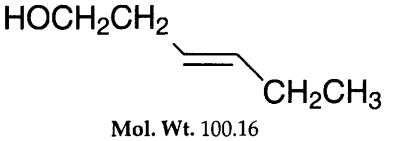
Irritancy

Dermal rabbit (24 hr) 500 mg caused an irritant effect (1).

References

1. *Food Cosmet. Toxicol.* 1974, **12**, 911

H73 (*E*)-3-hexen-1-ol



$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 928-97-2

Synonyms *trans*-3-hexenol

EINECS No. 213-193-3

Physical properties

B. Pt. 61-62°C at 12 mmHg **Flash point** 58°C **Specific gravity** 0.817

Ecotoxicity

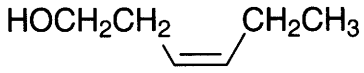
Fish toxicity

LC_{50} (96 hr) fathead minnow 271 mg l^{-1} (1).

References

1. Veith, G. D. et al *Xenobiotica* 1989, **19**(5), 555-565

H74 (*Z*)-3-hexen-1-ol



$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 928-96-1

Synonyms *cis*-3-hexenol; leaf alcohol

EINECS No. 213-192-8 **RTECS No.** MP 8400000

Occurrence Occurs in leaves of odorous plants, including shrubs and trees. Isolated from Japanese oil of peppermint.

Physical properties

B. Pt. 156-157°C **Flash point** 44°C **Specific gravity** 0.846 at 22°C with respect to water at 15°C
Solubility Organic solvents: ethanol, fixed oils, propylene glycol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 381 mg l^{-1} (1).

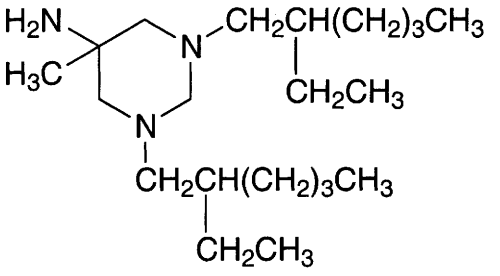
Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 4700, 7000 mg kg^{-1}, respectively (2,3).
LD_{50} intraperitoneal mouse, rat 400, 600 mg kg^{-1}, respectively (3).

References

1. Veith, G. D. et al *Xenobiotica* 1989, **19**(5), 555-565.
2. *Food Cosmet. Toxicol.* 1974, **12**, 109.
3. *Food Cosmet. Toxicol.* 1969, **7**, 451

H75 hexetidine



$C_{21}H_{45}N_3$ **Mol. Wt.** 339.61 **CAS Registry No.** 141-94-6

Synonyms 1,3-bis(2-ethylhexyl)hexahydro-5-methyl-5-pyrimidinamine; 5-amino-1,3-bis(2-ethylhexyl) hexahydro-5-methylpyrimidine; Glypesin; Hexocil; Oraldene; Sterisil; Triocil

EINECS No. 205-513-5

Uses Bactericidal and fungicidal antiseptic used as mouthwash.

Physical properties

B. Pt. at 0.4 mmHg **Flash point** 70°C **Specific gravity** 0.8889 at 20°C with respect to water at 20°C
Solubility Water: insoluble. Organic solvents: acetone, benzene, chloroform, ethanol, hexane, methanol

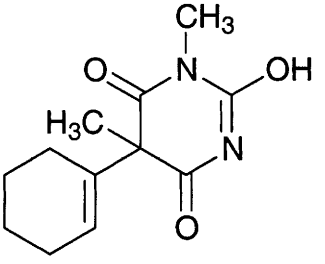
Mammalian & avian toxicity

Sensitisation
Allergic contact dermatitis reported in human therapeutic use (1).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK

H76 hexobarbital



$C_{12}H_{16}N_2O_3$ **Mol. Wt.** 236.27 **CAS Registry No.** 56-29-1

Synonyms 5-(1-cyclohexen-1-yl)-1,5-dimethylbarbituric acid; 5-(1-cyclohexen-1-yl)-1,5-dimethyl-2,4,6 (1*H*,3*H*,5*H*)-pyrimidinetrione; enhexymal; evipal; hexeral(barbiturate); hexabarbital; hexobarbitone; methylhexabital; Barbidorm; Cyclopan; Noreosan; Somnalert; Sombulex

EINECS No. 200-264-9 **RTECS No.** CQ 2625000

Uses Anaesthetic, sedative and hypnotic.

Physical properties

M. Pt. 145-147°C

Solubility Water: 0.3 g l^{-1}. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Ecotoxicity

Bioaccumulation

Bioconcentration factor for goldfish 1.74 and in frog 1.50 (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 470 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 250 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse, rat 280, 330 mg kg^{-1}, respectively (4,5).

Other effects

Other adverse effects (human)

Prolonged or repeated exposure may lead to dependence of the barbiturate-alcohol type (6).

Other comments

Metabolism and pharmacokinetics reviewed (7).

References

1. Nakatsugawa, T. et al in *Environmental Toxicology of Pesticides* 1972, Academic Press, New York, NY, USA.
2. *J. Pharmacol. Exp. Ther.* 1952, **106**, 444.
3. *Arzneim.-Forsch.* 1965, **15**, 688.
4. *J. Pharmacol. Exp. Ther.* 1948, **93**, 362.
5. *Arch. Int. Pharmacodyn. Ther.* 1970, **184**, 5.
6. Lewis, D. F. V. et al *Toxicol. Lett.* 1989, **45**(1), 1-13.
7. Van der Graaff, M. et al *Drug Metab. Rev.* 1988, **19**(2), 109-164

H77 *sec*-hexyl acetate

$$CH_3CO_2CH(CH_3)CH_2CH(CH_3)_2$$

$C_8H_{16}O_2$ **Mol. Wt.** 144.21 **CAS Registry No.** 108-84-9

Synonyms acetic acid, 1,3-dimethylbutyl ester; 1,3-dimethylbutyl acetate; MAAC; methylamyl acetate; methylisoamyl acetate; methylisobutylcarbinol acetate; 4-methyl-2-pentanol, acetate; 4-methyl-2-pentyl acetate

EINECS No. 203-621-7 **RTECS No.** SA 7525000

Uses In metalising paint for electrochemical cells.

Physical properties

M. Pt. -63.8°C **B. Pt.** 146.3°C **Flash point** 45°C **Specific gravity** 0.8598 at 20°C with respect to water at 20°C **Volatility** v.p. 3.8 mmHg at 20°C ; v.den. 4.97

Occupational exposure

DE-MAK 50 ppm (300 mg m^{-3})
FR-VME 50 ppm (300 mg m^{-3})
UK-LTEL 50 ppm (299 mg m^{-3}) **UK-STEL** 100 ppm (599 mg m^{-3})
US-TWA 50 ppm (295 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6160 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (1).
LD_{50} dermal rabbit 20 g kg^{-1} (1).

Irritancy

Irritant to the human eye at 100 ppm for 15 min (2).
500 mg applied to rabbit skin caused mild irritation (duration unspecified) (1).

Other comments

Reviews on human health effects, epidemiology, experimental toxicity and workplace experience listed (3).

References

1. *Union Carbide Data Sheet* 1966 Union Carbide Corp., New York, NY, USA.
2. *J. Ind. Hyg. Toxicol.* 1946, **28**, 262.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H78 hexyl acrylate

$$CH_2{=}CHCO_2(CH_2)_5CH_3$$

$C_9H_{16}O_2$ **Mol. Wt.** 156.22 **CAS Registry No.** 2499-95-8
Synonyms acrylic acid, hexyl ester; hexyl 2-propenoate; 2-propenoic acid, hexyl ester; Ageflux-n-HA
EINECS No. 219-698-5 **RTECS No.** AT 1450000
Uses Cross-linking agent; in electrophotographic liquid developers and UV-fixable toners.

Physical properties

M. Pt. –45°C **B. Pt.** 88-90°C at 24 mmHg **Flash point** 68°C **Specific gravity** 0.888 at 20°C

Occupational exposure

Supply classification irritant, dangerous for the environment
Risk phrases Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R36/37/38, R43, R51/53)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S24, S26, S37, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 1.09 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 26 g kg^{-1} (2).

LD_{50} dermal rabbit 5600 mg kg^{-1} (2).

Other comments

Reviews on human health effects and experimental toxicity listed (3).

References

1. Russom, C. L. et al *Bull. Environ. Contam. Toxicol.* 1988, **41**, 589-596.
2. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H79 hexyltrichlorosilane

$C_6H_{13}SiCl_3$

$C_6H_{13}Cl_3Si$ **Mol. Wt.** 219.61 **CAS Registry No.** 928-65-4

Synonyms trichlorohexylsilane

EINECS No. 213-178-1 **RTECS No.** VV 4320000

Uses Catalyst.

Physical properties

B. Pt. 191.6°C **Specific gravity** 1.07 at 20°C

Solubility Water: decomp.

Occupational exposure

UN No. 1784 **HAZCHEM Code** 4XE **Conveyance classification** corrosive substance

Mammalian & avian toxicity

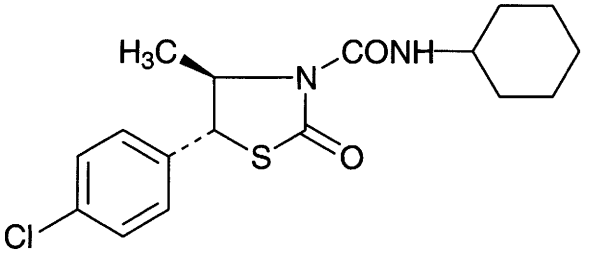
Irritancy

Severe eye, skin and mucous membrane irritant (1).

References

1. *Sax's Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA

H80 hexythiazox



$C_{17}H_{21}ClN_2O_2S$ **Mol. Wt.** 352.88 **CAS Registry No.** 78587-05-0

Synonyms (4*RS*5*RS*)-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxo-thiazolidine-3-carboxamide; *trans*-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxo-3-thiazolidinecarboxamide; Zeldox; Calibre; Stopper; Acaflor; Acorit; Metacar; Ordoval

RTECS No. XJ 5396000

Uses Non-systemic acaricide.

Physical properties

M. Pt. 108°C **Partition coefficient** log P_{ow} 2.53 **Volatility** v.p. 2.55×10^{-5} mmHg at 20°C
Solubility Water: 0.5 mg l^{-1} at 20°C. Organic solvents: acetone, acetonitrile, chloroform, hexane, methanol, xylene

Occupational exposure

Supply classification dangerous for the environment
Risk phrases Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R50/53)
Safety phrases This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout >300 mg l^{-1}, bluegill sunfish 11.6 mg l^{-1} (1).

Invertebrate toxicity
Non-toxic to bees (2).
LD_{50} topical application >200 μg bee^{-1} (1).

Environmental fate

Degradation studies
$t_{1/2}$ in clay loam at 15°C 8 days; undergoes oxidation to corresponding hydroxy and carbonyl compounds. Stable to light, air and heat (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck >2510 mg kg^{-1}, Japanese quail >5000 mg kg^{-1} (1).
LD_{50} oral rat, mouse >5000 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >2 mg l^{-1}.
LD_{50} dermal rat >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral mallard duck, bobwhite quail >5620 mg kg^{-1} in diet (1).
Rats fed 70 mg kg^{-1} diet 90-day trials showed no ill-effects (1).

Irritancy
Mild eye irritant (species, dose and duration unspecified); not irritating to rabbits skin (dose and duration unspecified) (1).

Sensitisation
Non-sensitising to guinea pig skin (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
WHO Toxicity Class Table 5 (4).
EPA Toxicity Class IV (1).
ADI 0.03 mg kg^{-1} (1).

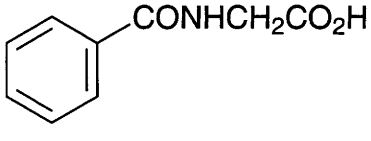
Other comments

Not harmful to egg or larval stages of the predatory mite *Phytoseiulus persimilis*, or to *Tydeus* (5).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Mayer, D. F. et al *Environ. Entomol.* 1986, **15**(5), 1047-1049.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
5. Sterk, G. et al *Meded. Fac. Landbouwwet. Rijksuniv. Gent* 1989, **54**(3b), 969-973

H81 hippuric acid



$C_9H_9NO_3$ **Mol. Wt.** 179.18 **CAS Registry No.** 495-69-2
Synonyms benzamidoacetic acid; benzoylamidoacetic acid; benzoylglycine; *N*-benzoylglycine
EINECS No. 207-806-3 **RTECS No.** MR 8150000

Occurrence In sewage effluent (1).
Present in urine of herbivorous animals, small amounts in human urine.

Physical properties

M. Pt. 188-191°C **Partition coefficient** log P_{ow} –0.07/–0.25 (calc.)
Solubility Water: 4 g l^{-1}. Organic solvents: chloroform, diethyl ether

Mammalian & avian toxicity

Acute data

LD_{50} redwing blackbird >100 mg kg^{-1} (2).

References

1. Dietz, F. et al *GWF, Gas- Wasserfach: Wasser/Abwasser* 1978, **119**(6).
2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382

H82 HN1

$$CH_3CH_2N(CH_2CH_2Cl)_2$$

$C_6H_{13}Cl_2N$ **Mol. Wt.** 170.08 **CAS Registry No.** 538-07-8

Synonyms ethylbis(2-chloroethyl)amine; 2-chloro-*N*-(2-chlorethyl)-*N*-ethylethanamine; 2,2'-dichlorotriethylamine; bis(2-chloroethyl)ethylamine

RTECS No. YE 1225000

Physical properties

M. Pt. –34°C **B. Pt.** 66°C at 3 mmHg **Specific gravity** 1.0861 at 23°C with respect to water at 4°C
Solubility Organic solvents: miscible with many organic solvents

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2.5 mg kg^{-1} (1).
LC_{50} (10 min) inhalation rat 750 mg m^{-3} (2).
LC_{50} (10 min) inhalation cat, dog, mouse, monkey 400, 800, 900, 1500 mg m^{-3}, respectively (2).
LD_{50} dermal mouse, rabbit, rat 13, 15, 17 mg kg^{-1}, respectively (3).
LD_{50} intravenous rat 0.5 mg kg^{-1} (1).

References

1. *NTIS Report* PB158-507, Natl. Tech. Inf. Ser., Springfield, VA, USA.
2. *NTIS Report* PB158- 508, Natl. Tech. Inf. Ser., Springfield, VA, USA.
3. *J. Pharmacol. Exp. Ther.* 1947, **91**, 224

H83 holmium

Ho

Ho **Mol. Wt.** 164.93 **CAS Registry No.** 7440-60-0

EINECS No. 231-169-0

Occurrence In rare earth minerals, which make up 0.7-1.2 ppm of the Earth's crust. Detected in human breast milk (1).

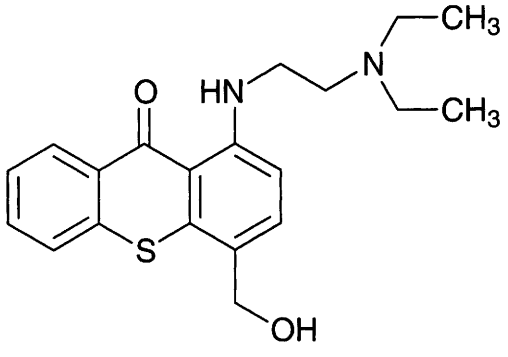
Physical properties

M. Pt. 1461°C **Specific gravity** 8.799

References

1. Durrant, S. F. et al *J. Micronutr. Anal.* 1989, 5(2), 111-126

H84 hycanthone



$C_{20}H_{24}N_2O_2S$ **Mol. Wt.** 356.49 **CAS Registry No.** 3105-97-3 (base); 23255-93-8 (mesylate)

Synonyms 1-[[2-(diethylamino)ethyl]amino]-4-(hydroxymethyl)-9*H*-thioxanthen-9-one; hycanthon; Etrenol (mesylate)

EINECS No. 221-463-7 **RTECS No.** XO 1590000

Uses Hycanthone is an anthelmintic effective against human *Schistosoma haematobium* and *S. mansoni* infections. It is administered intramuscularly as the mesylate salt.

Occurrence Not known to occur in nature.

Physical properties

M. Pt. 100.6-102.8°C (base), ~143°C (mesylate)

Solubility Water: slightly soluble (base), very soluble (mesylate). Organic solvents: freely soluble in 95% ethanol (mesylate), slightly soluble in chloroform (mesylate), very slightly soluble in acetone (mesylate), practically insoluble or insoluble in benzene and ether (mesylate)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 286, 1120 mg kg^{-1}, respectively (1).

LD_{50} subcutaneous mouse, rat 270, 286 mg kg^{-1}, respectively (1).

LD_{50} intramuscular mouse 253 mg kg^{-1} (2).

LD_{50} intravenous rat 75 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity of hycanthone mesylate to humans, insufficient evidence for carcinogenicity to animals, IARC classification group 3 (3).

Hepatocellular carcinomas were observed in *Schistosoma mansoni* infected ♀ mice administered a single dose of hycanthone mesylate. In uninfected mice, administration of a single dose of hycanthone mesylate produced neither hepatic hyperplasia nor hepatomas. The authors suggest that hepatic hyperplasia induced by the

deposition of schistosome eggs in the liver and enhanced by hycanthone mesylate is a predisposing factor for the hepatocarcinogenic effect of the compound (4).
Partially hepatectomised mice received a single intramuscular dose of 79 mg kg^{-1}. Of the mice living 200 days or longer, hepatocellular carcinoma was seen in 11.5% and liver sarcoma in 4.2%. This type of malignant neoplasm was not seen in controls (5).

Teratogenicity and reproductive effects
A single intramuscular dose of hycanthone mesylate (35 or 50 mg kg^{-1}) administered to mice on day-7 of gestation caused malformations in >7.3% of the litters, most frequently exencephaly and rib anomalies (6).
Intramuscular doses of hycanthone mesylate (50 mg kg^{-1}) administered to rabbits on days 7, 8, or 9 of gestation caused embryolethal and teratogenic effects (7).

Metabolism and toxicokinetics
Rhesus monkeys and ♂ Sprague-Dawley rats administered a single intramuscular injection of hycanthone mesylate (3 mg kg^{-1}) showed peak blood and tissue levels after 30-60 minutes. Highest concentrations occurred in the liver, spleen, kidneys and adrenals, but decreased to less than 20% of the administered dose after 48-72 hr. Unchanged hycanthone mesylate was found in blood and tissues except the liver, where it was rapidly metabolised to hycanthone sulfoxide in rats and the *N*-de-ethylated compound in monkeys (8).

Genotoxicity

Mammalian spot test (Fellfleckentest) with mice injected intraperitoneally with 0.03 mmol kg^{-1} hycanthone mesylate positive (9).
Hycanthone mesylate increased the mutant frequency in the thymidine kinase locus of heterozygous mutants of L5178Y mouse lymphoma cells (10).

Other effects

Other adverse effects (human)
Two of eight patients developed severe hepatocellular injury following a single intramuscular injection of 3 mg kg^{-1} hycanthone against infestation with *Schistosoma haematobium* (11).

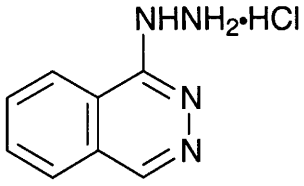
Other comments

Hycanthone mesylate is extremely sensitive to acid.
Mutagenic properties of hycanthone mesylate reviewed (12).

References

1. *Egypt. J. Bilharziasis* 1974, **1**(2), 181.
2. *J. Pharmacol. Exp. Ther.* 1977, **1**, 200.
3. *IARC Monograph* 1987, **Suppl. 7**, 64.
4. Haese, W. H. *J. Pharmacol. Exp. Ther.* 1973, **18**(2), 430-440.
5. Tsuda, H. et al *Cancer Res.* 1979, **39**(11), 4491-4496.
6. Moore, J. A. *Nature (London)* 1972, **239**(5367), 107-109.
7. Sieber, S. M. et al *Teratology* 1974, **10**, 227-236.
8. Hernandez, M. C. *Preclinical toxicology of hycanthone in dogs and monkeys* NSC 142982, Report 11TR1 TOX 32 pH 43671141, US Government Printing Office, Washington DC, USA.
9. Fahrig, R. *Arch. Toxicol.* 1977, **38**, 87-98.
10. Clive, D. et al *Mutat. Res.* 1972, **14**(2), 262-264.
11. Farid, Z. et al *Br. Med. J.* 1972, **ii**, 88-89.
12. Hartmann, P. E. et al *J. Toxicol. Environ. Health* 1975, **1**, 243-270

H85 hydralazine hydrochloride



$C_8H_9ClN_4$ **Mol. Wt.** 196.64 **CAS Registry No.** 304-20-1

Synonyms 1(2*H*)-phthalazinone hydrazone hydrochloride; 1-hydrazinophthalazine hydrochloride; hydralazine chloride; Aprelazine; Hyperazin; Lopress; Apresoline Hydrochloride

EINECS No. 206-151-0 **RTECS No.** TH 9000000

Uses Antihypertensive.

Physical properties

M. Pt. 273°C (decomp.)

Solubility Water: 44.2 g l^{-1} at 25°C. Organic solvents: 2.0 g l^{-1} in 95% ethanol, very slightly soluble in ether

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 188 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 73 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 83 mg kg^{-1} (3).
LD_{50} intravenous rat, mouse 34, 84 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal rat 35 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (5).
Oral mouse, hamster (drinking water) maximum tolerated dose for life 2.5, 5 g l^{-1}, respectively (6).
A survey of 1978 patients with lung or colorectal cancer and 6807 controls found no evidence that using hydralazine increased the risk of these neoplasms (7).

Teratogenicity and reproductive effects

No malformations were observed in the offspring of patients suffering from toxaemia or chronic hypertension treated with hydralazine hydrochloride during pregnancy (8).
Eight cases of malformation were reported in the children of 136 women taking hydralazine hydrochloride during pregnancy. This incidence was not statistically significantly different from the expected rate of 3.8 (9).

Metabolism and toxicokinetics

The main route of excretion of orally administered hydralazine hydrochloride in man is via the urine, as metabolites (10).
Acetylation has been proposed as the main pathway of hydralazine clearance in man (11).

Sensitisation

Previous industrial exposure to hydrazine compounds causing contact dermatitis may produce hypersensitivity in patients to hydralazine hydrochloride (12).

Genotoxicity

Salmonella typhimurium 500 μg $plate^{-1}$ mutation in microorganisms system positive (13).
Salmonella typhimurium TA100, TA1530, TA1537 with or without metabolic activation positive (14,15).

Active in the *Escherichia coli pol A+/A-1*test, indicating an interaction with DNA, but showed no DNA-damaging potency in the liver and lung of intraperitoneally dosed (1×0.42 or 5×0.14 nmole kg^{-1}) Swiss white mice investigated by the alkaline elution technique (15,16).

Other effects

Other adverse effects (human)

Side-effects are common with this antihypertensive drug and include tachycardia, angina pectoris, gastro-intestinal disturbances, fluid retention and lupus (17).

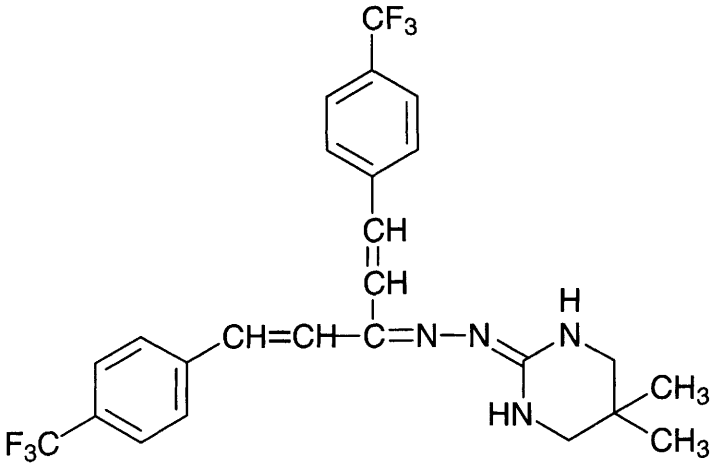
Other comments

Carcinogenic risk to humans reviewed (18).

References

1. McIsaac, W. M. et al *Pharmacol. Exp. Ther.* 1964, **143**, 7-13.
2. *Oyo Yakuri* 1969, **3**, 97.
3. *Drugs in Japan. Ethical Drugs* 6th ed., 1982, p. 619.
4. *J. Pharmacol. Exp. Ther.* 1951, **101**, 368.
5. *IARC Monograph* 1987, **Suppl. 7**, 64.
6. Shimizu, H. et al *Res. Commun. Chem. Pathol. Pharmacol.* 1974, **7**(4), 671-678.
7. Kaufman, D. W. et al *Eur. J. Clin. Pharmacol.* 1989, **36**, 259-264.
8. Curet, L. B. et al *Obstet. Gynecol.* 1979, **53**, 336-340.
9. Heinonen, O. P. et al *Birth Defects in Pregnancy* 1977, Publishing Sciences Group, Inc., Littleton, MA, USA, p. 441.
10. Lesser, J. M. et al *Drug Metab. Dispos.* 1974, **2**, 351-360.
11. Reidenberg, M. M. et al *Clin. Pharmacol. Ther.* 1973, **14**, 970-977.
12. Malten, K. E. et al *Ned. T. Geneesk.* 1962, **106**, 2219-2222.
13. *Res. Commun. Chem. Path. Pharmacol.* 1985, **49**, 415.
14. Tosk, J. et al *Mutat. Res.* 1979, **66**, 247-252.
15. Shaw, C. R. et al *Mutat. Res.* 1979, **68**, 79-84.
16. Parodi, S. et al *Cancer Res.* 1981, **41**(4), 1469-1482.
17. *Martindale. The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
18. *IARC Monograph* 1980, **24**, 85-100

H86 hydramethylnon



$C_{25}H_{24}F_6N_4$ **Mol. Wt.** 494.48 **CAS Registry No.** 67485-29-4

Synonyms tetrahydro-5,5-dimethyl-2(1*H*)-pyrimidinone [3-[4-(trifluoromethyl)phenyl]-1-[2-[4-(trifluoromethyl)phenyl]ethenyl]-2-propenylidene]hydrazone; Amdro; Combat; Maxforce; Cyaforce; Cyclon; Wipeout

RTECS No. UW 7583000

Uses Insecticide.

Physical properties

M. Pt. 185-190°C **Partition coefficient** log P_{ow} 2.31
Solubility Water: 5-7 μg l^{-1} at 25°C. Organic solvents: acetone, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) channel catfish, rainbow trout, bluegill sunfish 0.1, 0.16 and 1.7 mg l^{-1}, respectively (1).
LC_{50} (48 hr) carp 0.39 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* 1.14 mg l^{-1} (1).
Average calculated EC_{50} *Skeletonema costatum, Thalassiosira pseudonana, Isochrysis galbana, Dunaliella tertiolecta* and *Porphyridium cruentum* 1.3-1.9 mg l^{-1} (2).

Bioaccumulation
Low bioaccumulation potential (1).

Environmental fate

Abiotic removal
Decomposes rapidly in sunlight by photolysis, $t_{1/2}$ 1 hr; decomposition is unaffected by temperature (1).

Adsorption and retention
$t_{1/2}$ in sandy loam 7 days, $t_{1/2}$ when incorporated 28 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >2510 mg kg^{-1}, bobwhite quail 1828 mg kg^{-1} (1).
LD_{50} oral ♂, ♀ rat 1130, 1300 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation rat >5 mg l^{-1} (1).
LD_{50} dermal rabbit >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

No-effect level for 28- and 90-day feeding trials in rats 75, 50 mg kg^{-1} diet, respectively (1).
No-effect level for 90-day and 6-month feeding trials in beagles 3 mg kg^{-1} day^{-1} (1).
Leucopenia, with significant non-transient decreases in lymphocytes and eosinophils reported in calves fed 113.5 g day^{-1} for 7 wk (3).

Carcinogenicity and chronic effects

No effect level for 2-yr feeding trial in rats 50 mg kg^{-1} diet (1).
No-effect level for 18 month feeding trial in mice 25 mg kg^{-1} diet (1).

Teratogenicity and reproductive effects

Not teratogenic or embryotoxic in rats and rabbits (dose, duration and route of exposure unspecified) (1).
Foals of horses treated orally for 30 days (dose unspecified) developed clinical illness not observed in controls. No semen abnormalities were reported in treated males (4).

Metabolism and toxicokinetics

Rapidly eliminated in faeces and urine of rats after oral administration (dose unspecified) (1).
No residues found in milk of cows fed 0.05 mg kg^{-1} for 21 days, nor in milk or tissues of goats fed 0.2 mg kg^{-1} day^{-1} for 8 days (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
WHO Toxicity Class III (6).
EPA Toxicity Class III (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Walsh, G. E. et al *Environ. Toxicol. Chem.* 1987, **6**, 767-770.
3. Evans, D. L. et al *Am. J. Vet. Res.* 1984, **45**(5), 1023-1027.
4. Miller, D. M. et al *Proc. Annu. Meet. – Am. Assoc. Vet. Lab. Diagn.* 1984, 379-382.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

H87 hydrazine

$$NH_2NH_2$$

H_4N_2 **Mol. Wt.** 32.05 **CAS Registry No.** 302-01-2

Synonyms diamide; Levoxin; Liozan; Ultra Pure; Deoxy-Sol; Scav-Ox

EINECS No. 206-114-9 **RTECS No.** MU 7175000

Uses Reducing agent. Rocket fuel.

Physical properties

M. Pt. 2°C **B. Pt.** 113°C **Flash point** 52°C **Specific gravity** 1.011 at 15°C with respect to water at 4°C
Partition coefficient log P_{ow} −1.37 **Volatility** v.p. 16 mmHg at 20°C ; v.den. 1.1
Solubility Water: miscible. Organic solvents: miscible with ethanol, methanol, isobutanol, 1- and 2-propanol

Occupational exposure

FR-VME 0.1 ppm (0.1 mg m^{-3})
JP-OEL 0.01 ppm (0.013 mg m^{-3}) (provisional value)
SE-LEVL 0.1 ppm (0.1 mg m^{-3}) **SE-STEL** 0.3 ppm (0.4 mg m^{-3})
UK-LTEL MEL 0.02 ppm (0.03 mg m^{-3}) **UK-STEL** MEL 0.1 ppm (0.13 mg m^{-3})
US-TWA 0.01 ppm (0.013 mg m^{-3})

UN No. 2029 (anhydrous)

UN No. 3293 (aqueous solution with ≤37% hydrazine)

UN No. 2030 (aqueous solution with ≥37% but ≤64% hydrazine) **HAZCHEM Code** 2X (aqueous solution with ≤37% hydrazine) **HAZCHEM Code** 2P (aqueous solution with ≥37% but ≤64% hydrazine)
Conveyance classification corrosive substance, danger of fire (flammable liquid), toxic (anhydrous)
Conveyance classification toxic substance (aqueous solution with ≤37% hydrazine)
Conveyance classification corrosive substance, toxic (aqueous solution with ≥37% but ≤64% hydrazine)
Supply classification toxic
Risk phrases May cause cancer – Flammable – Toxic by inhalation, in contact with skin and if swallowed – Causes burns – May cause sensitisation by skin contact (R45, R10, R23/24/25, R34, R43)
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
LC_{50} (96 hr) *Poecilia reticulata* 0.61-3.85 mg l^{-1} (1).
LC_{50} (96 hr) *Lepomis macrochirus* 1.0-1.6 mg l^{-1} (2).
EC_{50} (96 hr) *Pimephales promelas* 6 mg l^{-1} (3).
LC_{50} (24 hr) roach, goldfish 0.54-0.95 mg l^{-1} (4).
LC_{50} (48 hr) Channel catfish, large mouth bass, green sunfish, 1.6, 3.6, 5.1 mg l^{-1}, respectively (5).

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 0.01 ppm Microtox test (6).
EC_{50} (48 hr) *Daphnia pulex* 0.16-0.19 mg l^{-1} (3).
EC_{50} (48 hr) green algae 10-100 mg l^{-1} (5).
Toxicity threshold (72 hr) *Entosiphon sulcatum* 0.93 mg l^{-1} (7).
Toxicity threshold (16 hr) *Pseudomonas putida* 0.019 mg l^{-1} (8).
Toxic to 10 species of Phaeophyta with *Pterygophora californica* being the most resistant, and *Nereocystis luetkeana* the least (9).

Environmental fate

Nitrification inhibition
75% inhibition of non-acclimated sewage sludge at 48 mg l^{-1} (10).
10 and 100 μg g^{-1} had no effect on nitrification after 49 days in Arredondo soil, no significant nitrification occurred in 500 μg g^{-1} treatment (11).

Degradation studies
Co-metabolised to nitrogen gas by *Nitrosomonas* (12).
Reduced to ammonia by nitrogenase isolated from *Azobacter vinelandii* (13).

When added continuously to a waste-water treatment plant, only concentrations <1 mg l^{-1} ensured complete absence of hydrazine from effluent without inhibiting treatment efficiency (14).
An *Achromobacter* species degraded hydrazine at concentrations <100 μg l^{-1} and had a short lag growth period. A *Bacillus* species and a *Pseudomonas* species degraded hydrazine at concentrations <25 μg l^{-1} with a lag growth period of 3-5 days when grown in glucose-amended basal mineral medium (15).
Low concentrations (10 μg g^{-1}) disappeared rapidly (1.5 hr) from Arredondo soil via autooxidation. 100 and 500 μg g^{-1} disappeared completely in 1 and 8 days, respectively; biodegradation accounted for 20% of the disappearance and there was no evidence of conversion into ammonia. Soil respiration was initially inhibited temporarily due to reduction of bacterial populations; CO_2 production recovered after 2 days and was then enhanced, levelling off after 6-7 days (11).
Achromobacter enhanced hydrazine degradation in water samples but not in Arredondo soil (16).

Adsorption and retention
Dilute hydrazine leached completely through a column of sand, but was adsorbed or, if soil contained a moderate amount of clay, decomposed in a column of soil (5).
Organic matter content influences soil adsorption (17).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 60 mg kg^{-1} (18).
LC_{50} (4 hr) inhalation mouse, rat (4 hr) 252, 570 ppm, respectively (19).
LD_{50} dermal rabbit 91 mg kg^{-1} (20).
LD_{50} intravenous rat, mouse 55, 57 mg kg^{-1}, respectively (18).
LD_{50} intraperitoneal rat, mouse 59, 62 mg kg^{-1}, respectively (18).

Sub-acute and sub-chronic data
Increased mortality and lethargy reported in mice, reduced blood cell count, haemocrit and haemoglobin values in dogs exposed to 1.3 mg m^{-3} continuously or 6.5 mg m^{-3}, 6 hr day^{-1}, 5 days wk^{-1} for 6 months (21).
Reversible megamitochondria and hepatic necrosis reported in rats and rabbits, respectively, fed 5-20 mg kg^{-1} for 3-10 days and 14.6-32.3 mg intravenously for 5 days, respectively (22,23).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (24).
Produced liver, lung and mammary tumours in F_0 and F_1 generations in mice after oral administration. Produced lung tumours, leukaemia and sarcomas in mice after intraperitoneal administration (24,25).
Produced lung and liver tumours in rats after oral administration (24).
Produced nasal tumours in rats, tumours and thyroid adenomas in hamsters, and a slight excess of lung adenomas in mice after inhalation (26).
Weakly carcinogenic in rats receiving 50 mg l^{-1} in drinking water for life; late occurrence of small, normally benign liver cell tumours reported (27).

Teratogenicity and reproductive effects
Reduced number of viable foetuses and reduced foetal weight, but no major malformations reported in rats after subcutaneous administration of 8 mg kg^{-1} on days 11-20 of pregnancy (28).
Increased resorptions reported in rats after intraperitoneal injection of 5 or 10 mg kg^{-1} on days 6-15 of pregnancy and increased incidence of foetal abnormalities (supernumerary and fused ribs, delayed ossification, hydronephrosis and brain ventricle dilation) in those receiving 10 mg kg^{-1} on days 7-9 (29).
Increased incidence of foetal abnormalities (exencephaly, hydronephrosis and supernumerary ribs) reported in mice after intraperitoneal administration of 12 or 20 mg kg^{-1} on days 6-9 of pregnancy (30).

Metabolism and toxicokinetics
55% of dermally applied hydrazine absorbed through skin of rabbits; maximum serum concentration occurred 1 hr after application (31).

After intraperitoneal administration to rats, $t_{1/2}$ in blood 44 min during first 3 hr after exposure, followed by a slower phase with $t_{1/2}$ 27 hr (32).
Distributed to and eliminated rapidly from most tissues after intraperitoneal or subcutaneous administration to rats and mice (33).
Significant part excreted unchanged or as acetylhydrazine in urine of dogs after subcutaneous, intraperitoneal or intravenous administration. Small amounts of diacetylhydrazine recovered from urine of treated rabbits, rats and mice but not dogs (34).
Urinary excretion and plasma $t_{1/2}$ decreased by pretreatment with microsomal enzyme inducers like phenobarbital in rats (35).
Oxyhaemoglobin in erythrocytes and liver microsomal oxygenases can catalyse oxidation to nitrogen *in vitro*; diazene may be the intermediate (36).
Rat liver cytochrome P_{450} implicated in formation of a free radical diazene precursor during microsomal oxidation (35).
20-30% of radio-labelled hydrazine was converted into nitrogen in rats and mice and excreted via the lungs in the first 2 hr (32,36).
Metabolism studied *in vivo* in rats after administration of single doses of 64 mg kg^{-1} [$^{15}N_2$]hydrazine. Urinary metabolites detected were: ammonia, unchanged hydrazine, acetylhydrazine, diacetylhydrazine, carbazic acid (from reaction of CO_2 and hydrazine), and hydrazone. Presence of ^{15}N-enriched urea as well as ammonia suggests *in vivo* cleavage of the N-N bond, possibly by N-oxidation and the resultant assigned to a metabolite resulting from cyclisation of the 2-oxoglutarate hydrazone (37).
Evidence for NADPH-cytochrome P_{450} reductase catalysed oxidation of hydrazine to its radical in the presence of O and NADPH reported in *in vitro* studies on rat liver microsomes (38).

Irritancy
Slight eye irritation reported in monkeys exposed to 1.3 mg m^{-3} continuously or 6.5 mg m^{-3}, 6 hr day^{-1}, 5 days wk^{-1} for 6 months (21).
Skin and eye irritation reported after occupational exposure (39).
Severe exposure to the vapour causes temporary blindness lasting 24 hr (40).
The liquid causes severe eye and skin burns (41).

Sensitisation
A case of systemic lupus erythmatosus-like disease due to occupational exposure has been reported. The individual patch-tested positive due to genetic predisposition (39).
Dermatitis and positive patch-tests reported in workers exposed to hydrazine in: pharmaceutical manufacturing, corrosion inhibitors, hydrazine sulfate production, and soldering flux in the electronics industry. Cross-sensitisation reported to hydrazine derivatives including isoniazid, phenylhydrazine and hydralazine (39).

Genotoxicity

Salmonella typhimurium TA100, TA1535, TA98 with metabolic activation positive. TA1537 with metabolic activation negative. TA1538 with metabolic activation negative. TA100, TA1535 without metabolic activation positive (42-44).
Escherichia coli WP2 *uvr*A without metabolic activation positive. *Saccharomyces cerevisiae* forward mutation assay without metabolic activation positive (45).
Mouse lymphoma L5178Y cell assay *in vitro* without metabolic activation positive, and negative results reported (46,47).
Chinese hamster cells *in vitro* without metabolic activation sister chromatid exchanges positive, and negative results reported (48,49).
Did not induce chromosomal aberrations in rat cells (type unspecified) *in vitro* without metabolic activation (50).
Induced unscheduled DNA synthesis in human fibroblasts *in vitro* with metabolic activation and in transformed human cells *in vitro* without metabolic activation (51,52).
Induced aneuploidy and sex-linked recessive lethal mutations in *Drosophila melanogaster* (53).
Micronucleus test and dominant lethal tests in mice negative (54,55).

Other effects

Other adverse effects (human)

Vomiting, weakness, somnolence and arrhythmia occurred in a laboratory technician who ingested 20-30 ml of a 6% aqueous solution. Violent behaviour, oliguria, confusion, peripheral neuropathy, haematuria, respiratory problems, liver disorder and coma have also been reported after accidental oral, inhalation and dermal exposure (39).

A high incidence of myocardial infarction reported in hydrazine manufacturing workers (39).

Observed mortality was close to that expected for lung cancer, other cancers and all other causes in 427 ♂ hydrazine manufacturing workers exposed to 0.6-13 mg m^{-3} for > 6 months between 1945 and 1971. The workers were followed until 1982 and the morbitities in the cohort are still being followed up (56).

Any other adverse effects

Rat hepatocyte suspensions incubated with various concentrations of hydrazine (0-20 mM) for 1, 2, and 3 hr suffered both concentration- and time-dependent loss of ATP, reduced glutathione (GSH) and cell viability. Experimental findings suggested that the cytotoxicity of hydrazine and its effects on urea synthesis and GSH levels are not a direct result of ATP depletion (57).

Legislation

Land disposal prohibited under U.S. Federal Resource Conservation and Recovery Act (58).

Emission from hazardous waste incinerators controlled by U.S. Federal Solid Waste Disposal Act and amendments (59).

Other comments

Human, experimental and ecotoxicity reviewed (39,60).

Toxicology reviewed (61-63).

References

1. Slonium, A. R. *Water. Res.* 1977, **11**, 889-895.
2. Hunt, T. P. et al *Bull. Environ. Contam. Toxicol.* 1981, **27**, 588-595.
3. Velte, J. S. *Bull. Environ. Contam. Toxicol.* 1984, **33**, 598-604.
4. Proteau, J. P. et al *Ann. Limnol.* 1979, **15**, 337-346.
5. Heck, W. W. et al *Environmental Pollution by Missile Propellants* 1963, Wright-Patterson Airforce Base, Aerospace Med. Res. Lab., OH, USA.
6. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
7. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser-Abwasser* 1981, **122**, 308-313.
8. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
9. James, D. E. et al *Hydrobiologia* 1987, 151-152.
10. Meink, F. et al *Les Eaux Residuaires Industrielles* 1970.
11. Ou, L. T. *Bull. Environ. Contam. Toxicol.* 1987, **38**(1), 179-183.
12. Kane, D. A. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 447-453.
13. Davis, L. C. *Arch. Biochem. Biophys.* 1980, **204**, 270-276.
14. Farmwald, J. A. et al *J. Water Pollut. Control Fed.* 1981, **53**, 565-575.
15. Ou, L. T. *Bull. Environ. Contam. Toxicol.* 1987, **39**(1), 78-85.
16. Ou, L. T. *Bull. Environ. Contam. Toxicol.* 1987, **39**(3), 541-548.
17. Isaacson, P. J. et al *J. Soil Sci.* 1984, **35**(1), 79-92.
18. *Med. Prac.* 1973, **24**, 71.
19. *Arch. Ind. Health* 1955, **12**, 609.
20. *Arch. Ind. Hyg. Occup. Med.* 1954, **9**, 199.
21. Haun, C. C. et al *Proc. 4th Ann. Conf. Environ. Toxicol. Fairborn, Ohio* 1973, Wright-Patterson Air Force Base, Aerospace Med. Res. Lab.
22. Wakabayashi, T. et al *Exp. Mol. Pathol.* 1983, **39**, 139-153.
23. Noda, A. et al *J. UOEH* 1983, **5**, 183-189.
24. *IARC Monograph* 1974, **4**, 127.

25. Menon, M. M. et al *J. Cancer Res. Clin. Oncol.* 1983, **105**, 258-261.
26. Vernot, E. H. et al *Fundam. Appl. Toxicol* 1985, **5**, 1050-1064.
27. Steinhoff, D. et al *Exp. Pathol.* 1988, **33**(3), 133-143.
28. Lee, S.H. et al *Arch. Environ. Health* 1970, **21**, 615-619.
29. Keller, W. C. et al *Evaluation of the Embryotoxicity of Hydrazine in Rats* 1982, Wright-Patterson Air Force Base, Aerospace Med. Res. Lab., OH, USA.
30. Lyng, R. D. et al *Effects of Hydrazine on Pregnant ICR Mice* 1980, Wright-Patterson Air Force Base, Aerospace Med. Res. Lab., OH, USA.
31. Anderson, M. E. et al in: Drill, V.A. et al (Eds.) *Cutaneous Toxicity* 1984, Raven Press, New York, NY, USA.
32. Springer, D. L. et al *J. Toxicol. Environ. Health* 1981, **8**, 21-29.
33. Kaneo, Y. et al *J. Pharmacobio-Dyn.* 1984, **7**, 556-562.
34. McKennis, H. et al *AMA Arch. Ind. Health* 1955, **12**, 511-514.
35. Noda, A. et al *Toxicol. Lett.* 1985, **25**, 313-317.
36. Nelson, S. D. et al *Adv. Exp. Med. Biol.* 1982, **136B**, 971-981.
37. Preece, N. E. et al *Biochem. Pharmacol.* 1991, **41**(9), 1319-1324.
38. Noda, A. et al *Biochem. Biophys. Res. Commun.* 1988, **153**(1), 256-260.
39. *Environmental Health Criteria 68: Hydrazine* 1987, WHO, Geneva, Switzerland.
40. Comstock, C. C. et al *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 476.
41. Clayton, G. D. et al (Eds.) *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, Interscience Publishers, New York, NY, USA.
42. Anderson, D. et al *Br. J. Cancer* 1978, **37**, 924-930.
43. Herbold, B. et al *Mutat. Res.* 1976, **40**, 73-84.
44. Wade, D. R. et al *Mutat. Res.* 1981, **89**, 9-20.
45. von Wright, A. in: Seeberg, E. et al (Eds.) *Chromosome Damage and Repair* 1981, Plenum Press, New York, NY, USA.
46. Rogers, A. M. et al *Mutat. Res.* 1981, **89**, 321-328.
47. Amacher, D. E. et al *Mutat. Res.* 1980, **72**, 447-474.
48. Perry, P. E. et al *Prog. Mutat. Res.* 1981, **1**, 560-569.
49. MacRae, W. D. et al *Mutat. Res.* 1979, **68**, 351-365.
50. Dean, B. J. *Prog. Mutat. Res.* 1981, **1**, 570-579.
51. Tsuchimoto, T. et al *Prog. Mutat. Res.* 1981, **1**, 705-711.
52. Epstein, S. S. et al *Toxicol. Appl. Pharmacol.* 1972, **23**, 288-325.
53. Agrelo, C. et al *Prog. Mutat. Res.* 1981, **1**, 528-532.
54. Martin, C. N. et al *Prog. Mutat. Res.* 1981, **1**, 533-537.
55. Shukla, P. T. *Mutat. Res.* 1972, **16**, 363-371.
56. Wald, N. et al *Br. J. Ind. Med.* 1984, **41**(1), 31-34.
57. Kerai, M. D. et al *Toxicology* 1997, **120**(3), 221-230.
58. US EPA *Fed. Regist.* 31 Jan. 1991, **56**(21), 3864-3928.
59. US EPA *Fed. Regist.* 21 Feb. 1991, **56**(35), 7134-7239.
60. *Dangerous Prop. Ind. Mater. Rep.* 1990, **10**(1), 21-58.
61. *Cah. Notes Doc.* 1989, **136**, 537-542.
62. Bressa, G. *DA Dif. Ambientale* 1989, **13**(2), 14-15.
63. Gigantesco, M. et al *Ann. Med. Nav.* 1987, **92**(4), 811-816

H88 hydrazine hydrate

$$NH_2NH_2H_2O$$

H_6N_2O **Mol. Wt.** 50.06 **CAS Registry No.** 10217-52-4

RTECS No. MV 4590000

Uses Reducing agent, solvent, in rocket propellant and in manufacture of 'Helman' catalyst.

Physical properties

M. Pt. –51.7°C **B. Pt.** 118°C **Flash point** 73°C **Specific gravity** 1.0305 at 21°C
Solubility Water: miscible with water. Organic solvents: miscible with ethanol

Occupational exposure

UN No. 2030 **HAZCHEM Code** 2P **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Irritancy
Causes delayed eye irritation (species and duration unspecified) (1).

Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation positive (2).
Induced direct DNA damage in *Escherichia coli* (2).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. De Flora, S. et al *Mutat. Res.* **1984, 133**, 161-198

H89 hydrazine sulfate

$$NH_2NH_2 \cdot H_2SO_4$$

$H_6N_2O_4S$ **Mol. Wt.** 130.12 **CAS Registry No.** 10034-93-2

Synonyms hydrazine hydrogen sulfate; hydrazine monosulfate; hydrazinium sulfate; hydrazonium sulfate; NSC-150014; HS

EINECS No. 233-110-4 **RTECS No.** MV 9625000

Uses In gravimetric analysis of nickel, cobalt and cadmium. In refining rare metals. Antioxidant in soldering flux for light metals. Reducing agent in mineral and slag analysis. For separating polonium from tellurium. Blood tests. For destroying fungi and moulds.

Physical properties

M. Pt. 254°C **Specific gravity** 1.370
Solubility Water: soluble

Occupational exposure

Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation, in contact with skin and if swallowed – May cause sensitisation by skin contact (R45, R23/24/25, R43)
Safety phrases 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)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 601, 740 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal mouse, rat 152, 230 mg kg^{-1}, respectively (3,2).

Carcinogenicity and chronic effects

Statistically significant excess of lung tumours reported in ♂ and ♀ mice fed 1.1 mg day^{-1} for life, and in their offspring (4).
0.2 ml $mouse^{-1}$ 1 × wk^{-1} for 8 wk by gavage or 0.1 ml $mouse^{-1}$ 1 × wk^{-1} for 8 wk by intraperitoneal injection had a weak carcinogenic effect, inducing lung tumours (5).
Oral administration to ♂ and ♀ rats of 18 and 12 mg kg^{-1} day^{-1} for 68 wk, respectively, and 1.13 mg kg^{-1} day^{-1} for 36 wk caused increased incidence of liver and lung tumours (6).

Irritancy

Caused moderate eye irritation in rabbits when applied at 20 mg for 24 hr (1).

Genotoxicity

Bacillus subtilis H17/M45 positive, HLL3g/HJ-15 negative; *Escherichia coli* without metabolic activation positive (7).
DNA repair test on mouse hepatocytes positive (8).
Induced unscheduled DNA synthesis in human fibroblasts *in vitro* (9).

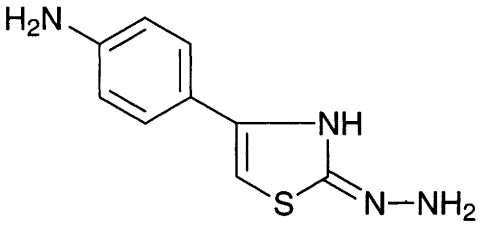
Other comments

Activity and clinical studies in cancer reviewed (10).

References

1. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechosiovakia.
2. *Russ. Pharmacol. Toxicol. (Engl. Transl.)* 1978, **41**, 74.
3. *Arch. Environ. Health* 1968, **17**, 315.
4. Menon, M. M. et al *J. Cancer Res. Clin. Oncol.* 1983, **105**, 258-261.
5. Kelly, M. G. et al *J. Natl. Cancer Inst.* 1969, **42**, 337-344.
6. Severi, L. et al *J. Natl. Cancer Inst.* 1968, **41**, 331-349.
7. Suter, W. et al *Mutat. Res.* 1982, **97**, 1.
8. Mori, H. et al *Jpn. J. Cancer Res.* 1988, **79**(2), 204-211.
9. Agrelo, C. et al *Prog. Mutat. Res.* 1981, **1**, 528-532.
10. Gold, J. *Nutr. Cancer* 1987, **9**, 59-66

H90 2-hydrazino-4-(*p*-aminophenyl)thiazole



$C_9H_{10}N_4S$ **Mol. Wt.** 206.27 **CAS Registry No.** 26049-71-8

Synonyms 2-hydrazino-4-(4-aminophenyl)thiazole

RTECS No. XJ 2880000

Uses Plant growth regulant.

Physical properties

M. Pt. 180°C

Solubility Organic solvents: benzene

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Mammary and salivary gland adenocarcinomas occurred in ♀ Sprague-Dawley rats fed a cumulative dose of 2.4 g rat^{-1} in the diet over 26 wk. Lymphosarcomas of the liver and spleen were also reported at low incidence (1).

Low incidences of lymphocytic leukaemia reported in ♀ Swiss mice fed a cumulative dose of 0.20 g $mouse^{-1}$ in the diet over 46 wk (2).

Mammary fibroadenomas and adenocarcinomas were observed in ♀ Sprague-Dawley rats fed a cumulative dose of 0.52 g rat^{-1} in diet over 46 wk. Splenic hyperplasia was also reported (3).

References

1. Cohen, S. M. et al *Cancer Res.* 1970, **30**, 897-901.
2. Cohen, S. M. et al *Cancer Res.* 1973, **33**, 1593-1597.
3. Cohen, S. M. et al *J. Natl. Cancer Inst.* 1973, **51**(2), 403-417

H91 2-hydrazinoethanol

$$NH_2NHCH_2CH_2OH$$

$C_2H_8N_2O$ **Mol. Wt.** 76.10 **CAS Registry No.** 109-84-2

Synonyms (2-hydroxyethyl)hydrazine; (β-hydroxyethyl)hydrazine; ethanolhydrazine; 2-hydrazinoethyl alcohol; hydrazinoethanol; Omaflora; Brombloom

EINECS No. 203-711-6 **RTECS No.** KL 2800000

Physical properties

M. Pt. –70°C **B. Pt.** 110-130°C at 17.5 mmHg **Flash point** 73°C **Specific gravity** 1.123

Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 139 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Turkey poults 2-6 wk posthatch fed 10 ppm showed severe depression of body weight. A significant increase in the ratio of granulocytes to agranulocytes was seen in poults fed 50 ppm (2).

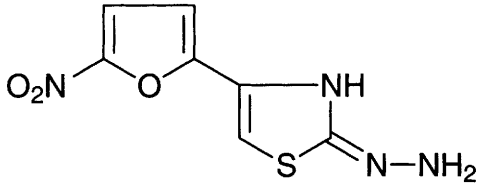
Genotoxicity

DNA-repair test on mouse and rat hepatocytes negative (3).

References

1. *Oyo Yakuri* 1968, **2**, 76.
2. Czarnecki, C. M. *Comp. Biochem. Physiol., C: Comp. Pharmacol. Toxicol.* 1988, **91C**(2), 607-611.
3. Mori, H. et al *Jpn. J. Cancer Res.* 1988, **79**(2), 204-211

H92 2-hydrazino-4-(5-nitro-2-furyl)thiazole



$C_7H_6N_4O_3S$ **Mol. Wt.** 226.22 **CAS Registry No.** 26049-68-3

Synonyms 2-hydrazino-4-(5-nitro-2-furanyl)thiazole

RTECS No. XJ 4900000

Physical properties

M. Pt. 189-191°C

Mammalian & avian toxicity

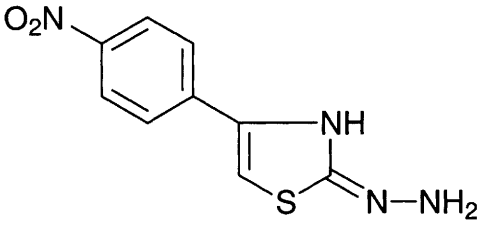
Carcinogenicity and chronic effects

Mammary and salivary gland adenocarcinomas occurred in ♀ Sprague-Dawley rats fed a cumulative dose of 4.2 g rat^{-1} in the diet over 46 wk. Liver cystic adenomas, perianal gland adenocarcinomas, bronchiolar adenomas, uterine fibroadenomas, renal cell carcinomas and kidney and liver sarcomas were also reported at low incidence (1). High incidence of forestomach tumours (papillomas and carcinomas) reported in ♀ Swiss mice fed a cumulative dose of 0.96 g $mouse^{-1}$. Two pulmonary alveolar carcinomas were also reported and leukaemia also occurred at low incidence (2).

References

1. Cohen, S. M. *Cancer Res.* 1970, **30**(4), 897-901.
2. Cohen, S. M. *Cancer Res.* 1973, **33**, 1593-1597

H93 2-hydrazino-4-(*p*-nitrophenyl)thiazole



$C_9H_8N_4O_2S$ **Mol. Wt.** 236.25 **CAS Registry No.** 26049-70-7

RTECS No. XJ 5075000

Physical properties

M. Pt. 166-169°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Mammary and salivary gland adenocarcinomas occurred in ♀ Sprague-Dawley rats fed a cumulative dose of 7.3 g rat^{-1} in diet over 46 wk. Lung alveolar cell carcinomas, perianal gland and ceruminous gland adenocarcinomas and squamous-cell carcinomas of the forestomach and skin were also reported at low incidence (1).

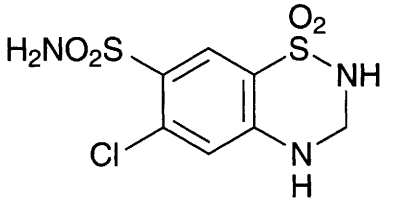
Low incidence of lymphocytic leukaemia reported in ♀ Swiss mice fed a cumulative dose of 0.2 g $mouse^{-1}$ in diet over 46 wk. A single mammary adenocarcinoma was reported in two mice (2).

Mammary fibroadenomas and adenocarcinomas were observed in ♀ Sprague-Dawley rats fed a cumulative dose of 0.54 g rat^{-1} in diet for 46 wk. Lymphoblastic lymphoma involving the spleen and bone marrow was also reported (3).

References

1. Cohen, S. M. et al *Cancer Res.* 1970, **30**(4), 897-901.
2. Cohen, S. M. et al *Cancer Res.* 1973, **33**, 1593-1597.
3. Cohen, S. M. et al *J. Natl. Cancer Inst.* 1973, **51**(2), 403-417

H94 hydrochlorothiazide



$C_7H_8ClN_3O_4S_2$ **Mol. Wt.** 297.74 **CAS Registry No.** 58-93-5

Synonyms 6-chloro-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide-1,1-dioxide; Aquarius; Diclotride; 3,4-dihydrochlorothiazide; Esidrex; Hypothiazide; Dichlorosuric; Hydrodiuril; Hydro-Saluric; Oretic

EINECS No. 200-403-3 **RTECS No.** DK 9100000

Uses Diuretic used in the treatment of oedema and hypertension.

Physical properties

M. Pt. 273-275°C

Solubility Water: Practically insoluble in water. Organic solvents: acetone, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1175 mg kg^{-1} (1).

LD_{50} intraperitoneal rat, mouse 234, 578 mg kg^{-1}, respectively (2).

LD_{50} subcutaneous rat, mouse 1270, 1470 mg kg^{-1}, respectively (2).

LD_{50} intravenous dog, rabbit, rat 250, 461, 990 mg kg^{-1}, respectively (2,3).

Sub-acute and sub-chronic data

F344 rats and B6C3F1 mice up to 50,000 ppm in feed for 15 day or 13 wk caused increased nephrosis and mineralisation of the kidney corticomedullary junction, but no deaths in rats, and nephrosis and calculi, inflammation, and epithelial hyperplasia in the urinary bladder, with deaths in ♂ mice at high doses (4).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice orally in feed. No evidence of carcinogenicity in rats or ♀ mice, equivocal evidence for carcinogenicity (marginal increase in neoplasms which may be chemically related) in ♂ mice (5).

♂ mouse 5000 ppm in feed equivocal evidence of liver adenoma/carcinoma (6).

0, 250, 500 and 2000 ppm in feed for 2 yr in rats caused severe renal disease with secondary parathyroid hyperplasia and fibrous osteodystrophy of the bone (4).

0, 2500, 5000 ppm in feed to mice for 2 yr caused no neoplasms in ♀ mice (4).

Teratogenicity and reproductive effects

Oral rat and mouse (days 6 to 15 of gestation). 0, 100, 300 or 1000 and 0, 100, 300 or 3000 mg kg^{-1} day^{-1}, respectively. Rats and mice were evaluated at days 20 and 17 of gestation, respectively. No maternal toxicity was observed; there was also no definite evidence of embryotoxicity or foetal toxicity (7).

Metabolism and toxicokinetics

2-amino-4-chloro-*m*-benzenedisulfonamide was detected in urine and erythrocytes of a patient receiving hydrochlorothiazide (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (9).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges positive, chromosomal aberrations negative (10).

In vitro mouse lymphoma L51784 forward mutation assay positive at tk locus without metabolic activation (11).

Other effects

Other adverse effects (human)

Phototoxic to human skin (12).

A 70-yr-old woman developed a noncardiac pulmonary oedema with initial symptoms of nausea, shortness of breath and diaphoresis after taking an Aldactazide tablet containing 25 mg hydrochlorothiazide (13).

A 54-yr-old woman with hypertension had seizures and a focal neurologic deficit associated with hyponatraemia when her duiretic was changed to Dyazide (50 mg hydrochlorothiazide, 50 mg triamterene) (14).

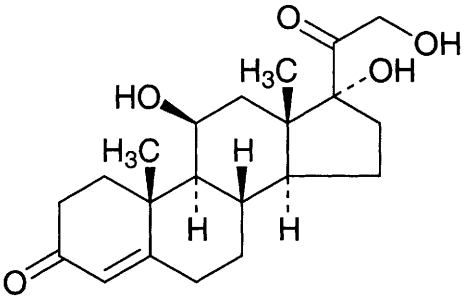
Legislation

Included in Schedule 4 and 6 (Release Into Air/Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (15).

References

1. *Farm. Zh. (Kiev)* 1983, **1**, 44.
2. Barnes, C. D. et al *Drug Dosages in Laboratory Animals – A Handbook* 1973, Univ. California Press, Berkeley, CA, USA.
3. *J. Pharmacol. Exp. Ther.* 1963, **140**, 249.
4. Bucher, J. R. *J. Appl. Toxicol.* 1990, **10**(5), 359-367.
5. *National Toxicology Program Research and Testing Division* 1992 Report No. PB90110156/AS, NIEHS, Research Triangle Park, NC 27709, USA.
6. Haseman, J. K. et al *Environ. Mol. Mutagen.* 1990, **16**(Suppl. 18), 15-31.
7. George, J. D. et al *Fundam. Appl. Toxicol.* 1995, **26**(2), 174-180.
8. Okuda, T. et al *Chem. Pharm. Bull.* 1987, **35**(8), 3516-3518.
9. Zeiger, E. et al *Environ. Mol. Mutagen.* 1990, **16**(Suppl. 18), 32-54.
10. Anderson, B. E. et al *Environ. Mol. Mutagen.* 1990, **16**(Suppl. 18), 55-137.
11. Myhr, B. et al *Environ. Mol. Mutagen.* 1990, **16** (Suppl. 18), 138-167.
12. Diffey, B. L. et al *Photochem. Photobiol.* 1988, **47**(1), 49-53.
13. Levay, I. D. *Drug Intell. Clin. Pharm.* 1984, **18**, 238-239.
14. Johnson, J. E. et al *South. Med. J.* 1983, **76**, 1363-1367.
15. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

H95 hydrocortisone



$C_{21}H_{30}O_5$ **Mol. Wt.** 362.47 **CAS Registry No.** 50-23-7

Synonyms 11,17,21-trihydroxypregn-4-ene-3,20-dione; cortisol; Corticreme; Hycortol; 17-hydroxycorticosterone; 11β,17,21-trihydroxyprogesterone; Barseb HC; Cetacourt; Dermacourt; Eldecort; Hydrocortone

EINECS No. 200-020-1 **RTECS No.** GM 8925000

Uses Anti-inflammatory hormone.

Occurrence Isolated from adrenal glands.

Physical properties

M. Pt. 212-213°C

Solubility Water: 0.25 mg ml^{-1} at 25°C. Organic solvents: acetone, chloroform, diethyl ether, ethanol, methanol

Ecotoxicity

Fish toxicity

Juvenile rainbow trout fed cortisol (dose unspecified) for 10 wk exhibited reduced growth and condition, liver glycogen and circulating lymphocytes, together with increased resting plasma glucose and haematocrit (1).

Freshwater rainbow trout injected 3 × wk^{-1} with 10 μg cortisol g^{-1} for 28 day had increased gill Cl^- cell number and Na^+/K^+ – ATPase activity with decreased muscle water (2).
Found to regulate rainbow trout fibroblast proliferation via the corticosteroid receptor (3).

Invertebrate toxicity
0.8, 0.5, 0.1, 0.01 and 0.001 μg μl^{-1} applied to lower abdomen of *Oncopeltus fasciatus* for 6 days increased the rate of development and significantly increased body weights of treated insects (4).

Environmental fate

Degradation studies
Δ-dehydrogenation to predisolone by *Arthrobacter simplex* By-2-13 did not follow Michaelis-Menten kinetics (5).

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal rat 150 mg kg^{-1} (6).
LD_{50} subcutaneous rat 449 mg kg^{-1} (7).

Carcinogenicity and chronic effects
Hydrocortisone enhanced growth of cells in a human undifferentiated gastric carcinoma cell line (MKN45) (8).

Teratogenicity and reproductive effects
250 μg administered neonatally to rat intraperitoneally delayed vaginal opening and the onset of the first oestrus. Ovarian oestradiol secretion and development of oestradiol secretion receptors in the uterus were not affected (8).
Hydrocortisone injected on day 11 of gestation (dose unspecified) prevented fusion of the palatal shelves (9).
Pregnant C57BL/10Sn mice dosed intramuscularly with 0, 200, 400, 600, 800 mg kg^{-1} on day 12 of gestation and evaluated on day 18 showed dose-dependent induction of cleft palate and retarded intra-uterine growth at all doses (10).
Five foetal lambs infused with 17 mg hydrocortisone day^{-1} at day 129 of gestation showed accelerated parenchymal maturation, expressed in terms of either morphogenesis of the gas exchange area or differentiation of type II alveolar cells (11).

Metabolism and toxicokinetics
16 hr after *in vitro* topical application of 10 μg to 2 cm^{-2} to mouse skin, extent of permeation was 18.1%; cortisone was identified as a metabolite (12).
Erythrocyte-to-plasma ratio in whole blood with 0.18-10.8 μg ml^{-1} hydrocortisone added was 2.4. Increasing the concentration to 0.18-0.68 μg ml^{-1} increased erythrocyte uptake by 16-28% of the amount of hydrocortisone added (13).
Metabolism by 17-dehydroxylation to a 17-deoxy-21-oic acid in mouse liver requires an enol aldehyde intermediate (14).
Oxidative metabolite 6β-hydroxycortisol detected in urine (15).
Metabolites 20α-dihydrocortisol and 5α,3β-tetrahydrocortisol detected in material serum of pregnant BIOA mice injected with 0-800 mg kg^{-1} hydrocortisone (10).

Genotoxicity

Salmonella typhimurium TA97a, TA98, TA100, TA1535 without metabolic activation caused decrease in his^+ revertants and inhibition of bacterial lawn formation (16).
In vitro human lymphocyte cells 1, 10 μg ml^{-1} showed dose-related increase in chromatid and chromosome type aberrations (16).
Swiss albino mice micronucleus assay 1 × 10^5 μg kg^{-1} body weight showed dose-dependent increases in micronucleated polychromatic erythrocytes and sister chromatid exchange frequency (16).

Other effects

Other adverse effects (human)

A low rate of catabolism by human lymphocytes correlates with a high sensitivity of the cells to the steroid and causes them to die at a greater rate than controls (17).

Any other adverse effects

30 mg kg^{-1} administered intramuscularly to ♂ albino rats elevated urinary excretion of H^+ in the form of titrated acids and NH^{4+} (18).

Injections of hydrocortisone to rats induced activity of digestive enzymes in the small intestine more than in the kidney or liver (19).

Hydrocortisone enhanced growth of cells in a human undifferentiated gastric carcinoma cell line (MKN45) (20).

References

1. Barton, B. A. et al *Dis. Aquat. Org.* 1987, **2**(3), 173-185.
2. Hadsen, S. S. *Comp. Biochem. Physiol., A: Comp. Physiol.* 1990, **95A**(1), 171-175.
3. Lee, L. E. J. *Cell Tissue Kinet.* 1989, **22**(4), 291-301.
4. Gawienowski, A. M. et al *Life Sci.* 1987, **40**(17), 1725-1730.
5. Zhong, L. et al *Weishengwu Xuebao* 1987, **27**(1), 45-51 (Ch.) (*Chem. Abstr.* **106**, 172712g).
6. *Jpn. J. Med.* 1971, **11**, 377.
7. *Toxicol. Appl. Pharmacol.* 1966, **8**, 250.
8. Tinnikov, A. A. et al *Probl. Endokrinol.* 1988, **34**(6), 76-79 (Russ.) (*Chem. Abstr.* **110** 51508u).
9. Shah, R. M. et al *J. Craniofacial Genet. Dev. Biol.* 1986, **2**, 277-283.
10. Roberts, L. G. et al *J. Craniofacial Genet. Dev. Biol.* 1987, **7**, 341-356.
11. Kendall, J. Z. et al *J. Dev. Physiol.* 1990, **13**(3), 165-172.
12. Kao, J. et al *J. Pharmacol. Exp. Ther.* 1987, **241**(2), 482-487.
13. Driessen, O. et al *Ther. Drug Monit.* 1989, **11**(4), 401-407.
14. Singer, C. J. et al *Endocrinology (Baltimore)* 1986, **19**(3), 1356-1361.
15. Morita, K. et al *Rinsho Yakuri* 1987, **18**(3), 509-513.
16. Bali, D. et al *Environ. Mol. Mutagen.* 1990, **16**(4), 250-254.
17. Klein, A. et al *Biochem. Cell Biol.* 1990, 68(4), 810-813.
18. Krishtal, N. V. et al *Fiziol. Zh. (Kiev)* 1989, **35**(1), 59-62 (Russ.) (*Chem. Abstr.* **110** 108584x).
19. Nikitina, A. A. et al *Zh. Evol. Biokhim. Fiziol.* 1990, **26**(2), 273-276.
20. Motoyama, T. et al *Acta Med. Biol. (Niigata)* 1986, **34**(2), 39-45

H96 hydrogen

$$H_2$$

H_2 **Mol. Wt.** 2.02 **CAS Registry No.** 1333-74-0

Synonyms protium; dihydrogen; molecular hydrogen; orthohydrogen; parahydrogen

EINECS No. 215-605-7 **RTECS No.** MW 8900000

Uses Used in welding. Manufacture of ammonia, synthetic methanol, hydrochloric acid, tungsten. Hydrogenation of oils, fats, naphthalene, phenol. In balloons and airships. In thermonuclear reactions. Liquid used in bubble chambers to study subatomic particles and as a coolant. As a fuel.

Occurrence The most abundant element in the known universe.

Physical properties

M. Pt. –259.18°C **B. Pt.** –252.8°C **Specific gravity** 0.0899 g l^{-1}

Volatility v.p. 1570 mm Hg at –250°C (liquid); v.den. 0.069

Occupational exposure

UN No. 1049 (compressed); 1966 (refrigerated liquid) **HAZCHEM Code** 2SE (compressed); 2WE (refrigerated liquid) **Conveyance classification** flammable gas
Supply classification extremely flammable
Risk phrases Extremely flammable (R12)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Environmental fate

Nitrification inhibition
Alcaligenes faecalis induces hydrogen uptake hydrogenase, with a maximum activity of 26.2 μg H_2-uptake ml^{-1} hr^{-1}. Nitrogen fixing activity was supported by hydrogen in the presence and absence of carbon source in the culture medium. Nitrogenase activity decreased when the hydrogen content was >30% in the absence of carbon source and 25% in the presence of carbon source, respectively (1).

Carbonaceous inhibition
Hydrogenase activity in *Pseudomonas saccharophila* was induced by hydrogen under low partial pressure of oxygen and under air, in autrophic as well as in heterotrophic conditions, provided the sucrose concentration was relatively low (2).
The metabolite pattern of *Escherichia coli* was affected when the hydrogen partial pressure was <1 atm: high hydrogen partial pressures increased formate formation, low pressures gave rise to increased acetate production and higher cell yields (3).

Anaerobic effects
Sulfate-reducing bacteria outcompeted methanogenic bacteria for the mutual substrate hydrogen in human faecal slurries from methane- and non methane-producing individuals mixed together (4).
Utilised in methane production by anaerobic bacteria (5).

Degradation studies
Arthrobacter, Calderobacterium hydrogenophilum and *Nocardia opaca* in liquid culture and immobilised on solid surface, were found to absorb hydrogen from gaseous phase at concentrations of several ppm. Thus, they are potentially involved in hydrogen oxidation at low concentrations in gaseous phase (6).
Soil enriched with aerobic, autotrophic hydrogen-oxidising microflora (mainly dinitrogen fixers) which could oxidise 84.5 ml H_2 dm^{-2} hr^{-1} in the first 25 cm layer may act as a biological shield between hydrogen-rich environments and air and may be utilised as a biofilter e.g. in the waste processing industry (7).

Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (8).

References

1. Lin, X. et al *Zhiwu Shengli Xuebao* 1989, **15**(1), 30-34 (Ch.) (*Chem. Abstr.* **111**, 83954d).
2. Barraquio, W. L. et al *J. Gen. Microbiol.* 1988, **134**(4), 893-901.
3. De Corte, B. et al *Biotechnol. Lett.* 1989, **11**(8), 583-588.
4. Gibson, G. R. et al *J. Appl. Bacteriol.* 1988, **65**(3), 241-247.
5. Conrad, R. et al *FEMS Microbiol. Ecol.* 1989, **62**(5), 852-856.
6. Bodnar, I. V. et al *Zh. Obshch. Biol.* 1986, **47**(6), 780-789 (Russ.) (*Chem. Abstr.* **106**, 81386n).
7. Dugnari, L. et al *FEMS Microbiol. Ecol.* 1986, **38**(6), 347-351.
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H97 hydrogen azide

HN_3

HN_3 **Mol. Wt.** 43.03 **CAS Registry No.** 7782-79-8

Synonyms hydrazoic acid; azoimide; diazoimide; hydronitric acid; triazoic acid

EINECS No. 231-965-8 **RTECS No.** MW 2800000

Uses In preparation of heavy metal azides for shell detonators.

Physical properties

M. Pt. –80°C **B. Pt.** 37°C **Specific gravity** 1.09 at 20°C with respect to water at 4°C
Solubility Water: soluble

Occupational exposure

DE-MAK 0.1 ppm (0.18 mg m^{-3}) **UK-STEL** 0.1 ppm (0.18 mg m^{-3}) (vapour)

Mammalian & avian toxicity

Acute data
LC_{Lo} (1 hr) inhalation rat 1100 ppm (1).
LD_{50} intraperitoneal mouse 22 mg kg^{-1} (2).
Major effects observed are respiratory stimulation, fall in blood pressure, convulsions followed by depression. Inhalation caused bronchiolar inflammation and oedema (3).

Irritancy
Human eye irritant (2).

Other effects

Other adverse effects (human)
Central nervous system and cardiovascular effects reported in a human exposed to 300 ppb by inhalation (2). Acute effects in humans include cough, headache, reduced blood pressure, weakness and collapse. Chronic toxicity includes hypotension, weakness, palpitation and ataxia (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

References

1. *Publ. Health Rep.* 1943, **58**, 607.
2. *J. Ind. Hyg. Toxicol.* 1948, **30**, 98.
3. Clayton, G. D. et al (Eds.) *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, Interscience Publishers, New York, NY, USA.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H98 hydrogen bromide

HBr

HBr **Mol. Wt.** 80.91 **CAS Registry No.** 10035-10-6

Synonyms hydrobromic acid; anhydrous hydrobromic acid

EINECS No. 233-113-0 **RTECS No.** MW 3850000

Uses Sedative. Manufacture of inorganic and organic bromides. As reducing agent and as a catalyst in controlled oxidation in the alkylation of aromatic compounds in the isomerisation of conjugated diolefins.

Physical properties

M. Pt. –87°C **B. Pt.** –66.5°C

Solubility Water: miscible. Organic solvents: miscible with ethanol

Occupational exposure

DE-MAK 2 ppm (6.7 mg m^{-3})

UK-STEL 3 ppm (10 mg m^{-3})

US-STEL ceiling limit 3 ppm (9.9 mg m^{-3})

UN No. 1788 **HAZCHEM Code** 2R **Conveyance classification** corrosive substance

Supply classification corrosive

Risk phrases Causes burns – Irritating to the respiratory system (R34, R37)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7/9, S26, S45)

Mammalian & avian toxicity

Acute data

LC_{50} (1 hr) inhalation mouse, rat 814, 2858 ppm, respectively (1).

Rats exposed to 1300 ppm HBr for 30 min via nose breathers showed tissue injury in the nasal region (epithelial and submucosal necrosis, accumulations of inflammatory cells, exudates and extravasation of erythrocytes). Rats similarly exposed by mouthpiece had higher mortality, major tissue disruption of the trachea, including epithelia submucosal, glandular and cartilage necrosis, and peripheral lung damage (2).

Legislation

Included in Schedule 4 and 6 (Release Into Air/Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

Air pollutant in riboflavin manufacture and vehicle exhausts.

Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology and workplace experience listed (4).

References

1. *NTIS Report* No. PB214-270, Natl. Tech. Inf. Ser., Springfield, VA, USA.
2. Stavert, D. M. et al *Fundam. Appl. Toxicol.* 1991, **16**, 636-655.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H99 hydrogen chloride

HCl

HCl **Mol. Wt.** 36.46 **CAS Registry No.** 7647-01-0

Synonyms anhydrous hydrochloric acid; hydrochloric acid; chlorohydric acid; muriatic acid; dilute hydrochloric acid

EINECS No. 231-595-7 **RTECS No.** MW 4025000

Uses Used in manufacture of inorganic and organic hydrochlorides, vinyl chloride, alkyl chlorides, arsenious chloride, and in the chlorination of rubber. Used in isomerisation, polymerisation and alkylation organic reactions and as a gaseous flux for babbitting operations.
Occurrence In gastric juice.

Physical properties

M. Pt. –144.22°C **B. Pt.** –85.05°C **Specific gravity** 1.639 at 0°C (gas); 1.194 at –26°C (liquid, conc. acid)
Volatility v.p. 4 atm at 17.8°C ; v.den. 1.27
Solubility Water: 673 g l^{-1} at 30°C. Organic solvents: methanol, ethanol, diethyl ether

Occupational exposure

DE-MAK 5 ppm (7 mg m^{-3})
FR-VLE 5 ppm (7.5 mg m^{-3})
JP-OEL ceiling limit 5 ppm
SE-CEIL 5 ppm (8 mg m^{-3})
UK-LTEL 1 ppm (2 mg m^{-3}) **UK-STEL** 5 ppm (8 mg m^{-3})
US-STEL ceiling limit 5 ppm (7.5 mg m^{-3})

UN No. 1050 (anhydrous); 2186 (refrigerated liquid) **HAZCHEM Code** 2RE (anhydrous)
Conveyance classification toxic gas, corrosive
Supply classification toxic
Supply classification corrosive
Risk phrases Toxic by inhalation – Causes severe burns (R23, R35)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S26, S36/37/39, S45)

Ecotoxicity

Fish toxicity
Arctic char exposed to pH 4.5 (HCl) for 2 wk were initially hyperactive but became hypoactive with continued exposure. Thigmotaxis was greater than in controls and feeding intensity and attraction to food was depressed. Haematocrit, protein, cortisol and glucose increased but osmolality and plasma Na^+ and Cl^- decreased (1).

Invertebrate toxicity
Acidification of soy broth containing *Listeria monocytogenes* to pH 4.4 inhibited microbial activity (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit (aqueous) 900 mg kg^{-1} (3).
LC_{50} (1 hr) inhalation rat, mouse 1108, 3124 ppm, respectively (4,5).
LC_{Lo} (5 min) inhalation human 3000 ppm (6).

LD_{50} intraperitoneal mouse 1449 mg kg^{-1} (7).
20 ml min^{-1} of 9.13 g l^{-1} HCl (aqueous) infused into anaesthetised cats via an extracorporeal arteriovenous shunt between the femoral artery and vein caused a transient increase in right ventricular blood pressure and respiratory frequency but a fall in tidal volume and therefore no elevation in total ventilation (8).

Sub-acute and sub-chronic data
Aspiration of 2.5 ml kg^{-1} HCl on unanaesthetised sheep with a chronic lung lymph fistula for ≤148 hr caused increased lymph flow, lipid peroxidation, and bronchial blood flow; decreased cardiac index in the airway and pulmonary vasoconstriction also occurred. Long term acid-injured animals survived for ≤1 wk following aspiration (9).
Four groups of three anaesthetised baboons exposed in a head-only mode to 500, 5000 or 10,000 ppm HCl for 15 min showed a concentration-related increase in respiratory frequency and minute volume with a marked decrease in blood pulmonary oxygen at the two highest concentrations. No significant alterations in pulmonary function parameters were measured at 3-day or 3-month post-exposure (10).

Irritancy
100 mg instilled into rabbit eye (72 hr) caused mild irritation (11).
Dermal irritant (12).
Collagen fibres with increased affinity for eosin and irregular cross-striation in polarised light, together with shrunken cells with dark stained nuclei, found just beneath the epidermis after application of hydrochloric acid to pig skin (13).

Other effects

Any other adverse effects
Aerosols of hydrochloric acid solution are widely dispersed in alveoli causing alveolar hyperplasia (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides guide level 25 mg l^{-1} (15).
Included in Schedule 4 and 6 (Release Into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, environmental effects, exposure levels, ecotoxicity, workplace experience and epidemiology listed (17).

References

1. Jones K. A. et al *Can. J. Fish Aquat. Sci.* 1987, **44**(2), 373-381.
2. Sorrells, K. M. et al *J. Food Prot.* 1989, **52**(8), 571-573.
3. *Biochem. Z.* 1923, **134**, 437.
4. *J. Combust. Toxicol.* 1976, **3**, 61.
5. *Aerospace Medical Research Laboratory Report* No. TR-74-78, 1974, Aerospace Tech. Div., Air Force Systems Command, Wright-Patterson Air Force Base, OH, USA.
6. *Tabulae Biol.* 1933, **3**, 231.
7. *C. R. Hebd. Seances Acad. Sci.* 1963, **256**, 1043.
8. Orr, J. A. et al *J. Appl. Physiol.* 1987, **62**(6), 2362-2370.
9. Stothert, J. C. et al *Circ. Shock* 1990, **30**(3), 237-254.
10. Kaplan, H. I. et al *J. Toxicol. Environ. Health* 1988, **23**(4), 473-493.
11. *Toxicology* 1982, **23**, 281.
12. Loden, M. et al *Gov. Rep. Announce. Index (U. S.)* 1986, **86**(7), Abstr. No. 613,483.
13. Karlsmark, T. et al *Forensic Sci. Int.* 1988, **39**(3), 227-233.
14. Vozumi, M. et al *Osaka-furitsu Koshu Eisei Kenkyusho Kenkyu Hokoku, Kogai Eisei Hen* 1988, **9**, 1-9 (Japan.) (*Chem. Abstr.* **110**, 226769j).
15. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.

16. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
17. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H100 hydrogen cyanide

HCN

CHN **Mol. Wt.** 27.03 **CAS Registry No.** 74-90-8

Synonyms hydrocyanic acid; prussic acid; formonitrile; formic anammonide; Cyclon; Cyclone B; Evercyn; Cyanosil; Tritox; Uragan D

EINECS No. 200-821-6 **RTECS No.** MW 6825000

Uses Compressed gas used as rodenticide and insecticide on ships. Used in manufacture of methyl methacrylate, acrylonitrile, herbicides, ferro-cyanide, lactic acid and pharmaceuticals.
Occurrence In cigarette smoke; cyanatogenic plants.

Physical properties

M. Pt. −13.4°C **B. Pt.** 25.6°C **Flash point** −18°C **Specific gravity** 0.6876 at 20°C with respect to water at 4°C
Volatility v.p. 400 mm Hg at 9.8°C ; v.den. 0.932
Solubility Water: miscible. Organic solvents: diethyl ether; miscible with ethanol

Occupational exposure

DE-MAK 10 ppm (11 mg m^{-3})
FR-VME 2 ppm (2 mg m^{-3}) **FR-VLE** 10 ppm (10 mg m^{-3})
JP-OEL 5 ppm (5.5 mg m^{-3})
SE-CEIL 5 mg m^{-3} (as CN)
UK-STEL MEL 10 ppm (11 mg m^{-3})
US-STEL ceiling limit 4.7 ppm (5 mg m^{-3}) (as CN)

UN No. 3294 (solution in alcohol with ≤45% hydrogen cyanide); 1051 (stabilised containing <3% water); 1614 (stabilised containing <3% water and absorbed in a porous inert material) **HAZCHEM Code** 3W (solution in alcohol with ≤45% hydrogen cyanide) **Conveyance classification** toxic substance, flammable (solution in alcohol with ≤45% hydrogen cyanide and stabilised containing <3% water) **Conveyance classification** toxic substance (stabilised containing <3% water and absorbed in a porous inert material)
Supply classification extremely flammable, very toxic
Risk phrases Extremely flammable – Very toxic by inhalation (R12, R26)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and in a well ventilated place – Keep away from sources of ignition – No smoking – Wear suitable protective clothing and gloves – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7/9, S16, S36/37, S38, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 0.125 mg l^{-1} (1).
LC_{50} (96 hr) rainbow trout 0.057 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (96 hr) *Gammarus pseudolimnaeus* 0.17 mg l^{-1} (2).
LC_{50} (96 hr) *Asellus communis* 2.29 mg l^{-1} (2).
EC_{50} (5 min) *Photobacterium phosphoreum* 8.55 ppm Microtox test (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 3.7 mg kg^{-1} (4).
LD_{Lo} oral human, pig 0.57, 2.0 mg kg^{-1}, respectively (4).
LC_{50} (5 min) rat 544 ppm (5).
LC_{50} (30 min) mice 169 ppm (5).
LC_{50} (3 min) dog 300 ppm (5).
Inhalation rabbit 300 ppm caused death with blood cyanide levels up to 0.70 μg ml^{-1} or below (6).

Teratogenicity and reproductive effects

Pregnant rats exposed to 15 ppm on day 0-6, 7-13 and 14-20 of gestation showed no effect on foetal weight (7).

Metabolism and toxicokinetics

In animals, cyanide ion is metabolised mainly to thiocyanate (8).

Other effects

Other adverse effects (human)

Causes death in man after exposure to 100-200 ppm for 30-60 min. Combines with methaemoglobin to form cyanomethaemoglobin, preventing tissues removing oxygen from the blood. At lower concentrations causes cyanosis, headache, dizziness, unsteadiness of gait, nausea and a feeling of suffocation leaving no disability on recovery (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Cyanides: maximum admissible concentration 50 μg l^{-1} (10).
EPA Toxicity Class I (formulation) (11).
ADI 0.05 mg kg^{-1} body weight (11).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology, exposure levels, workplace experience and environmental effects listed (12).

References

1. Broderius, S. J. et al *J. Fish Res. Bull. Can.* 1979, **36**, 164.
2. Oseid, D. M. et al *Bull. Environ. Contam. Toxicol.* 1979, **21**, 439-447.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. Lewis, R. J. et al *Registry of Toxic Effects of Chemical Substances* 1984, National Institute for Occupational Safety and Health No. 81-116.
5. Back, et al *Reclassification of Materials Listed as Transportation Health Hazards* (TSA-20-72-3; PB214-270).
6. Morikawa, T. et al *Nippon Kasai Gakkai Ronbunshu* 1990, **39**(2), 65-70 (Japan.) (*Chem. Abstr.* **114**, 137570c).
7. Tachi, N. *Nagoya-shiritsu Daigaku Igakkai Zasshi* 1987, **38**(4), 535-560 (Japan.) (*Chem. Abstr.* **108**, 126475a).
8. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
9. Lewis, R. J. (Ed.) *Sax's Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
12. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H101 hydrogen fluoride

HF

HF **Mol. Wt.** 20.01 **CAS Registry No.** 7664-39-3

Synonyms hydrofluoric acid gas; anhydrous hydrofluoric acid; antisal 2b; fluorhydric acid

EINECS No. 231-634-8 **RTECS No.** MW 7875000

Uses Catalyst, particularly in petroleum industry. Used in fluorination processes, in separating uranium isotopes and in dye chemistry.

Physical properties

M. Pt. –83.1°C **B. Pt.** 19.54°C **Specific gravity** 0.878 g l^{-1} at 25°C and 760mmHg
Volatility v.p. 400 mm Hg at 2.5°C
Solubility Water: soluble. Organic solvents: benzene, tetralin, toluene, *m*-xylene

Occupational exposure

DE-MAK 3 ppm (2.5 mg m^{-3})
FR-VLE 3 ppm (2.5 mg m^{-3})
JP-OEL 3 ppm (2.5 mg m^{-3})
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 3 ppm (2.5 mg m^{-3}) (as F)
US-STEL ceiling limit 3 ppm (2.3 mg m^{-3})

UN No. 1052 (anhydrous) **HAZCHEM Code** 2XE (anhydrous) **Conveyance classification** corrosive substance, toxic (anhydrous)
Supply classification very toxic, corrosive
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Causes severe burns (R26/27/28, R35)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7/9, S26, S36/37/39, S45)

Ecotoxicity

Toxicity to other species
LD_{Lo} subcutaneous frog 112 mg kg^{-1} (1).
Pinus sylvestris seedlings exposed to hydrogen fluoride suffered needle necrosis (2).

Mammalian & avian toxicity

Acute data
LC_{50} (1 hr) inhalation mouse, rat, monkey 342, 966, 1744 ppm, respectively (3-5).
LC_{Lo} (30 min) inhalation human 50 ppm (6).
Rats exposed to 1300 ppm for 30 min via nose breathers showed tissue injury in the nasal region (epithelial and submucosal necrosis, accumulations of inflammatory cells, exudates and extravasation of erythrocytes). Rats similarly exposed by mouthpiece had higher mortality, major tissue disruption of the trachea, including epithelia submucosal, glandular and cartilage necrosis, and peripheral lung damage (7).
LD_{Lo} dermal mouse 500 mg kg^{-1} (8).

Sub-acute and sub-chronic data
Male albino guinea pigs inhaling 5 mg hydrogen fluoride for 4 days had increased plasma cholesterol levels and reduced isocitrate dehydrogenase activity leading to an accumulation of citric acid (9).

Metabolism and toxicokinetics
Urine of workers exposed to hydrogen fluoride showed the presence of fluoride ions (F^-) (10).

Sensitisation
Allergic dermatoses were observed in workers occupationally exposed to HF (11).

Genotoxicity

Mild intoxication of rats caused chromosomal aberrations in bone marrow cells (12).

Other effects

Other adverse effects (human)
Employees at an incinerator 500 m downwind from a toxic gas release containing HF and HBr experienced eye and respiratory irritation (13).
Occupational exposure to HF caused moderate changes in the functional state of the pituitary gland-thyroid gland system in industrial workers, attributed to disorders of the endocrine regulatory chain and the effects of HF on thyroid hormone metabolism at the target cell level (14).
A group of 20 volunteers were exposed to constant hydrogen fluoride (HF) concentrations of 0.2 to 5.2 mg m^{-3} for 1 hr, concentrations known to occur in aluminium potroom atmospheres. Eye and upper and lower airway symptoms were recorded and graded with a standardised questionnaire. The total symptom score was increased significantly at the end of exposure for all volunteers and for volunteers exposed to <0.6 mg m^{-3} HF, the current Norwegian standard for total fluorides. No change was detected in forced expiratory volume in 1 sec, although there was a significant decrease in forced vital capacity in the group exposed to fluorides below the hygienic standard and for the entire group. Almost all symptoms had disappeared 4 hr after exposure ceased. Symptom scores from the upper airways correlated significantly with HF concentration, the change in plasma fluoride concentration and the maximum plasma fluoride concentration. A significant correlation was also found between the total symptom score for airways and HF concentration (15).

Any other adverse effects
Rabbits and guinea pigs exposed to various concentrations of gas exhibited: respiratory irritation, slowed respiratory rate, damage to the conjunctiva, cornea and nasal mucous membrane; cardiac dilatation, congestion and myocardial injury; pulmonary haemorrhage, congestion, emphysema and oedema, with bronchopneumonia in some cases; hepatic congestion; splenic congestion and oedema; renal congestion and oedema of other organs. Lung damage was greater in guinea-pigs (16).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) and Schedule 6 (Release Into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (17).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluoride maximum admissible concentration 1500 µg l^{-1} at 8-12°C, 700 µg l^{-1} at 25-30°C (18).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, workplace experience, environmental effects and epidemiology listed (19).

References

1. *C. R. Seances Soc. Biol. Ses Fil.* 1937, **124**, 133.
2. Oleksyn, J. et al *Acta Soc. Bot. Pol.* 1988, **57**(1), 107-115.
3. *J. Combust. Toxicol.* 1976, **3**, 61.

4. *Toxicol. Appl. Pharmacol.* 1977, **42**, 417.
5. *Aerospace Medical Research Laboratory Report* No. TR-70-77/70, Aerospace Technical Div., Air Force Systems Command, Wright-Patterson Air Force Base, OH, USA.
6. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
7. Stavert, D. M. et al *Fundam. Appl. Toxicol.* 1991, **16**(4), 636-655.
8. *Sangyo Igaku* 1975, **17**, 281.
9. Dousset, J. C. et al *Fluoride* 1987, **20**(3), 137-141.
10. Levchenko, N. I. *Gig. Tr. Prof. Zabol.* 1987, (9), 52-54 (Russ.) (*Chem. Abstr.* **108**, 43173z).
11. Budina, L. V. et al *Gig. Tr. Prof. Zabol.* 1991, (10), 32-34 (Russ.) (*Chem. Abstr.* **115**, 262347g).
12. Tazhibeer, S. *Vopr. Pitan.* 1987, (4), 63-66 (Russ.) (*Chem. Abstr.* **107**, 196917z).
13. *Energy Res. Abstr.* 1987, **12**(17), Abstr. No. 35872.
14. Tokar, V. I. et al *Gig. Tr. Prof. Zabol.* 1989, (9), 19-22 (Russ.) (*Chem. Abstr.* **112**, 144853j).
15. Lund, K. et al *Occup. Environ. Med.* 1997, **54**(1), 32-37.
16. Machle, W. et al *J. Ind. Hyg.* 1934, **16**, 129-145.
17. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
18. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
19. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H102 hydrogen iodide

HI

HI **Mol. Wt.** 127.91 **CAS Registry No.** 10034-85-2

Synonyms hydriodic acid; anhydrous hydriodic acid

EINECS No. 233-109-9 **RTECS No.** MW 3760000

Uses Expectorant. Manufacture of hydroiodic acid, organic iodo compounds; to remove iodine from iodo compounds.

Physical properties

M. Pt. –50.8°C **B. Pt.** –35.38°C **Specific gravity** 1.701

Solubility Water: miscible. Organic solvents: diethyl ether, miscible with ethanol

Occupational exposure

UN No. 2197 (anhydrous) **HAZCHEM Code** 2RE (anhydrous) **Conveyance classification** toxic gas, corrosive (anhydrous)

Supply classification corrosive

Risk phrases Causes severe burns (R35)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S26, S36/37/39, S45)

Legislation

Included in Schedule 4 and 6 (Release Into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (1).

Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (2).

References

1. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H103 hydrogen peroxide

H_2O_2

H_2O_2 **Mol. Wt.** 34.01 **CAS Registry No.** 7722-84-1

Synonyms dihydrogen dioxide; hydrogen dioxide; Albone; Tripwite; Amitex B; Durox; Oxypure; Interoxselect; Perone; Tysul; Valsan

EINECS No. 231-765-0 **RTECS No.** MX 0899000

Uses A 90% solution used in rocket propulsion. Dough conditioner, maturing and bleaching agent in food. Disinfectant, deodorant, antiseptic. Bleaching hair and fabrics.
Occurrence Key component and product of the earth's lower atmospheric photochemical reactions. In plant tissues. Produced metabolically in human intact cells and tissues.

Physical properties

M. Pt. –0.43°C **B. Pt.** 152°C **Flash point** 1.463 at 0°C with respect to water at 4°C
Solubility Water: miscible. Organic solvents: diethyl ether

Occupational exposure

DE-MAK 1 ppm (1.4 mg m^{-3})
FR-VME 1 ppm (1.5 mg m^{-3})
SE-LEVL 1 ppm (1.4 mg m^{-3}) **SE-CEIL** 2 ppm (3 mg m^{-3})
UK-LTEL 1 ppm (1.4 mg m^{-3}) **UK-STEL** 2 ppm (2.8 mg m^{-3})
US-TWA 1 ppm (1.4 mg m^{-3})

UN No. 2984 (aqueous solutions with ≥8% but ≤20% hydrogen peroxide, stabilised as necessary); 2014 (aqueous solutions with ≥20% but ≤60% hydrogen peroxide, stabilised as necessary); 2015 (hydrogen peroxide, stabilised or aqueous solution, stabilised, with >60% hydrogen peroxide)
HAZCHEM Code 2P (aqueous solutions with ≥8% but ≤20%, or ≥20% but ≤60% hydrogen peroxide, stabilised as necessary); 2PE (hydrogen peroxide, stabilised or aqueous solutions, stabilised, with >60% hydrogen peroxide)
Conveyance classification oxidising substance (aqueous solutions with ≥8% but ≤20% hydrogen peroxide, stabilised as necessary); oxidising substance, corrosive (aqueous solutions with ≥20% but ≤60% hydrogen peroxide, stabilised as necessary or hydrogen peroxide, stabilised or aqueous solution, stabilised, with >60% hydrogen peroxide)
Supply classification oxidising, corrosive
Risk phrases ≥60% – Contact with combustible material may cause fire – Causes burns (R8, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep in a cool place – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S3, S28, S36/39, S45)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 42 mg l^{-1}. Yellow tail, red sea bream and striped jack exposed to 300, 900, 1500 mg^{-1} (3 min) caused no mortality but yellow tail exposed to 900 mg l^{-1} and red sea bream exposed to 300 and 1500 mg l^{-1} showed slight anaemia due to formation of methaemoglobinaemia (1).
LC_{50} (24 hr) rabbit fish, striped goby and jack mackerel 224-289 mg l^{-1} (2).

Invertebrate toxicity

4.5-6 mg l^{-1} hydrogen peroxide sorbed in porous calcium silicate granules destroyed *Gymnodinium nagasakiense* within 30 min (1).

Environmental fate

Degradation studies

Degradation in natural waters was initiated by *Chlorella vulgaris*, *Microcystis aeruginosa* and *Ankistrodesmus quadricauda*. No degradation was observed in absence of algae. Degradation was inhibited by NaN_3 and ethanol (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2 g kg^{-1} (4).
LC_{Lo} inhalation mouse 227 ppm (5).
LD_{50} dermal rat 4060 mg kg^{-1} (6).
LD_{50} intravenous rabbit 15 g kg^{-1} (7).
Lungs of rabbits and cats that died after intravenous administration were pale and emphysematous, with considerable amounts of gas in the great veins and right side of the heart (8).
A single topical application of 15-30% to mouse dorsal skin produced extensive epidermolysis, inflammation and vascular injury, followed by quick regeneration and epidermal hyperplasia, together with extensive endothelial damage to the dorsal blood vessels (9).

Sub-acute and sub-chronic data

Young ♂ rats receiving 1.5% hydrogen peroxide in drinking water for 8 wk showed dose-related growth retardation, induction of dental caries and pathological changes in the periodontium (10).
Treatment of 16 mice for 35 wk with 0.15% hydrogen peroxide resulted in hydropic degeneration of hepatic and renal tubular epithelial tissues, necrosis, inflammation irregularities of tissue structure of the stomach wall, hypertrophy of the lymphatic tissue of the small intestinal wall. Concentrations >1% caused death within 2 wk (11).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (12).
Groups of 100 C57BL/6J mice given 0, 0.1 and 0.4% hydrogen peroxide in drinking water for 100 wk showed one adenoma of the duodenum in controls, 6 adenomas and one carcinoma of the duodenum in the 0.1% group and 2 duodenal adenomas and 5 carcinomas in the 0.4% group (13).
138 ♂ and ♀ C57BL/6N mice treated with 0.4% hydrogen peroxide in drinking water showed gastric erosions and duodenal plaques after 30 days and hyperplastic lesions, adenomas and carcinomas after day-90 in the duodenum and stomach. Atypical hyperplasia appeared late in the experiment and 5% of the animals developed duodenal adenocarcinoma (14).
Mice injected with 0.1 ml of a 0.5% solution in saline of hydrogen peroxide showed no tumours in animals surviving longer than 200 days (15).
30/303 newborn AB and C57BIxA/JAX mice which received one subcutaneous injection of 0.1 ml of 0.6% hydrogen peroxide survived >6 month. Of these, 6 developed tumours at various sites. 42/346 mice injected 3 × with the same dose as above survived >6 month; of these, 14 developed tumours. (16).
Twice wkly topical applications of 30% hydrogen peroxide on the buccal epithelium of Syrian hamsters for 22 wk caused hyperkeratosis and hyperplasia in all animals with hyperchromatic cells and mild dysplasia in 4/9; no tumours were seen (17).

Teratogenicity and reproductive effects

Female rats drinking 0.45% hydrogen peroxide for 5 wk produced normal litters when mated with untreated males (18).

1% solution administered to 3-month-old ♂ mice for 7-28 day as sole drinking-fluid caused no infertility (19).

47-374 μg egg^{-1} aqueous solution of 30% hydrogen peroxide injected into the airspace of White Leghorn chicken eggs on day-3 of incubation caused embryonic deaths and dose-related malformations on day-14 at doses >95 μg egg^{-1} (20).

Metabolism and toxicokinetics

Hydrogen peroxide is decomposed in the bowel by catalase to produce oxygen, before absorption occurs (21).

Erythrocytes are affected by low concentrations and it is decomposed by glutathione peroxidase and in higher concentrations by catalase; with hepatocytes, cystolic hydrogen peroxide from drug metabolism was decomposed by glutathione peroxidase; peroxisomal hydrogen peroxide was decomposed by catalase (22-24).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA102, TA1537 without metabolic activation weakly positive (25).

Escherichia coli exposed to increasing concentrations of hydrogen peroxide exhibits two different modes of killing at <2.5 mM or >10-12.5 mM with a region of partial resistance between. Mode 1 lethality requires active cellular metabolism and is enhanced by DNA repair deficient strains and anoxia-induced cell function, while hydroxyl radicals are important, in modes 1 and 2 (26,27).

Saccharomyces cerevisiae gene conversion and mitotic recombination positive (28).

0.68 mg l^{-1} hydrogen peroxide had little effect on micronucleus frequency of splenocytes from 10-wk ♂ mice C57BL/6J but in conjunction with Fe^{2+} (27.9-55.9 mg l^{-1}) micronucleus count increased 3-4 fold without loss of cell viability (29).

34×10^{-3} to 34×10^{-5} g l^{-1} in 0.9% NaCl solution (24 hr) human embryonic fibroblasts single treatment caused chromosome- and chromatid-type aberrations in a dose-response relationship. Chromosome-type aberrations were predominantly dicentrics and deletions (30).

Other effects

Any other adverse effects

Local intra-arterial infusion of hydrogen peroxide 20.4-44.2 μg kg^{-1} min^{-1} induced gastric mucosal injury in the rat (31).

Experiments using cultures of rabbit colonic epithelial cells suggest that H_2O_2 is more toxic to these cells than $O_2^{\cdot-}$ and OH· in the extracellular space. H_2O_2 enters the intracellular space and is converted into the more reactive and harmful OH· leading to cellular injury in the presence of intracellular iron (32).

Soft contact lenses soaked in hydrogen peroxide at 100 ppm and 300 ppm worn in rabbit eye for 2 hr increased central corneal thickness by 4.6% and 5.8%, respectively. A 160% increase in hydrogen peroxide in the aqueous humour was detected after using 300 ppm soaked lenses (33).

300 ppm damaged human corneal epithelial cells *in vitro*; 70-100 ppm caused cell death in minutes (34).

Other comments

Hydrogen peroxide is formed intracellularly by mitochondria, endoplasmic reticulum peroxisomes and soluble enzymes as a metabolic by-product. It is formed in the liver and large quantities have been identified in rat kidney (35).

Reviews on human health effects, experimental toxicity, physico-chemical properties, epidemiology and workplace experience listed (36).

References

1. Miyazaki, T. et al *Bull. Fac. Bioresour., Mie Univ.* 1990, (4), 165-173 (Japan.) (*Chem. Abstr.* **114**, 76516r).
2. Kanda, T. et al *Suisan Zoshoku* 1989, **37**(3), 221-224 (Japan.) (*Chem. Abstr.* **112**, 113796p).
3. Batovskaya, L. O. et al *Dokl. Akad. Nauk SSSR* 1988, **301**(6), 1513-1516 (Russ.) (*Chem. Abstr.* **109**, 208092h).

4. *Hyg. Sanit. (USSR)* 1983, **48**(6), 28.
5. *Arch. Environ. Health* 1962, **4**, 327.
6. *Gig. Trud. Prof. Zabol.* 1977, **21**(10), 22.
7. *US Army Chemical Corps, Medical Laboratories Research Reports* No. 75, 1951, Army Chemical Centre, Edgewood, Arsenal, MD, USA.
8. Lorincz, A. L. et al *Anaesthesiology* 1948, **9**, 162-174.
9. Klein-Szanto, A. J. P. et al *J. Invest. Dermatol.* 1982, **79**, 30-34.
10. Shapiro, M. et al *J. Dent. Res.* 1960, **39**, 332-343.
11. Aoki, M. et al *Igaku to Seibutsugaku* 1972, **84**, 159-162 (Japan).
12. *IARC Monograph* 1987, **Suppl. 7**, 64.
13. Ito, A. et al *Gann* 1981, **72**, 174-175.
14. Ito, A. et al *Gann* 1982, **73**, 315-322.
15. Nakahara, W. et al *Gann* 1959, **50**, 17-21.
16. Schmidt, F. *Acta Biol. Med. Ger.* 1964, **20**, 574-584 (Ger.).
17. Weitzmann, S. A. *J. Periodontol.* 1986, **57**(11), 685-688.
18. Hankin, L. *Nature (London)* 1958, **182**, 1453.
19. Wales, R. G. et al *J. Endocrinol.* 1959, **18**, 236-244.
20. Korhonen, A. et al *Environ. Res.* 1984, **33**, 54-61.
21. Sheehan, J. F. et al *Lab. Invest.* 1960, **9**, 150-168.
22. Cohen, G. et al *Biochemistry* 1963, **2**, 1420-1428.
23. Nicholls, P. *Biochem. Biophys. Acta* 1972, **279**, 306-309.
24. Jones, D. P. et al *Arch. Biochem. Biophys.* 1981, **210**, 505-516.
25. Kensese, S. M. et al *Teratog., Carcinog., Mutagen.* 1989, **9**, 211-218.
26. Imlay, J. A. et al *J. Bacteriol.* 1986, **166**, 519-527.
27. Brandi, G. et al *Environ. Mol. Mutagen.* 1991, **18**(1), 22-27.
28. Kaneko, M. et al *Mutat. Res.* 1988, **207**(1), 17-22.
29. Dreosti, I. E. et al *Mutat. Res.* 1990 **244**(4), 337-343.
30. Oya, Y. et al *Mutat. Res.* 1986, **172**(3), 245-253.
31. Esplugues, J. V. et al *Br. J. Pharmacol.* 1989, **97**(4), 1085-1092.
32. Hata, Y. et al *Life Sci.* 1997, **60**(24), 2221-2230.
33. Yuan, N. et al *Acta Ophthalmol.* 1991, **69**(2), 241-246.
34. Tripathi, B. J. et al *Arch. Ophthalmol. (Chicago)* 1989, **107**, 1516-1519.
35. Chance, B. et al *Physiol. Rev.* 1979, **59**, 527-605.
36. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels

H104 hydrogen selenide

H_2Se

H_2Se **Mol. Wt.** 80.98 **CAS Registry No.** 7783-07-5

Synonyms selenium hydride; dihydrogen selenide; selane

EINECS No. 231-978-9 **RTECS No.** MX 1050000

Physical properties

M. Pt. –64°C **B. Pt.** –41.4°C **Specific gravity** 3.614g (gas); 2.12 at –42°C (liquid)
Volatility v.p. 10 atm at 23.4°C
Solubility Organic solvents: carbon disulfide

Occupational exposure

DE-MAK 0.05 ppm (0.17 mg m^{-3})
FR-VME 0.02 ppm (0.08 mg m^{-3})
JP-OEL 0.05 ppm (0.17 mg m^{-3})
SE-LEVL 0.01 ppm (0.03 mg m^{-3}) **SE-STEL** 0.05 ppm (0.2 mg m^{-3})
UK-LTEL 0.05 ppm (0.17 mg m^{-3}) (as Se)
US-TWA 0.05 ppm (0.16 mg m^{-3})

UN No. 2202 (anhydrous) **Conveyance classification** toxic gas, danger of fire (flammable gas) (anhydrous)
Supply classification toxic
Risk phrases Toxic by inhalation and if swallowed – Danger of cumulative effects (R23/25, R33)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – When using do not eat, drink or smoke – After contact with skin, wash immediately with plenty of water – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S20/21, S28, S45)

Mammalian & avian toxicity

Acute data
LC_{50} (8 hr) inhalation guinea pig 300 ppb (1).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (3).

References

1. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H105 hydrogen sulfide

$$H_2S$$

H_2S **Mol. Wt.** 34.08 **CAS Registry No.** 7783-06-4
Synonyms sulfurated hydrogen; hydrosulfuric acid; dehydrogen monosulfide; stink damp; sulfur hydride
EINECS No. 231-977-3 **RTECS No.** MX 1225000
Uses Analytical reagent. Used in metallurgy.
Occurrence In coal pits, gas wells, sulfur springs. From decaying organic matter containing sulfur.

Physical properties

M. Pt. –85.5°C **B. Pt.** –60.4°C **Specific gravity** 1.539 at 0°C **Volatility** v.p. 20 mm Hg at 25.5°C ; v.den. 1.189
Solubility Water: 4.1 g l^{-1} at 20°C. Organic solvents: alcohol

Occupational exposure

DE-MAK 10 ppm (14 mg m^{-3})
FR-VME 5 ppm (7 mg m^{-3}) **FR-VLE** 10 ppm (14 mg m^{-3})
JP-OEL 10 ppm (14 mg m^{-3})
SE-LEVL 10 ppm (14 mg m^{-3}) **SE-CEIL** 15 ppm (20 mg m^{-3})
UK-LTEL 10 ppm (14 mg m^{-3}) **UK-STEL** 15 ppm (21 mg m^{-3})
US-TWA 10 ppm (14 mg m^{-3}) **US-STEL** 15 ppm (21 mg m^{-3})

UN No. 1053 (liquefied) **HAZCHEM Code** 2WE (liquified) **Conveyance classification** toxic gas, danger of fire (flammable gas) (liquified)
Supply classification extremely flammable
Supply classification very toxic
Supply classification dangerous for the environment
Risk phrases Extremely flammable – Very toxic by inhalation – Very toxic to aquatic organisms (R12, R26, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S9, S16, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow, American char, 0.007-0.55 mg l^{-1} at 6-24°C (1).

Invertebrate toxicity
Black sea mussels exposed to hydrogen sulfide exhibited changes in protein-carbohydrate metabolism, total proteins, lactate and pyruvate, and transamination enzyme activity in the mussel haemolymph (2).
LC_{50} (96 hr) *Asellus* 0.11 mg l^{-1} (1).
Active transport of carbon dioxide in *Synechococcus* was inhibited by 0.05 µg hydrogen sulfide (3).

Toxicity to other species
Yield of *Trifolium pratense* L. was decreased by 32% by fumigation with 0.25 mm^3 dm^{-3} for 2 wk. Yield of *Phaseolus vulgaris* L. was increased by 11% (4).

Bioaccumulation
Does not have bioaccumulation or food chain contamination potential (5).

Environmental fate

Anaerobic effects
Measurement of methanogenic activity of granular sludge indicated a 50% inhibition at free H_2S concentrations of 250 and 90 mg S l^{-1} at pH 6.4-7.2 and 7.8-8.0, respectively (6).
100% bacterial lactose utilisation was achieved in sludge up to 250 mg hydrogen sulfide l^{-1}, but only 40% at 450 mg hydrogen sulfide l^{-1} (7).

Degradation studies
Specific uptake rate of hydrogen sulfide by *Thiobacillus* sp. HA43 isolated from a H_2S-acclimated peat biofilter was 2.22×10^{-12} g S $cell^{-1}$ hr^{-1} (8).
Calyptogena found in subduction zones in the Japan trench metabolise hydrogen sulfide by chemoautotrophic process (9).

Mammalian & avian toxicity

Acute data
LC_{50} (1 hr) inhalation mouse 673 ppm (10).
LC_{50} (8 hr) inhalation guinea pig 1 mg m^{-3} (11).

LC_{Lo} (30 min) inhalation man 600 ppm (12).
Slight congestion of the lungs was reported in Wistar rats exposed to 75 ppm for 20-60 min (13).

Sub-acute and sub-chronic data
Albino mice exposed to 0.1 mg l^{-1} for 6 hr day^{-1} for 9 month exhibited declined muscular strength, static and dynamic performance, and endurance capacity, together with decreased glycogen, ATP and creatinine phosphoric acid levels and increased lactic acid levels in the muscles and liver (13).
3-100 mg hydrogen sulfide m^{-3} in natural gas inhaled by rats dose-dependently decreased bacteriocidal, lysozyme and complement activities and increased β-lysine concentrations of blood serum compared to controls. Lysozyme concentrations decreased also in the liver, kidney, lung and spleen. Similar effects were seen after 1 month inhalation of 3 mg m^{-3} (14).

Teratogenicity and reproductive effects
Gravid rats exposed to ≤75 ppm from day 6-21 had normal reproductive parameters until parturition when delivery time was extended in a dose-dependent manner with a maximum increase of 42% at 75 ppm. Exposure to 75 ppm for 6 wk caused significantly elevated maternal liver cholesterol content on day-21 postpartum. Pups exposed *in utero* and neonatally to day-21 postpartum showed only a slight decrease in time of ear detachment and hair development (15).

Metabolism and toxicokinetics
Converted into alkali sulfide in the blood stream. The hydrosulfide radical is excreted by the lungs and in urine. Part of the sulfide is oxidised to sulfate and thiosulfate (16).
Urinary thiosulfate can be used as an indicator of hydrogen sulfide exposure (17).
Levels of hydrogen sulfide in ♂ Wistar rats exposed to 75 ppm for 20-60 min were higher in tissues than blood shortly after exposure, especially in the heart (13).

Irritancy
Viscose rayon washers exposed to up to 9 mg m^{-3} showed associated irritative eye complaints at levels below the threshold limit of 14 mg m^{-3} (18).

Other effects

Other adverse effects (human)
89 people accidentally exposed to hydrogen sulfide in a chemical plant showed symptoms of dizziness, weakness, nausea, headache, loss of consciousness, confusion and somnalence. 52 showed signs of poisoning and 12 died (19).
In 4 cases of fatal poisoning where victims fell into sludge, sulfhaemoglobin formed in the blood and greenish skin discoloration was noted (20).
26 ♂ pulp mill workers exposed daily to hydrogen sulfide showed no significant changes in respiratory function or bronchial responsiveness (21).
Data associated with health effects suggest a public health risk from accidental releases of hydrogen sulfide at 300 ppm (lethal effects) and 50 ppm (sublethal effects) (22).
A group of 9 men and 10 women inhaled 10 ppm of hydrogen sulfide (H_2S), the occupational exposure limit, for 15 min during cycle exercise at 50% of their maximal aerobic power. Pulmonary function tests were administered at rest and immediately after the 2-hr exposure. Variables derived from flow volume hoop, maximum ventilation volume and diffusion capacity of the lung for carbon monoxide exhibited no significant changes for any of the subjects (23).

Any other adverse effects
Inhibited the oxidation-energy metabolism and membrane transport processes in the brain regions in ♂ rats intoxicated with hydrogen sulfide (24).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (25).
Included in Schedule 4 (Release Into Air: Prescribed Substances) of Statutory Instrument No. 472, 1991 (26).

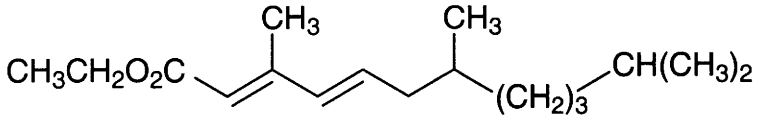
Other comments

The toxicology of hydrogen sulfide its mechanism of action and health effects reviewed. At high concentrations it causes olfactory paralysis, loss of consciousnes and risk of pulmonary oedema; at low levels it may result in mucosal irritation and kerato-conjunctivities. Treatment consists of a combination of sodium nitrite and hyperbaric oxygen, although the therapy carries some risk (27).
Reviews on human health effects, experimental toxicology, physico-chemical properties, environmental effects, workplace experience and exposure levels listed (28).
Human health effects and epidemiology reviewed (19).

References

1. Smith, L. L. et al *Prog. Water Technol.* 1975, **7**, 599.
2. Galina, M. S. *Gidrobiol. Zh.* 1990, **26**(6), 56-59 (Russ.) (*Chem. Abstr.* **115**, 152678h).
3. Espie, G. S. et al *Curr. Res. Photosynth., Proc. Int. Conf. Photosynth, 8th* 1989, **4**, 513-516.
4. Maas, F. M. et al *J. Exp. Bot.* 1987, **38**(194), 1459-1469.
5. *Tech. Info. for Problem Spills: Hydrogen Sulfide (Draft)* 1981, 1, Environment Canada.
6. Koster, I. W. et al *Water Res.* 1986, **20**(12), 1561-1567.
7. Hilton, B. L. et al *Proc. Ind. Waste Conf.* 1987, **42**, 739-747.
8. Cho, K. S. et al *J. Ferment. Bioeng.* 1991, **71**(1), 44-49.
9. Boulegue, J. et al *Earth Planet. Sci. Lett.* 1987, **83**(1-4), 343-355.
10. *NTIS Report* No. PB214-270, Natl. Tech. Inf. Ser., Springfield, VA, USA.
11. Lewis, R. J. et al *Registry of Toxic Effects of Chemical Substances* 1984, Natl. Inst. Occup. Saf. Health. No. 81-86.
12. Lefaux, R. *Practical Toxicology of Plastics* 1968, 207, Chemical Rubber Co., Cleveland, OH, USA.
13. Braginskaya, L. L. et al *Gig. Tr. Prof. Zabol.* 1968, **12**(8), 46-50 (Russ.) (*Chem. Abstr.* **96**, 47159f).
14. Setko, N. P. et al *Gig. Sanit.* 1989, (3), 24-26 (Russ.) (*Chem. Abstr.* **110**, 149468f).
15. Hayden, L. J. et al *Toxicol. Ind. Health* 1990, **6**(3-4), 389-401.
16. Booth, N. H. et al *Veterinary Pharmacology and Therapeutics* 5th ed. 1982, 959, Iowa State University Press, IA, USA.
17. Kangas, J. et al *Clin. Chim. Acta* 1987, **164**(1), 7-10.
18. Vanhoorne, E. et al *Cah. Notes Doc.* 1990, **139**, 456-465 (Fr.) (*Chem. Abstr.* **114**, 253173z).
19. Glass, D. C. *Ann. Occup. Hyg.* 1990, **34**(3), 323-327.
20. Tatsuno, Y. et al *Nippon Hoigaku Zasshi* 1986, **40**(3), 308-315 (Japan.) (*Chem. Abstr.* **106**, 170381z).
21. Jappinen, P. et al *Br. J. Ind. Med.* 1990, **47**(12), 824-828.
22. Layton, D. W. et al *J. Air Pollut. Control Assoc.* 1987, **37**(10), 1185-1190.
23. Bhambhani, Y. et al *J. Occup. Environ. Med.* 1996, **38**(10), 1012-1017.
24. Sandu, V. D. et al *Stud. Cercet. Biol., Ser. Biol. Anim.* 1993, **45**(1), 69-72 (Rom.) (*Chem. Abstr.* **120**, 237723).
25. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
26. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
27. Guidotti, T. L. *Occup. Med.* 1996, **46**(5), 367-371.
28. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H106 hydroprene



$C_{17}H_{30}O_2$ **Mol. Wt.** 266.42 **CAS Registry No.** 41205-09-8

Synonyms ethyl 3,7,11-trimethyldodeca-2,4-dienoate; ethyl (2*E*,4*E*)-3,7,11-trimethyl-2,4-dodecadienoate; ethyl (2*E*,4*E*)-3,7,11-trimethyldodeca-2,4-dienoate; Altozar; Gencor; Gentrol; Mator; Protol

RTECS No. JR 1700000

Uses Insecticide.

Physical properties

B. Pt. 174°C at 19 mmHg, 138-40°C at 1.25 mmHg **Specific gravity** 0.892 at 25°C
Partition coefficient log P_{ow} 3.06 **Volatility** v.p. 1.9-3.0 × 10^{-4} mmHg (25°C)
Solubility Water: 2 mg l^{-1} (pH 7, 20°C). Organic solvents: soluble in common organic solvents

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, trout >100 mg l^{-1} (1).

Invertebrate toxicity
First stage *Blattella germanica* nymphs 100 μg μl^{-1} toxic (2).
Hydroprene applied topically (dose unspecified) to *Leptocoris coimbatorensis* 5th-instar nymphs and adults inhibited sperm formation and caused degeneration of the testes (3).
Application to post-diapause pupae of *Scirpophaga incertulas* produced deformaties in anatomy and histology of ovaries, accessory glands and bursa copulatrix (4).
LD_{50} oral and contact >1 mg bee^{-1} (1).

Environmental fate

Degradation studies
Rapidly decomposed: $t_{1/2}$ few days. In plants, degradation involves ester hydrolysis, *O*-demethylation and oxidative splitting of the double bond (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral dog, rat >10,000->34,000 mg kg^{-1} (5).
LC_{50} (4 hr) inhalation rat 5.4 mg l^{-1} (1).
LD_{50} dermal rabbit 4550 mg kg^{-1} (6).

Sub-acute and sub-chronic data
In 90-day feeding trial, no-effect level for rats was 50 mg kg^{-1} body weight daily (1).

Teratogenicity and reproductive effects
Non-teratogenic in rabbits at 90 mg kg^{-1} day^{-1} (1).
1 mg g^{-1} injected into mice on day-9 of pregnancy caused a 75% incidence of morphological abnormalities in foetuses including curly tail, cleft palate, misshaped limbs and haematoma (7).

Irritancy
Mild eye irritant in rabbits (1).

Genotoxicity

Non-mutagenic in mice at 1300 mg kg^{-1} (1).

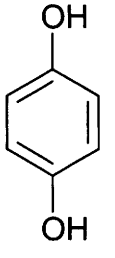
Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (9).
The log P_{ow} exceeds the European Community recommended value 3.0 (6th and 7th amendments) (10).
WHO Toxicity Class Table 5 (11).
EPA Toxicity Class IV (formulation) (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. King, J. E. et al *J. Econ. Entomol.* 1988, **81**(1), 225-227.
3. Kaur, A. et al *J. Anim. Morphol. Physiol.* 1987, **34**(1-2), 39-44.
4. Chakravorty, S. et al *Acta Entomol. Bohemoslov.* 1986, **83**(6), 401-410.
5. Thompson, W. T. *Agricultural Chemicals, Book I* 1977, Thompson Publications, Fresno, CA, USA.
6. *Farm Chemicals Handbook* 1983, **C12**, Meister Publishing, Willoughby, OH, USA.
7. Unsworth, B. et al *Life Sci.* 1974, **15**, 1649-1655.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
9. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
10. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
11. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

H107 hydroquinone



$C_6H_6O_2$ **Mol. Wt.** 110.11 **CAS Registry No.** 123-31-9

Synonyms 1,4-benzenediol; quinol; *p*-benzenediol; *p*-hydroxyphenol; Eldopaque; Eldoquin; Tecquinol

EINECS No. 204-617-8 **RTECS No.** MX 3500000

Uses Photographic reducer and developer. Antioxidant. Depigmentation agent for the skin.

Physical properties

M. Pt. 170-171°C **B. Pt.** 285-287°C **Flash point** 165°C **Specific gravity** 1.332 at 15°C
Solubility Water: 1 g in 14 ml water. Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 2 mg m^{-3}
SE-LEVL 0.5 mg m^{-3} **SE-STEL** 1.5 mg m^{-3}
UK-LTEL 2 mg m^{-3} **UK-STEL** 4 mg m^{-3}
US-TWA 2 mg m^{-3}

UN No. 2662 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful by inhalation and if swallowed (R20/22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes – Wear eye/face protection (S2, S24/25, S39)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 0.1-0.18 mg l^{-1} (1).
In stickleback and steelhead trout (10 mg l^{-1}) death occurred in 1-2 and 0-1 hr, respectively (2).
Exposure to 5 ppm caused death of trout, bluegill sunfish and goldfish in 2-6 hr. Exposure to 1 ppm caused death of trout in 7 hr (3).
LC_{50} (96 hr) rainbow trout 0.097 mg l^{-1} (4).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 0.05 mg l^{-1} (1).
EC_{50} (30 min) *Photobacterium phosphoreum* 0.0382 mg l^{-1} Microtox test (5).
IC_{50} *Saccharomyces cerevisiae* yeast test 330 mg l^{-1} (6).

Bioaccumulation
Estimated bioconcentration factor for golden ide 40. Experimental 24 hr bioconcentration factor range in algae was 40-65. Data indicate that bioconcentration in fish and aquatic organisms is insignificant (7-9).

Environmental fate

Degradation studies
BOD_5 7.5%, 0.05 mg l^{-1} when inoculated with an activated sludge seed (7).
Pure culture oxidation produced 1,4-benzoquinone, 2-hydroxy-1,4-benzoquinone and β-keto-adipic acid (10).
BOD_{10} 0.48% reduction of dissolved oxygen concentration using a sewage seed inoculum (11).
COD (<120 hr) 54.2%, 200 mg l^{-1} using a thickened adapted activated sludge under aerobic conditions (12).
$ThOD_5$ 53% reduction of dissolved oxygen concentration in a settled raw waste water seed inoculum (13).
Bacteria from soil and related environments raised on a wide variety of different phenolic compounds utilised 95% of 300 ppm 1,4-benzenediol within 1-2 days under aerobic conditions (14).
Complete degradation of 0.55-2.2 g l^{-1} using a mixed microbial seed under anaerobic conditions (15).
Biodegradable (16).

Abiotic removal
Photolysis in water by natural sunlight produced superoxide anion and ultimately hydrogen peroxide (17).
Photolysis in dilute aqueous solutions and in the presence of oxygen produced quinone through the intermediary of semiquinoic radicals (18,19).
$t_{1/2}$ 12 min for oxidation by alkylperoxy radicals present in sunlit waters in organic solvents (20).
Estimated photochemical $t_{1/2}$ 15.7 hr (21).

Adsorption and retention
Estimated soil adsorption coefficients of 9 and 50 suggest that 1,4-benzenediol will display high to very high mobility in soil (22,23).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 320 mg kg^{-1} (24).
LD_{50} oral mouse 400 mg kg^{-1} (6).
LD_{Lo} oral human 29 mg kg^{-1} (25).
LD_{50} intraperitoneal rat 170 mg kg^{-1} (26).
LD_{50} intravenous rat 115 mg kg^{-1} (24).
LD_{50} 72, 96 hr old chick embryos (injected into air sac) 8.59 and 15.63 μg egg^{-1}, respectively (27).
Oral ♂ Fischer 344 rats 1.8 or 4.5 mmol kg^{-1}. The lower dose was nephrotoxic in some rats and cell proliferation in proximal tubular cells of the S3M region correlated with the degree of toxicity in individual rats. The higher dose caused significant increases in the urinary excretion of γ-glutamyl transpeptidase, alkaline phosphatase, and glutathione-S-transferase activities (28).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (29).
National Toxicology Program tested rats and mice via gavage. No evidence of carcinogenicity in ♂ mice, some evidence for carcinogenicity (increased incidence of chemically related neoplasms, malignant, benign or combined) in ♂ rats and ♀ rats and ♀ mice (30).
Oral ♂/♀ rat, mouse (2 yr) 0.8% in diet. The studies strongly indicated that hydroquinone is a potential renal carcinogen in ♂ rats and a potential hepatocarcinogen in ♂ mice (31).
Oral ♂ F344 rats (2 yr) 0.8% hydroquinone in diet. Retardation of body weight and elevated relative liver weights were noted. Formalin-fixed and paraffin embedded liver tissues from rats killed terminally were cut and stained for glutathione S-transferase placental form (GST-P) and tumour growth factor α (TGFα) immunohistochemistry. Numbers and areas of GST-P+ve foci per unit area of liver section were measured, and the treated/control proportional values were calculated to be 71% and 71%. Long-term inhibitory effects of phenolic compounds on liver carcinogenesis, predicted from the Ito test, were thus confirmed (32).
Oral Wistar/Crj ♂ rats (36 weeks) 0.89% in diet potently enhanced the 2nd stage of *N*-ethyl-*N*-hydroxyethylnitrosamine-induced renal carcinogenesis (0.1% EHEN in drinking water for 3 wk) (33).
Gavage ♂/♀ rats (2 yr) 0, 25, 50 mg kg^{-1} 5 days wk^{-1}. Gavage ♂/♀ mice (2 yr) 0, 50, 100 mg kg^{-1}. There was evidence of hydroquinone-related carcinogenicity in ♂ F344/N rats as indicated by increased incidences of tubular cell adenomas of the kidney, and in ♀ rats as shown by increases in mononuclear cell leukaemia, and in ♀ mice based on increases in hepatocellular neoplasms, mainly adenomas. There was no evidence of carcinogenicity in ♂ mice (34).

Teratogenicity and reproductive effects

Gavage Sprague-Dawley rats (10 wk prior to cohabitation, during cohabitation, and until scheduled termination) 0, 15, 50, or 150 mg kg^{-1} day^{-1}. No adverse effects on reproduction or fertility were observed in either generation (F0 or F1). The no-observed-effect levels for general and reproductive toxicity are 15 and 150 mg kg^{-1} day^{-1}, respectively (35).
Cultured whole rat conceptuses 100% mortality at 0.1mM (36).
Gavage rats (6-15th days of gestation) 0-300 mg kg^{-1} day^{-1}. Hydroquinone was not selectively toxic to the developing rat conceptus and appears not to have the properties of a developmental toxicant. The no-observable-effect level for both maternal and developmental toxicity was 100 mg kg^{-1}, the no-observable-adverse-effect level was 300 mg kg^{-1} (37).
Gavage New Zealand White rabbits (6-18th days of gestation) 0-150 mg kg^{-1}. Hydroquinone 150 mg kg^{-1} produced minimal developmental alterations in the presence of maternal toxicity. The no-observed-effect level for developmental toxicity was 75 mg kg^{-1} day^{-1} (38).
Hydroquinone (0.0625 to 40 μg) was injected into the air sacs of chicken eggs 72 and 96 hr after incubation, producing gross malformations such as body haemorrhage, curled claws, everted viscera, defective beak, exencephaly and monophthalmia in developing chick embryos at dosages ranging from 20 down to 0.0625 μg egg^{-1}. Malformations and their incidence were higher in both groups compared with controls, but not statistically significant, revealing that the teratogenic potential of hydroquinone is unremarkable. At higher concentrations the compound was embryotoxic (27).

Metabolism and toxicokinetics

Absorbed from gastro-intestinal tract and possibly through skin and is partially excreted in urine as 1,4-benzenediol and in conjugation with hexuronic, sulfuric and other acids (39).

Irritancy

A 2-5% solution applied to human skin caused mild to severe irritation (40).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (41).
Human lymphocyte HL-60 cells treated with 1,4-benzenediol produced DNA adducts at levels from 0.05-10 adducts per 10^7 nucleotides as a function of treatment time and concentration. Induced a three-fold increase in micronucleated cells (42).
Drosophila melanogaster sex-linked recessive lethal (SLRL) assay; by feed equivocal, by injection negative (43).

Other effects

Other adverse effects (human)

Ingestion of 1 g by humans has caused tinnitus, nausea, vomiting, sense of suffocation, shortness of breath, cyanosis, convulsions, delirium and collapse. Death has followed ingestion of 5 g. Irritation of intestinal tract occurs with oral ingestion and dermatitis can result from skin contact. Staining and opacification of cornea occur in workers exposed for prolonged periods to concentrations of vapour not high enough for production of systemic effects (44).
Patchy pigmentation of the palm, forefinger and base of the neck was reported in a West Indian woman after using a cosmetic cream containing 1,4-benzenediol (45).
Localised exogenous ochronosis of the face developed in a black woman who had used a proprietary bleaching cream containing 2% hydroquinone up to 6 times daily for about 30 months. Eighteen months after discontinuing use, there was clearing of the hyperpigmentation except for some residual changes in the periorbital areas (46).
The incidence of malignant melanoma (MM) in a group of 837 lithographers born in 1933 to 1942 was followed in the Danish Cancer Register from 1974 to 1989. Five MM cases were identified, against 1.5 expected. Materials used in the printing industry contain many known and suspected carcinogens; a photographic chemical, hydroquinone, which causes depigmentation and changes in skin melanocytes may be implicated (47).

Any other adverse effects

Exposure of human T lymphoblasts *in vitro* to 50 μM hydroquinone decreased IL-2-dependent DNA synthesis and cell proliferation by >90% with no effect on cell viability. There is evidence that hydroquinone may inhibit ribonucleotide reductase (48).

Other comments

Human health effects, experimental toxicology and environmental fate reviewed (49-51).

References

1. *Env. Eff. Photoproc. Chem.* 1974, **18**, 219.
2. *Fish Toxicity Screening Data* 1989, EPA 560/6-89-001, Washington, DC, USA.
3. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, Washington, DC, USA.
4. DeGraeve, G. M. et al *Arch. Environ. Contam. Toxicol.* 1980, **9**, 543-555.
5. Kaiser, K. L. E. et al *Water Pollut. Res. J. Canada* 1991, **26**(3), 361-431.
6. Koch, H. P. et al *Methods Find. Exp. Clin. Pharmacol.* 1993, **15**(3), 141-152.
7. Freitag, D. et al *Chemosphere* 1985, **14**, 1589-1616.
8. Freitag, D. et al *Ecotox. Environ. Saf.* 1982, **6**, 60-81.
9. Geyer, H. et al *Chemosphere* 1981, **10**, 1307-1313.
10. Harbison, K. G. et al *Environ. Toxicol. Chem.* 1982, **1**, 9-15.
11. Heukelekian, H. et al *J. Water Pollut. Control Fed.* 1955, **29**, 1040-1053.
12. Pitter, P. *Water Res.* 1976, **10**, 231-235.
13. Young, R. H. F. et al *J. Water Pollut. Control Fed.* 1968, **40**, 354-368.

14. Tabak, H. H. et al *J. Bacteriol.* 1964, **87**, 910.
15. Szewzyk, U. et al *Appl. Microbiol. Technol.* 1989, **32**, 346-349.
16. *MITI Report* 1984, Ministry of International Trade and Industry, Tokyo, Japan.
17. Choudhry, G. G. et al *Res. Rev.* 1985, **96**, 19-136.
18. Perbet, G. et al *J. Chimie Physique* 1979, **76**, 89-96.
19. Tissot, A. et al *Chemosphere* 1985, **14**, 1221-1230.
20. Mill, T. *Environ. Toxicol. Chem.* 1982, **1**, 135-141.
21. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
22. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, McGraw-Hill, New York, NY, USA.
23. Swann, R. L. et al *Res. Rev.* 1983, **85**, 17-28.
24. Woodward, G. et al *Fed. Proc. Fed. Am. Soc. Expt. Biol.* 1949, **8**, 348.
25. Deichmann, W. B. et al *Toxicology of Drugs and Chemicals* 1969, 321, Academic Press, London, UK.
26. *J. Ind. Hyg. Toxicol.* 1949, **31**, 79.
27. Burgaz, S. et al *Drug Chem. Toxicol.* 1994, **17**(2), 163-174.
28. Peters, M. M. C. G. et al *Carcinogenesis* 1997, **18**(12), 2393-2401.
29. *IARC Monograph* 1977, **15**, 169.
30. *National Toxicology Program Research Testing Division* 1992, Report No. TR-366, NIEHS, Research Triangle Park, NC, USA.
31. Shibata, M. et al *Jpn. J. Cancer Res.* 1991, **82**(11), 1211-1219.
32. Hagiwara, A. et al *Teratog. Carcinog. Mutagen.* 1997, **16**(6), 317-325.
33. Okazaki, S. et al *Teratog., Carcinog. Mutagen.* 1993, **13**(3), 127-137.
34. Kari, F. W. et al *Food Chem. Toxicol.* 1992, **30**(9), 734-747.
35. Blacker, A. M. et al *Fundam. Appl. Toxicol.* 1993, **21**(4), 420-424.
36. Chapman, D. E. et al *Toxicol. Appl. Pharmacol.* 1994, **128**(1), 129-137.
37. Krasavage, W. J. et al *Fundam. Appl. Toxicol.* 1992, **18**(3), 370-375.
38. Murphy, S. J. et al *Fundam. Appl. Toxicol.* 1992, **19**(2), 214-221.
39. Florin, I. et al *Toxicology* 1979, **15**, 219-232.
40. *Archives of Dermatology* 1966, **93**, 589.
41. McCann, J. et al *Proc. Nat. Acad. Sci. USA* 1975, **72**(12), 5135-5139.
42. Robertson, M. L. et al *Mutat. Res.* 1991, **249**(1) 201-209.
43. Foureman, P. et al *Environ. Mol. Mutagen.* 1994, **23**, 51-63.
44. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
45. Ridley, C. M. et al *Br. Med. J.* 1984, **288**, 1537.
46. Cullison, D. et al *J. Am. Acad. Derm.* 1983, **8**, 882.
47. Nielsen, H. et al *Scand. J. Work, Environ. Health* 1996, **22**(2), 108-111.
48. Li, Q. et al *Fundam. Appl. Toxicol.* 1997, **38**(2), 158-165.
49. *Dangerous Prop. Ind. Mater. Rep.* 1988, **8**(1), 51-60.
50. Devillers, J. et al *Ecotoxiol. Environ. Saf.* 1990, **19**(3), 327-354.
51. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H108 hydrotalcite

$$Mg_6(CO)_3[Al(OH)_6]_2(OH)_4{\cdot}4H_2O$$

$C_3H_{24}Al_2Mg_6O_{23}$ **Mol. Wt.** 628.00 **CAS Registry No.** 12304-65-3

Synonyms aluminium magnesium carbonate hydroxide hydrate; Altacite; DHT 4A; Nacid; Talcid; Kyowaad 1000

RTECS No. MX 8420000

Uses Antacid.

Occupational exposure

UK-LTEL 2 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse >10,000 mg kg^{-1} (1).

Other effects

Other adverse effects (human)

Oral human volunteer (24 hr) 2 tablets every 6 hr (concentration unspecified), reduced gastric acidity by an average of 31-37% with reductions of ≤65% during the 2-hr immediately following a dose (2).

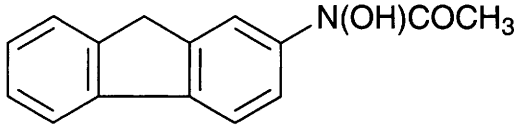
Other comments

Soluble in dilute mineral acids.

References

1. *Drugs in Japan (Ethical Drugs)* 1982, **6**, 629.
2. Dreyer, M. et al *Arzneim.-Forsch.* 1991, **41**(7), 738-41 (Ger.) (*Chem. Abstr.* **115**, 105807q)

H109 *N*-hydroxy-2-acetylaminofluorene



$C_{15}H_{13}NO_2$ **Mol. Wt.** 239.27 **CAS Registry No.** 53-95-2

Synonyms *N*-(9*H*-fluoren-2-yl)-*N*-hydroxyacetamide; *N*-fluoren-2-ylacetohydroxamic acid; *N*-2-fluorenylacetohydroxamic acid; 2-(*N*-hydroxyacetamido)fluorene; *N*-hydroxy-*N*-acetyl-2-aminofluorene

RTECS No. AK 8575000

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 52 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 1500 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Heterotopic bladder implanted in ♂ F344 rat (53 wk) was instilled with 240 μg l^{-1} once a wk for 30 wk. Transitional cell carcinomas were observed in 15/35 animals (3).

♂ $B6C3F_1$ mouse (10 month) single dose of 7, 14 or 29 μg l^{-1} g^{-1} induced liver tumours. Deacetylation to *N*-hydroxy-2-aminofluorene is suggested as one of the metabolic steps in the formation of liver DNA adducts and the initiator of hepatic tumours (4).

Metabolism and toxicokinetics

Metabolised to *N*-sulfoxy-2-aminofluorene, the main electrophile and hepatocarcinogen in infant ♂ mice (5).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation positive (6).
Salmonella typhimurium TA98, TA100, TA1537, TA1538 with metabolic activation positive (7).
In vitro Chinese hamster ovary HGPRT direct-acting mutagen positive (8).
In vitro rat hepatocyte unscheduled DNA synthesis positive (9).
In vitro Chinese hamster ovary cells with and without metabolic activation equivocal results (10).
Levels of metabolism and cell-mediated *Salmonella typhimurium* TA98 mutagenesis higher with *in vitro* human hepatocytes compared to *in vitro* rat hepatocytes. There is inter-individual variation with human hepatocytes in metabolism and mutagenesis (11).

Other effects

Any other adverse effects
In vitro ♂ rat hepatocytes 240 mg l^{-1} caused 90% cell death within 6 hr preceded by loss of intracellular ATP (12).

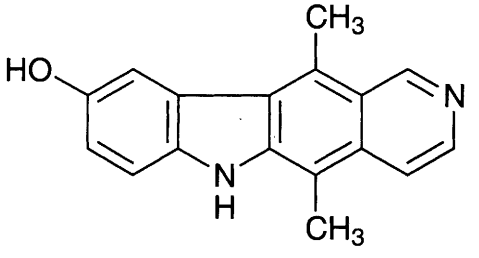
Other comments

Metabolite of 2-acetylaminofluorene *in vitro* rat human kidney cells (13).
Mutagenic and carcinogenic activity reviewed (14).

References

1. *Cancer Res.* 1975, **35**, 2959.
2. *J. Natl. Cancer Inst.* 1979, **62**, 911.
3. Wang, C. Y. et al *Cancer Res.* 1987, **47**(13), 3406-3409.
4. Lai, C. C. et al *Carcinogenesis (London)* 1988, **9**(7), 1295-1302.
5. King, C. M. et al (Ed.) *Proceedings of the International Conference on Carcinogenic and Mutagenic N-Substituted Aryl Compounds*, 1988, 249-257, Elsevier, New York, NY, USA.
6. Gao, N. et al *Teratog., Carcinog., Mutagen.* 1991, **11**(2), 65-76.
7. Khudoley, V. V. et al *Arch. Geschwulstforsch.* 1987, **57**(6), 453-462.
8. Okinaka, R. T. et al *Mutat. Res.* 1988, **200**(1-2), 45-50.
9. Chipman, J. K. et al *Mutat. Res.* 1988, **207**(3-4), 193-198.
10. Heflich, R. H. et al *Environ. Mol. Mutagen.* 1988, **11**(2), 167-181.
11. Rudo, K. et al *Cancer Res.* 1987, **47**(22), 5861-5867.
12. Kroese, E. D. et al *Biochem. Pharmacol.* 1990, **40**(8), 1885-1892.
13. Rudo, K. M_t et al *Cancer Res.* 1989, **49**(5), 1187-1192.
14. Park, B. K. et al *Kich'o Kwahak Yongu (Yeungnam Taehakkyo)* 1985, **5**, 137-144 (Korean) (*Chem. Abstr.* **106**, 170719r)

H110 9-hydroxyellipticine



$C_{17}H_{15}N_2O$ **Mol. Wt.** 263.32 **CAS Registry No.** 51131-85-2

Synonyms 5,11-dimethyl-6*H*-pyrido[4,3-*b*]carbazol-9-ol

EINECS No. 257-000-0 **RTECS No.** UU 8886500

Physical properties

M. Pt. 324-325°C

Genotoxicity

5-10 mg kg^{-1} injected intraperitoneally caused sister chromatid exchanges, chromatid aberrations, chromosome clumping and micronuclei in mouse bone marrow cells (1).

References

1. Renault, G. et al *Toxicol. Appl. Pharmacol.* 1987, **89**(2), 281-286

H111 1-(2-hydroxyethyl)-1-nitrosourea

$$H_2NC(O)N(NO)CH_2CH_2OH$$

$C_3H_7N_3O_3$ **Mol. Wt.** 133.11 **CAS Registry No.** 13743-07-2

Synonyms HENU; HNU; nitroso-2-hydroxyethylurea

RTECS No. YT 4915000

Physical properties

M. Pt. 51-55°C

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 120 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Increased incidence of lymphoma reported in ♂, ♀ mice given 37.5 or 75 mg l^{-1} in drinking water for life (2).

A variety of neoplasms was reported including lung, colon, thyroid, forestomach, tongue, duodenum, ileum, Zymbal's gland, thymus and mammary gland adenocarcinomas in rats receiving 1.4 or 14 mg kg^{-1} by gavage 2 × wk^{-1} for 18 wk. All animals died by 34 wk at the higher dose (3).

In ♂ Wistar rats receiving an unspecified dose in drinking water for 1 yr, 48% had bone tumours, 32% intestinal tumours and 53% lymphoma-leukaemia (4).

Induced neoplasms in Swiss mice after topical application of 35 mg ml^{-1} in oil for 25 wk (total dose 350 mg) (5).

Skin carcinomas, lung adenocarcinomas, leukaemia, thymus lymphosarcomas, and tumours of the stomach, mammary gland and uterus reported in mice after skin painting with 2 × wk^{-1} application of total dose 12 mg (median survival 78 wk) (6).

Teratogenicity and reproductive effects

Reduced survival of undifferentiated A spermatogonia 5 days after intraperitoneal injection of 57-284 mg kg^{-1} to ♂ mice (7).

Genotoxicity

Salmonella typhimurium TA1535 with or without metabolic activation positive (8-10).

Active in prophage induction assay with *Escherichia coli* BR339 (lambda) (9).

E. coli B(Arg)H/r30R (wild type) and Hs30R (*uvrA*) positive (11).

Other comments

The compound is a direct-acting alkylating agent.

References

1. *J. Natl. Cancer Inst.* 1976, **56**, 445.
2. Mirvish, S. S. et al *Cancer Lett. (Shannon, Irel.)* 1990, **54**(1-2), 101-106.
3. Lijinsky, W. et al *Jpn. J. Cancer Res.* 1988, **79**(2), 181-186.
4. Mirvish, S. S. et al *J. Natl. Cancer Inst.* 1987, **78**(2), 387-393.
5. Lijinsky, W. et al *Cancer Res.* 1983, **43**, 214-221.
6. Lijinsky, W. et al *J. Cancer Res. Clin. Oncol.* 1988, **114**, 245-249.
7. Oakberg, E. F. et al *Mutat. Res.* 1983, **108**, 337-344.
8. Andrews, A. W. et al *Top. Chem. Mutagen.* 1984, **1**, 13-43.
9. Lijinsky, W. et al *Mutat. Res.* 1987, **178**, 157-165.
10. Lee, K. et al *Mutat. Res.* 1977, **48**, 131-138.
11. Kohda, K. H. et al *Mutat. Res.* 1987, **177**, 219-228

H112 hydroxylamine

NH_2OH

H_3NO **Mol. Wt.** 33.03 **CAS Registry No.** 7803-49-8

Synonyms hydroxyamine; oxammonium

EINECS No. 232-259-2 **RTECS No.** NC 2975000

Physical properties

M. Pt. 34°C **B. Pt.** 110°C **Flash point** explodes at 130°C **Specific gravity** 1.227
Volatility v.p. 10 mmHg at 47.2°C
Solubility Water: decomposes. Organic solvents: methanol

Occupational exposure

Supply classification harmful
Supply classification dangerous for the environment
Risk phrases Heating may cause an explosion – Harmful if swallowed – Irritating to respiratory system and skin – Risk of serious damage to eyes – May cause sensitisation by skin contact – Harmful: danger of serious damage to health by prolonged exposure if swallowed – Very toxic to aquatic organisms (R5, R22, R37/38, R41, R43, R48/22, R50)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S22, S26, S36/37/39, S61)

Environmental fate

Nitrification inhibition
Inhibited ammonia oxidation in chemostat cultures of *Thiosphaera pantotropha*, but was itself fully oxidised (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat, mouse 60 mg kg^{-1} (2,3).

LD_{50} subcutaneous rat 30 mg kg^{-1} (4).

A single 24-hr dermal exposure to hydroxylamine sulfate (dose unspecified) produced haematotoxic effects in rabbits, including anaemia, methaemoglobin formation and reticulocytosis (5).

Genotoxicity

Salmonella typhimurium TA1535/pSK1002 with or without metabolic activation negative in *umu* test (6).

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).

DNA synthesis test in human fibroblasts negative (8).

Drosophila melanogaster wing spot test positive – hydroxylamine hydrochloride (9).

Active in inducing reversion of dark variant of *Photobacterium leiognathi* to the luminescent state (10).

Induced sister chromatid exchanges in Chinese hamster V-79 cells *in vitro* (11).

Other comments

Reviews on human health effects, experimental toxicity, environmental effects and workplace experience listed (12).

Hazards reviewed (13).

References

1. Robertson, L. A. et al *Antonie van Leeuwenhoek* 1989, **56**(4), 301-309.
2. *Cancer Res.* 1966, **26**, 1448.
3. *J. Pharmacol. Exp. Ther.* 1969, **165**, 30.
4. *J. Pharmacol. Exp. Ther.* 1957, **119**, 444.
5. Derelanko, M. J. et al *Fundam. Appl. Toxicol.* 1987, **8**(4), 583-594.
6. Nakamura, S. et al *Mutat. Res.* 1987, **192**, 239-246.
7. McCann, J. et al *Proc. Natl. Acad. Sci. U. S. A.* 1975, **72**,(12), 5135-5139.
8. Yanagisawa, K. et al *Mutat. Res.* 1987, **183**, 89-94.
9. Graf, U. et al *Mutat. Res.* 1989, **222**, 359-373.
10. Ulitzur, S. et al *Mutat. Res.* 1980, **74**, 113-124.
11. Speit, G. et al *Hum. Genet.* 1980, **54**, 155-158.
12. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
13. *Dangerous Prop. Ind. Mater. Rep.* 1988, **8**(4), 40-41

H113 *N*-(hydroxymethyl)acrylamide

$$H_2C{=}CHCONHCH_2OH$$

$C_4H_7NO_2$ **Mol. Wt.** 101.11 **CAS Registry No.** 924-42-5

Synonyms *N*-(hydroxymethyl)-2-propenamide; *N*-methanolacrylamide; monomethylolacrylamide; Uramine T80

EINECS No. 213-103-2 **RTECS No.** AS 3600000

Physical properties

M. Pt. 74°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 420, 474 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal rat 563 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Gavage (2 yr) ♂/♀ rats and mice, 6 or 12 mg kg^{-1} day^{-1}, no evidence of carcinogenicity in ♂/♀ rats, clear evidence of carcinogenicity in ♂/♀ mice based on increased incidence of neoplasms of the Harderian gland (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with or without metabolic activation, negative (4).
In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations were induced (metabolic activation unspecified) (4).
In vitro B6C3F1 mice bone marrow, no increase in micronucleated polychromatic erythrocytes was observed (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Other comments

Toxicity reviewed (6).
Reviews on experimental toxicity and human health effects listed (7).

References

1. *Jpn. J. Hyg.* 1979, **34**, 183.
2. Grayson, M. et al (Eds.) *Kirk-Othmer Encyclopedia of Chemical Technology* 1978, 306, John Wiley & Sons, New York, NY, USA.
3. *Biochem. Pharmacol.* 1970, **19**, 2591.
4. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-352, NIEHS, Research Triangle Park, NC, USA.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *BIBRA Toxicity Profile* 1991, British Industrial Biological Research Association, Carshalton, UK.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H114 4-hydroxy-2-nonenal

$$CH_3(CH_2)_4CH(OH)CH{=}CHCHO$$

$C_9H_{16}O_2$ **Mol. Wt.** 156.22 **CAS Registry No.** 29343-52-0

Synonyms HNE
Uses Food flavouring agent.

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat, mouse 35, 69 mg kg^{-1}, respectively (1,2).

Genotoxicity

Reduced plating efficiency in Chinese hamster ovary cells, with some DNA fragmentation (3).
Cerebral endothelial cells (species unspecified) incubated for 3 hr with ≥1 μM 4-hydroxy-2-nonenal suffered significantly elevated levels of chromosomal aberrations; at ≥ 10 μM increased numbers of micronuclei were seen compared with controls. Cytotoxicity was observed at 50 μM (4).

Other effects

Any other adverse effects
In vitro rat heart and lung caused profound depletion of cardiac GSH and slight ethane and pentane evolution (5).
In vitro Chinese hamster fibroblast HA-1 cell line cytotoxic. In resistant cell lines total glutathione and glutathione transferase activity were increased (2-3 fold) suggesting that cell lines adapted or maintained in a highly peroxidative environment are also resistant to the cytotoxicity of aldehydes formed during lipid peroxidation. The formation of aldehydes may contribute significantly to the mechanisms of oxidant-induced injury (6).

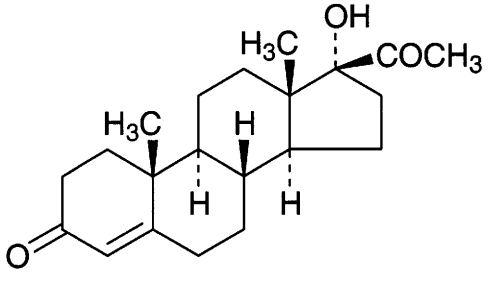
Other comments

Reacts with sulfhydryl groups. Inhibits tubulin polymerisation in a dose-dependent manner (7).
Metabolism reviewed (8).

References

1. *Toxicology* 1984, **4**, 100.
2. Lewis, R. J. *Sax's Dangerous Properties of Industrial Materials* (Ed.) 8th ed., 1992, **3**, 1949, Van Nostrand Reinhold, New York, NY, USA.
3. Brambilla, G. et al *Mutat. Res.* 1986, **171**, 169.
4. Karlhuber, G. M. et al *Mutat. Res.* 1997, **381**(2), 209-216.
5. Dutta, S. et al *Toxicol. Lett.* 1988, **44**(1-2), 55-64.
6. Spitz, D. R. et al *Biochem. J.* 1990, **267**(2), 453-459.
7. Gabriel, L. et al *Chem.-Biol. Interact.* 1985, **56**, 201.
8. Pryor, W. A. *Free Radical Biol. Med.* 1990, **8**(6), 541-543

H115 hydroxyprogesterone



$C_{21}H_{30}O_3$ **Mol. Wt.** 330.47 **CAS Registry No.** 68-96-2

Synonyms 17α-hydroxyprogesterone; 17-hydroxypregn-4-ene-3,20-dione; 4-pregnen-17α-ol-3,20-dione; Gestageno; Prodox

EINECS No. 200-699-4 **RTECS No.** TU 5060000

Uses Progestogen

Occurrence Isolated from adrenal glands.

Physical properties

M. Pt. 222-223°C
Solubility Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Increased tumour incidence and ratio of malignant to benign tumours in ♀ Wistar rats, ♂ and ♀ mice and Syrian golden hamsters after intramuscular injection of 5-100 × human contraceptive dose 1-2 × month^{-1} over 5-32 month (1).

References

1. Gao, F. et al *Sci. China, Ser. B* 1990, **33**(3), 311-322

H116 2-hydroxypropyl acrylate

$$CH_2=CHCO_2CH_2CH(OH)CH_3$$

$C_6H_{10}O_3$ **Mol. Wt.** 130.14 **CAS Registry No.** 999-61-1

Synonyms 1,2-propanediol 1-acrylate; 2-propenoic acid, 2-hydroxypropyl ester; propylene glycol monoacrylate; Bisomer HPA

EINECS No. 213-663-8 **RTECS No.** AT 1925000

Uses In photocurable resins, photohardenable ink-resists, photopolymerisable compounds.

Physical properties

B. Pt. 77°C at 5 mmHg **Flash point** 89°C **Specific gravity** 1.044

Occupational exposure

FR-VME 0.5 ppm (3 mg m^{-3})
UK-LTEL 0.5 ppm (2.7 mg m^{-3})
US-TWA 0.5 ppm
Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Causes burns – May cause sensitisation by skin contact (R23/24/25, R34, R43)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36/37/39, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 3.10-3.61 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 250 mg kg^{-1} (2).

LD_{50} oral mouse 1056 mg kg^{-1} (3).
LD_{50} subcutaneous rabbit 160 mg kg^{-1} (4).

Other comments

Reviews on human health effects, experimental toxicity, physico-chemical effects and workplace experience listed (5).

References

1. Russon, C. L. et al *Bull. Environ. Contam. Toxicol.* 1988, **41**, 589-596.
2. *Documentation of Threshold Limit Values for Substances in Workroom Air* 1986, ACGIH, Cincinnati, OH, USA.
3. *Toxicol. Lett.* 1982, **11**, 125.
4. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H117 2-hydroxypropyl methacrylate

$$CH_2=C(CH_3)CO_2CH_2CH(OH)CH_3$$

$C_7H_{12}O_3$ **Mol. Wt.** 144.17 **CAS Registry No.** 923-26-2

Synonyms 2-methyl-2-propenoic acid, 2-hydroxypropyl ester; methacrylic acid, 2-hydroxypropyl ester; β-hydroxypropyl methacrylate; Bisomer HPMA; Bisomer CF

EINECS No. 213-090-3 **RTECS No.** OZ 4750000

Uses Manufacture of resins.

Physical properties

M. Pt. below –70°C **B. Pt.** 96°C at 9.8 mm Hg **Flash point** 121°C (open cup) **Specific gravity** 1.027 at 25°C

Occupational exposure

Supply classification irritant
Risk phrases Irritating to eyes and skin (R36/38)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water (S2, S26, S28)

Mammalian & avian toxicity

Sensitisation
A dental technician with allergic contact dermatitis patch-tested positive to 2-hydroxypropyl methacrylate (1).

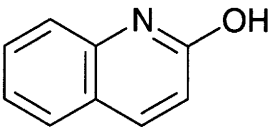
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (2).

References

1. Kanerva, L. et al *Contact Dermatitis* 1988, **18**(1), 10-15.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H118 2-hydroxyquinoline



C_9H_7NO **Mol. Wt.** 145.16 **CAS Registry No.** 59-31-4

Synonyms carbostyril; 2-quinolinol; 2(1*H*)-quinolone; *o*-aminocinnamic acid

EINECS No. 200-420-6 **RTECS No.** FG 7175000

Physical properties

M. Pt. 198-199°C

Solubility Water: 1.05 g l^{-1} at 22°C. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 1 ppm, Microtox test (1).

Mammalian & avian toxicity

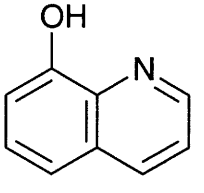
Acute data

LD_{50} intraperitoneal mouse 150 mg kg^{-1} (2).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. *NTIS Report* No. AD607-9J2, Natl. Tech. Inf. Ser., Springfield, VA, USA

H119 8-hydroxyquinoline



C_9H_7NO **Mol. Wt.** 145.16 **CAS Registry No.** 148-24-3

Synonyms 8-quinolinol; oxyquinoline; oxine; hydroxybenzopyridine; phenopyridine; oxychinolin; Bioquin; Quinophenol

EINECS No. 205-711-1 **RTECS No.** VC 4200000

Uses Slimicide. Fungistat; chelating agent in determination of trace metals; disinfectant. Antimicrobial used in human medicine to treat minor burns and piles. In dye manufacture.

Physical properties

M. Pt. 72-74°C **B. Pt.** 267°C
Solubility Organic solvents: acetone, benzene, chlorofrom, ethanol, aqueous mineral acids

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bleak 18 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (96 hr) *Nitocra spinipes* 11.5 mg l^{-1} (1).
EC_{50} (30 min) *Photobacterium phosphoreum* 2.30 ppm Microtox test (2).

Environmental fate

Nitrification inhibition
75% inhibition of nitrification in non-acclimated sludge at 73 mg l^{-1} (3).

Degradation studies
COD: 80% of ThOD (0.05 normality Cr_2O_7), $KMnO_4$: 44% of ThOD (0.01 N $KMnO_4$), ThOD: 0.02 mg l^{-1} O_2 (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1200 mg kg^{-1} (5).
LD_{50} oral mouse 2 g kg^{-1} (6).
LD_{50} oral redwing blackbird 104 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 48 mg kg^{-1} (8).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (9).
NTP tested rats and mice via gavage. No evidence of carcinogenicity in ♂ mice, ♂ and ♀ rats (10).
No evidence of carcinogenicity in rats fed 400 mg kg^{-1} day^{-1} for 78 wk, or 50 mg kg^{-1} day^{-1} for 104 wk, or in a two-stage skin painting study in mice (11).
Increased tumour incidence (lymphomas, lung adenomas, liver and subcutaneous haemangiomas, and ovary adenoma) reported in mice after subcutaneous injection of 1.5 mg $mouse^{-1}$, 3 × $month^{-1}$ for 660 days (9).
Increased incidence of bladder tumours reported in mice 40 wk after bladder implantation of a 9-11 mg cholesterol pellet containing 20% 8-hydroxyquinoline, but not when paraffin wax pellets were used (9).

Irritancy
Severe skin irritation, redness and purpuritic eruption may occur in sensitive people (11).
Application to skin of mice caused hair depigmentation (11).
A 1.45 g l^{-1} aqueous solution caused slight eye irritation to rabbits (11).

Genotoxicity

Salmonella typhimurium TA97, TA100 with metabolic activation positive (12).
Did not induce unscheduled DNA synthesis in human cells *in vitro* (11).
Did not induce sex-linked recessive lethal mutations in *Drosophila melanogaster* (11).
Did not induce micronuclei in mice given intraperitoneal injections of 87 mg kg^{-1} (11).

Other effects

Other adverse effects (human)
A child suffered methaemoglobinaemia and damage to the liver and kidneys after an enema containing 6 g (11).

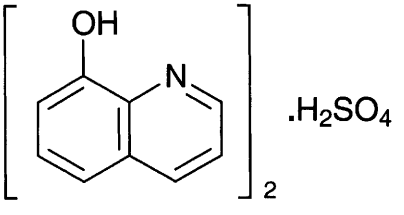
Other comments

Reviews on human health effects and experimental toxicology listed (13).

References

1. Linden, E. et al *Chemosphere* 1979, **11/12**, 843-851.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Meinck, F. et al *Les Eaux Residuaires Industrielles* 1970.
4. Wolters, N. *Unterschiedliche Bestimmungsmethoden zur Erfassung der organischen Substanz in einer Verbindung* Lehrauftrag Wasserbiol. Tech. Hochschule, Darmstadt, Germany.
5. *Pesticide Chemicals Official Compendium* 1966, Assoc. Am. Pest. Contr. Officials, KS, USA.
6. *Drugs in Japan* 6th ed. 1982, Jap. Pharm. Info. Center, Tokyo, Japan.
7. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
8. Bernstein et al *Toxicol. Appl. Pharmacol.* 1963, **5**, 599.
9. *IARC Monograph* 1977, **13**, 101-112.
10. *National Toxicology Program Research and Testing Division* 1992, Report No. TR366, NIEHS, Research Triangle Park, NC, USA.
11. *BIBRA Toxicity Profile: 8-Hydroxyquinoline* 1987, British Industrial Biological Research Association, Carshalton, UK.
12. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
13. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

H120 hydroxyquinoline sulfate



$C_{18}H_{16}N_2O_6S$ **Mol. Wt.** 388.40 **CAS Registry No.** 134-31-6

Synonyms 8-hydroxyquinoline sulfate; bis(8-hydroxyquinolinium) sulfate; 8-quinolinol sulfate; oxyquinoline sulfate; oxine sulfate; Albisal; Chinosol

EINECS No. 205-137-1 **RTECS No.** VC 8260000

Uses Superseded systemic fungicide and bactericide. Antiseptic, antiperspirant, deodorant. Topical antiseptic, disinfectant.

Physical properties

M. Pt. 175-178°C

Solubility Water: 300 g l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform, ethanol

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed (R22)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing (S2, S36)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 280, 2038 mg kg^{-1}, respectively (1).
LD_{50} dermal rat >4000 mg kg^{-1} (2).

Metabolism and toxicokinetics

Metabolised in mammals via conjugation with glucuronic acid. 95% eliminated in urine 24-36 hr after oral administration (species and dose unspecified) (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (3).
Salmonella typhimurium TA1537 with metabolic activation weakly positive; TA1535, TA98 with or without metabolic activation negative; TA100 without metabolic activation negative (4).
Induced chromatid aberrations in human leukocytes *in vitro* (4).

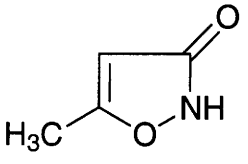
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
EPA Toxicity Class III (formulation) (2).

References

1. Perkow, W. *Wirksubstanzen der Planzenschutz und Schaedlingsbekaempfungsmittel* 1971/1976, Verlag Paul Parey, Berlin, Germany.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
4. Epler, J. L. et al *Mutat. Res.* 1977, **39**, 285-296.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

H121 hymexazol



$C_4H_5NO_2$ **Mol. Wt.** 99.09 **CAS Registry No.** 10004-44-1

Synonyms 5-methylisoxazol-3-ol; 5-methyl-3(2*H*)-isoxazolone; 3-hydroxy-5-methylisoxazole; 5-methyl-3-isoxazolol; Tachigaran

EINECS No. 233-000-6 **RTECS No.** NY 2932000

Uses Systemic soil and seed fungicide.

Physical properties

M. Pt. 86°C **Partition coefficient** log P_{ow} –0.658 **Volatility** v.p. 1.37×10^{-3} mmHg at 25°C
Solubility Water: 65.1 g l^{-1} at 20°C. Organic solvents: acetone, chloroform, dimethylformamide, ethanol, ethylene glycol, methanol

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp, Japanese killifish 165, >40 mg l^{-1}, respectively (1).

Environmental fate

Degradation studies
Degraded to 5-methyl-2(3*H*)-oxazolone in soil (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral Japanese quail 1700 mg kg^{-1} (1).
LD_{50} oral ♀, ♂ rat 3909, 4678 mg kg^{-1}, respectively (1).
LD_{50} oral ♀, ♂ mice 1968, 2148 mg kg^{-1}, respectively (1).
LD_{50} dermal rabbit, rat 2000, >10,000 mg kg^{-1}, respectively (1).
LD_{50} subcutaneous mouse, rat 1167, 1884 mg kg^{-1}, respectively (2).
LD_{50} intravenous mouse 445 mg kg^{-1} (2).

Sub-acute and sub-chronic data
Dose- and time-dependent increases in alanine aminotransferase and amidopyrine *N*-demethylase activities, cytochrome P450, free radicals, iron-containing protein concentrations and lipid peroxidation rates in the liver observed in rats exposed to 5-2060 mg m^{-3} by inhalation for ≤4 months (3).

Carcinogenicity and chronic effects
No-effect level for rats and dogs in 2-yr feeding trials 20 and 15 mg kg^{-1} day^{-1}, respectively; no evidence of carcinogenicity (1).
No evidence of carcinogenicity in ♂, ♀ rats receiving 1 or 100 mg kg^{-1} for prolonged periods (route and duration unspecified) (4).

Teratogenicity and reproductive effects
No evidence of embryotoxicity or teratogenicity in rats receiving 28 and 280 mg kg^{-1} (route and duration unspecified) (4).

Genotoxicity

Increased incidence of chromosomal aberration reported in mice following single or daily dose for 14 days, orally or by inhalation (dose unspecified) (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
WHO Toxicity Class Table 5 (8).
EPA Toxicity Class III (formulation) (1).

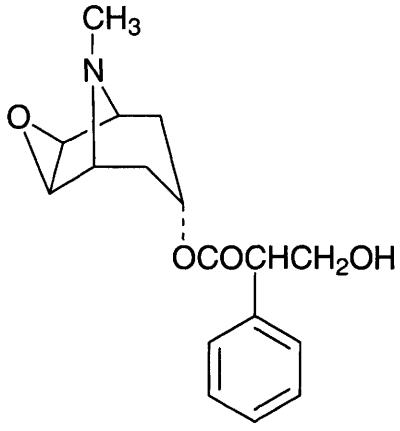
Other comments

Not toxic to bees (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *Noyaku Kagaku* 1975, **2**, 165.
3. Sinitskaya, T. A. et al *Gig. Sanit.* 1989, (5), 87-89 (Russ.) (*Chem. Abstr.* **111**, 52071d).
4. Martson, L. V. et al *Gig. Sanit.* 1991, (4), 53-55 (Russ.) (*Chem. Abstr.* **115**, 24128s).
5. German, I. V. *Gig. Sanit.* 1990, (5), 72-74 (Russ.) (*Chem. Abstr.* **113**, 93130g).
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

H122 hyoscine



$C_{17}H_{21}NO_4$ **Mol. Wt.** 303.36 **CAS Registry No.** 51-34-3

Synonyms scopolamine; scopine tropate; 6β-,7β-expoxy-3α-tropanyl *S*-(−)-tropate; atrochin; hyosol

EINECS No. 200-090-3 **RTECS No.** VR 3675000

Uses Antimuscarinic agent used in prevention and control of motion sickness, visceral spasms and as a cycloplegic and mydriatic.

Occurrence In the plant *Atropa belladonna*.

Physical properties

M. Pt. 59°C

Solubility Organic solvents: acetone, chloroform, diethyl ether, ethanol

Occupational exposure

Supply classification very toxic

Risk phrases Very toxic by inhalation, in contact with skin and if swallowed (R26/27/28)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the eyes – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S25, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1275 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 400 mg kg^{-1} (2).

LD_{50} subcutaneous rabbit, mouse 75, 1700 mg kg^{-1}, respectively (3,4).

LD_{50} intravenous rabbit, mouse 50, 100 mg kg^{-1}, respectively (3,5).

Teratogenicity and reproductive effects

Increased incidence of malformations reported in foetuses of mice following injection of 4.6 or 59 μg g^{-1} into the abdominal cavity daily on days 6-16 of gestation (6).

Rats were given up to 900 mg kg^{-1} day^{-1} on days 6-15 of pregnancy by gavage. There was no clear evidence of teratogenicity, but marginal evidence of retarded intra-uterine growth, and a non-dose-related trend to an increased incidence of malformation at maternally toxic doses (7).

Aggression was increased among offspring of mice injected with 1 mg kg^{-1} intraperitoneally on days 3, 7, 10, 13 or 16 of pregnancy (8).

Hyoscine toxicity has been reported in a neonate following administration of 1.8 mg (plus pethidine and levorphanol) prior to delivery; the neonate was lethargic, barrel chested and had a heart rate of 200 (9).

Metabolism and toxicokinetics

Readily absorbed from the gastro-intestinal tract and almost entirely metabolised, probably in the liver; only a small proportion is excreted unchanged in urine. Crosses the blood-brain barrier, placenta, and is well absorbed through the skin (9).

Irritancy

Contact dermatitis reported following transdermal use for motion sickness in men treated for 1.5-15 months (9).

Genotoxicity

Induced chromosomal aberrations and sister chromatid exchanges in cultured human lymphocytes (6).

Other effects

Other adverse effects (human)

Dysarthria, severely impaired immediate recall, visual illusions, ataxia and visuospatial apraxia reported in a volunteer after subcutaneous injection of 1 mg (~ 0.014 mg kg^{-1}). Another reported dry mouth, blurred vision, sedation and dizziness after ~ 6 μg kg^{-1} (10).

Bilateral mydriasis reported during transdermal use may have been due to contamination of a finger while applying the patch and then rubbing the eye (11).

Psychotic reactions have been reported following transdermal use and after instillation of eye drops (12).

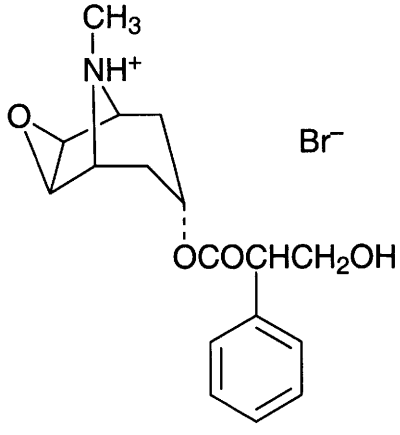
Legislation

Use in cosmetics in the UK prohibited (7).

References

1. *Arch. Int. Pharmacodyn. Ther.* 1961, **134**, 255.
2. *Arzneim.-Forsch.* 1971, **21**, 1721.
3. *Abdernalden's Handbuch der Biologischen Arbeitsmethoden* 1935, **4**, 1289.
4. *J. Pharmacol. Exp. Ther.* 1936, **56**, 85.
5. *J. Med. Chem.* 1983, **26**, 1772.
6. Yu, J. et al *Chin. Med. J. (Beijing, Engl. Ed.)* 1988, **101**(5), 339-345.
7. *NTIS Report RTI-170 NTP-87-145* 1987, Natl. Tech. Inf. Ser., Springfield, VA, USA.
8. Richardson, D. L. et al *Fed. Proc.* 1972, **31**, 596.
9. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
10. Serby, M. et al *Am. J. Psychiatry* 1984, **141**, 1010.
11. Biena, R. A. et al *Ann. Intern. Med.* 1983, **99**, 572-573.
12. Barker, D. B. et al *DICP, Ann. Pharmacother.* 1990, **24**, 847-850

H123 hyoscine bromide



$C_{17}H_{22}BrNO_4$ **Mol. Wt.** 384.27 **CAS Registry No.** 114-49-8

Synonyms hyoscine hydrobromide; scopolamine bromide; benzeneacetic acid, α-(hydroxymethyl)-, 9-methyl-3-oxa-9-azatricyclo [3.3.1.0^{2,4}]non-7-yl ester, hydrobromide, [7(*S*)-(1α,2β,4β,5α,7β]-; Beldavrin; Euscopol; Kwells

EINECS No. 204-050-6 **RTECS No.** YM 4550000

Uses Anticholinergic; sedative; a pre-anaesthetic; control of motion sickness.

Physical properties

M. Pt. 196-197°C

Occupational exposure

Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed (R26/27/28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the eyes – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S25, S45)

Mammalian & avian toxicity

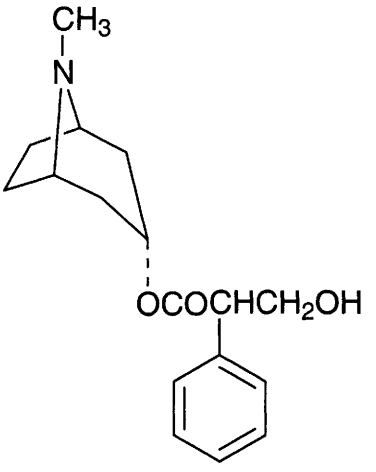
Acute data
LD_{50} oral rat, mouse 1270, 1880 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous rat 3800 mg kg^{-1} (1).

Teratogenicity and reproductive effects
Major embryo malformations including gastroschisis, exencephaly, reduction limb deformities, microphthalmia and buphthalmia reported in hen eggs after injection of 100 or 200 μg (3).
No adverse effects on prenatal viability and no evidence of teratogenesis reported in mice after administration of 10-900 mg kg^{-1} day^{-1} on days 6-15 of pregnancy (4).

References

1. *Arch. Int. Pharmacodyn. Ther.* 1969, **180**, 155.
2. *Arzneim.-Forsch.* 1968, **18**, 1132.
3. McBride, W. G. et al *Aust. J. Biol. Sci.* 1982, **35**, 173-178.
4. *NTIS Report RTI-171, NTP-87-102* 1987, Natl. Tech. Inf. Ser., Springfield, VA, USA

H124 hyoscyamine



$C_{17}H_{23}NO_3$ **Mol. Wt.** 289.37 **CAS Registry No.** 101-31-5

Synonyms (–)-atropine; α-(hydroxymethyl)benzeneacetic acid, 8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester; 1α*H*,5α*H*-tropan-3α-ol (–)-tropate; tropine tropate; Cystospaz; Daturine

EINECS No. 202-933-0 **RTECS No.** NH 0875000

Uses Antimuscarinic with the effects of atropine, used in relief of conditions associated with visceral spasm. It has also been used for colds and to treat Parkinsonism.

Occurrence In Solanaceae such as *Atropa belladonna*.

Physical properties

M. Pt. 106-108°C.

Solubility Organic solvents: chloroform, ethanol

Occupational exposure

Supply classification very toxic

Risk phrases Very toxic by inhalation and if swallowed (R26/28)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the skin – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S24, S45)

Mammalian & avian toxicity

Acute data

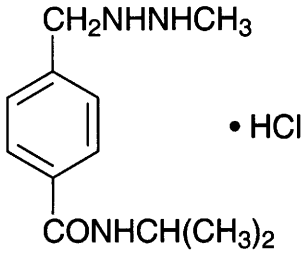
LD_{50} intravenous mouse 95 mg kg^{-1} (1).

LD_{Lo} route unspecified human 1470 μg kg^{-1} (2).

References

1. *Br. J. Pharmacol. Chemother.* 1965, **24**, 138.
2. Arena, J. M. *Poisoning* 1970, Charles C. Thomas, Springfield, IL, USA

I1 ibenzmethyzin hydrochloride



$C_{12}H_{20}ClN_3O$ **Mol. Wt.** 257.76 **CAS Registry No.** 366-70-1

Synonyms *N*-isopropyl-α-(2-methylhydrazino)-*p*-toluamide monohydrochloride; *N*-(1-methylethyl)-4-[(2-methylhydrazino)methyl]benzamide; IBZ; *N*-4-isopropylcarbamoyl benzyl-*N'*-methylhydrazine hydrochloride; Procarbazine hydrochloride; Natulan

EINECS No. 206-678-6 **RTECS No.** XS 4725000

Uses Chemotherapeutic agent.

Physical properties

M. Pt. 223°C

Solubility Organic solvents: chloroform, diethyl ether, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1320 mg kg^{-1} (1).

LD_{50} oral rabbit 145 mg kg^{-1} (1).

LD_{50} intravenous rat, mouse 350, 560 mg kg^{-1}, respectively (2,3).

LD_{50} subcutaneous rat, mouse 490, 710 mg kg^{-1}, respectively (3,4).

LD_{50} intraperitoneal mouse 699 mg kg^{-1} (5).

Carcinogenicity and chronic effects

Sufficient evidence for the carcinogenicity in mice and rats. Limited evidence of its carcinogenicity in monkeys. There is inadequate evidence of the carcinogenicity of the substance alone in humans, IARC classification group 2A (6).

Mice were given (route unspecified) 300 mg kg^{-1} once a wk for 8 wk. By 6-11 wk 9/14 had lung tumours and 2/14 had leukaemia and by 12-16 wk 21/21 had lung tumours and 17/21 had leukaemia (7).

Ten ♀ Sprague-Dawley rats received single 50, 100 or 150 mg doses or 3 doses of 50 mg by gavage. All animals showed mammary tumours by 20 wk after treatment (8).

♂ and ♀ Sprague-Dawley rats received intraperitoneal doses of 15 or 30 mg kg^{-1} in buffered saline 3 × wk^{-1} for 26 wk. Neoplasms, including those of the neuroepithelial tissues, mammary gland, haematopoietic system and lymphoreticular tissue, were observed in 19/30 ♂ and 27/30 ♀ of the low-dose group and in 30/33 ♂ and 30/31 ♀ of the high-dose group. Other cancers detected were lymphomas, leukaemia, olfactory neuroblastomas, adenocarcinomas of the mammary gland and oligodendroglioma (9).

Intravenous injections of 24 mg kg^{-1} to ♂ BR46 rats once every wk for 52 wk. 1/34 and 14/34 rats died with, respectively, benign and malignant neoplasms. Malignant: 3 renal sarcomas, 1 adenocarcinoma, 2 intra-abdominal spindle-cell sarcomas, 1 rectal carcinoma, 1 testicular carcinoma, 1 squamous-cell carcinoma of the ear duct, 1 subaxillary sarcoma and 1 neurilemmoma. Benign: 1 prostatic adenoma and 1 subcutaneous fibromas (2).

Teratogenicity and reproductive effects

Single intraperitoneal injection 5-550 mg kg^{-1} to ♀ Wistar (CF) rats. After single injection of 100 mg kg^{-1} on days

5-8 of pregnancy and a single dose >75 mg kg^{-1} on days 9-14 or 17, 100% embryomortality was reported. Single doses of 25-75 mg kg^{-1} on days 10, 11, 12, 14 or 17 were teratogenic with defects including tail and limb malformations, exencephaly, omphalocele, encephalocoele and short maxilla or mandible (10).
0, 1, 5 or 15 mg kg^{-1} administered to pregnant rats from gestation days 13 to 16. Offspring brains at age 12 to 15 wk showed cerebral atrophy, which increased with dose, and a reduction in neuronal numbers. Astrocyte and oligodendrocyte populations were unaffected (11).
♂ rats aged 10-90 days given a daily intraperitoneal (5 or 9 wk) 30 mg kg^{-1} or gavage (9 wk) doses 5 or 50 mg kg^{-1} showed substantial mortality in immature rats and at high oral doses. Body weight gain and the weights of testes and epididymis were reduced. Spermatogenic architecture was disrupted. The number of Sertoli cells was not affected, but a dysfunction was seen in cases of severe disruption of spermatogenesis. Leydig cells were moderately affected and epididymal sperm reserves were reduced. Foetus number was low in ♀ mated with treated ♂ (12).

Metabolism and toxicokinetics
Levels in the plasma and the cerebrospinal fluid equilibrated, following 100 mg kg^{-1} intravenous dose, within 30 min in a dog study (13).
After intraperitoneal injection of 20 or 200 mg kg^{-1} of ^{14}C-radiolabelled compound to rats, 7-10% of the dose was exhaled as methane and 11-22% as CO_2 within 8 hr. It was suggested that metabolism proceeded via formation of methylhydrazine (14).
Following human oral administration 70% appeared within 24 hr in urine. Most appeared as the metabolite *N*-isopropyl terephthalaminic acid with only 5% as the unmodified compound. Little excreted in the faeces (15,16).

Sensitisation
4/44 and 8/23 patients with Hodgkin's disease and non-Hodgkin's lymphoma, respectively, showed allergic skin reactions (17).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (18-20).
Salmonella typhimurium (strain unspecified) without metabolic activation positive (21).
Saccharomyces cerevisiae without metabolic activation mitotic cross-over, gene conversions and reverse mutations positive (20).
Drosophila melanogaster recessive lethal mutations, total sex chromosome loss and dominant lethality positive (22).
In vitro mouse lymphoma L5178Y with metabolic activation positive (23).
In vivo mouse foetal liver and blood cells after transplacental treatment caused micronuclei (24).

Other effects

Other adverse effects (human)
Daily oral doses 250-300 mg caused dose-related reversible depression of peripheral leucocyte and platelet counts with a low 2-3 wk into the programme. Vomiting and nausea are common. Somnolence, hallucinations, agitation and lethargy are frequent with oral and intravenous injection, being more aggravated via the latter route (25). Peripheral neuropathy has been reported (26).

Other comments

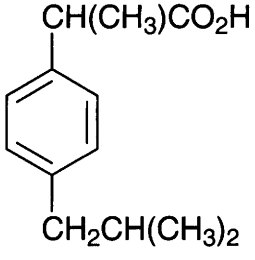
Antitumour activity, metabolism, pharmacology and mode of action reviewed (1,27).

References

1. Reed, D. J. *Antineoplastic and Immunosuppresive Agents* 1975, Part 2, Springer, New York, NY, USA.
2. Schmahl, D. et al *Arzneim.-Forsch.* 1970, **20**, 1461-1467.
3. *Iyakuhin Kenkyu* 1973, **4**, 467.
4. *Drugs in Japan. Ethical Drugs* 6th ed., 1982, Japan Pharmaceutical Information Centre, Yakugyo Jiho Co. Ltd., Tokyo, Japan.
5. *Arch. Toxicol.* 1979, **41**, 287.
6. *IARC Monograph* 1987, **Suppl. 7**, 327.

7. Kelly, M. G. et al *Cancer Chemother. Rep.* 1964, **39**, 77-80.
8. Henson, J. C. et al *Eur. J. Cancer* 1966, **2**, 385-386.
9. National Cancer Institute *NCI Carcinog. Tech. Rep. Ser.* 1979, No. 19.
10. Chaube, S. et al *Teratology* 1969, **2**, 23-32.
11. Wright, J. A. et al *J. Comp. Pathol.* 1989, **101**(4), 421-427.
12. Velez de la Calle, J. F. et al *J. Reprod. Fertil.* 1988, **84**(1), 51-61.
13. Oliverio, V. T. et al *Cancer Chemother. Rep.* 1964, **42**, 1-7.
14. Dost, F. N. et al *Biochem. Pharmacol.* 1967, **16**, 1741-1746.
15. Bollag, W. *Natulan* 1965, Wright, Bristol, UK.
16. Schwartz, D. E. et al *Arzneim.-Forsch.* 1967, **17**, 1389-1393.
17. Anderson, E. et al *Scand. J. Haematol.* 1980, **24**, 149-151.
18. Heddle, J. A. et al *Progress in Genetic Toxicology* 1977, 265-274, Elsevier/North-Holland Biomedical Press, Amsterdam, Netherlands.
19. Painter, R. B. et al *Mutat. Res.* 1978, **54**, 113-115.
20. Bronzetti, G. et al *Mutat. Res.* 1979, **68**, 51-58.
21. Pueyo, C. *Mutat. Res.* 1979, **67**, 189-192.
22. Blijleven, W. G. H. et al *Mutat. Res.* 1977, **45**, 47-59.
23. Clive, D. et al *Mutat. Res.* 1979, **59**, 61-108.
24. Cole, R. J. et al *Nature (London)* 1979, **277**, 317-318.
25. DeVita, V. T. et al *Clin. Pharmacol. Ther.* 1966, **7**, 542-546.
26. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
27. Sartorelli, A. C. et al *Ann. Rev. Pharmacol.* 1969, **9**, 51-72

12 ibuprofen



$C_{13}H_{18}O_2$ **Mol. Wt.** 206.28 **CAS Registry No.** 15687-27-1

Synonyms α-methyl-4-(2-methylpropyl)benzeneacetic acid; *p*-isobutylhydratropic acid; 2-(4-isobutylphenyl)propionic acid; Actifen; Brufen; Ibufen; Motrin

EINECS No. 239-784-6 **RTECS No.** MU 6640000

Uses Anti-inflammatory, analgesic and antipyretic drug.

Physical properties

M. Pt. 75-77°C ((±)-form)

Solubility Organic solvents: acetone, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 636, 740 mg kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal mouse, rat 320-626 mg kg^{-1}, respectively (3,4).

Teratogenicity and reproductive effects

Oral near-term rat 6 mg kg^{-1} caused foetal ductal constriction of 70% within 1 to 8 hr, 60% dilation of both ventricles and 120% increase in pericardial fluid. These changes partly disappeared at 24 hr. Cardiac failure was induced in some animals (5).

Metabolism and toxicokinetics

Following ingestion by human, peak plasma concentrations occur at 1 to 2 hr. Bound extensively to plasma proteins with $t_{1/2}$ of ~2 hr. Rapidly excreted in urine mainly as metabolites and their conjugates; 1% as unmodified compound and 14% as conjugated compound (6).

After 400 mg single dose in healthy volunteers, one preparation produced peak plasma concentration of 30.0 μg ml^{-1} at 1.6 hr and the other 23.2 μg ml^{-1} at 2.3 hr (7).

90 and 120 min after dermal application to guinea pig, detectable levels were observed in blood and plasma. Concentrations of 13-228 μg, dependent on depth, were found in muscle tissue below the application area (8).

Sensitisation

A fatal asthma attack occurred in a 65-yr-old woman, adult-onset asthma, 30 min after taking 800 mg dose (9). Hypersensitivity reactions may occur and include rashes (10).

Other effects

Other adverse effects (human)

Reversible amblyopia has been reported (11,12).

Can cause dyspepsia, nausea and vomiting, gastro-intestinal bleeding, peptic ulcers and perforation (13,14).

Acute renal failure (15-17).

In an evaluation of hepatic toxicity involving 1468 patients with rheumatoid arthritis and osteoarthritis, no aspartate aminotransferase elevation was observed (18).

Any other adverse effects

In vitro rat hepatocyte toxic effects at ten-fold therapeutic plasma concentration for 48 hr. Impaired gluconeogenesis from lactate after 6 hr at therapeutic level. 40% inhibition of albumin synthesis after 6 hr exposure to five-fold therapeutic level (19).

Other comments

Central nervous system adverse effects reviewed (20).

Metabolism and pharmacokinetics reviewed (21-23).

No increase in δ-aminolaevulinic acid synthetase activity in rat, suggesting the drug is safe to be used by porphyria sufferers (24).

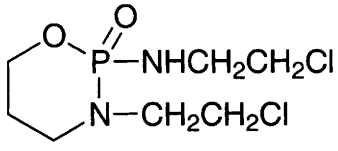
Chemopreventive agent against carcinogenesis in *in vitro* mouse mammary gland (25).

References

1. *Arzneim.-Forsch.* 1984, **34**, 280.
2. *Pharm. Chem. J. (Engl. Transl.)* 1980, **14**, 119.
3. *Toxicol. Appl. Pharmacol.* 1969, **15**, 310.
4. *Arzneim.-Forsch.* 1977, **27**, 1006.
5. Momma, K. et al *Am. J. Obstet. Gynecol.* 1990, **162**(5), 1304-1310.
6. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
7. Karttunen, P. et al *Int. J. Clin. Pharmacol. Ther. Toxicol.* 1990, **28**(6), 251-255.
8. Giese, U. *Arzneim.-Forsch.* 1990, **40**(1), 84-88.
9. Ayres, J. G. et al *Lancet* 1987, **i**, 1082.
10. Sternlieb, P. et al *Ann. Intern. Med.* 1980, **92**, 570.
11. Collum, L. M. T. et al *Br. J. Ophthalmol.* 1971, **55**, 472-477.
12. Palmer, C. A. L. *Br. Med. J.* 1972, **3**, 765.
13. Ravi, S. et al *Postgrad. Med. J.* 1986, **62**, 773-776.
14. Clements, D. et al *Br. Med. J.* 1990, **301**, 987.
15. Brandstetter, R. D. et al *Br. Med. J.* 1978, **2**, 1194-1195.

16. Kimberly, R. P. et al *Arthritis Rheum.* 1979, **22**, 281-285.
17. Spierto, R. J. et al *Ann. Pharmacother.* 1992, **26**, 714.
18. Freeland, G. R. et al *Clin. Pharmacol. Ther. (St. Louis)* 1988, **43**(5), 473-479.
19. Castell, J. V. et al *Xenobiotica* 1988, **18**(6), 737-745.
20. Hoppmann, R. A. et al *Arch. Intern. Med.* 1991, **151**, 1309-1313.
21. Brune, K. et al *Dtsch. Apoth. Ztg.* 1989, **129**(5) (Suppl. 12), 3-15 (Ger.) (*Chem. Abstr.* **110**, 107468a).
22. Dinnendahl, V. *Pharm. Ztg.* 1989, **134**(1), 9-14 (Ger.) (*Chem. Abstr.* **110**, 107412c).
23. Brune, K. *Agents Actions Suppl.* 1988, **25**, 9-19.
24. McColl, K. E. L. et al *Ann. Rheum. Dis.* 1987, **46**(7), 540-542.
25. Mehta, R. G. et al *Anticancer Res.* 1991, **11**(2), 587-591

13 ifosfamide



$C_7H_{15}Cl_2N_2O_2P$ **Mol. Wt.** 261.09 **CAS Registry No.** 3778-73-2

Synonyms isophosphamide; *N,N*-bis(β-chloroethyl)amino-*N'*-*O*-propylenephosporic acid ester diamide; *N,*3-bis(2-chloroethyl)tetrahydro-2*H*-1,3,2-oxazaphosphorin-2-amine 2-oxide; 3-(2-chloroethyl)-2-[(2-chloroethyl)amino]tetrahydro-2*H*-1,3,2-oxazaphosphorine-2-oxide

EINECS No. 223-237-3 **RTECS No.** RP 6050000

Uses Antineoplastic agent used to treat solid tumours of the lung, ovary and testis, and for sarcomas and lymphomas. Some suggest its superiority over its congener cyclophosphamide is unsubstantiated, particularly in childhood neoplasms, and because of its toxicity argue its use may be unjustified.

Physical properties

M. Pt. 40°C
Solubility Organic solvents: isopropanol, methanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 143 mg kg^{-1} (1).
LD_{50} oral mouse 1005 mg kg^{-1} (1).
LD_{50} intraperitoneal rat, mouse 140, 397 mg kg^{-1}, respectively (2,3).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity in humans, limited evidence for carcinogenicity in animals, IARC group 3 (4).
National Toxicology Program tested rats and mice by intraperitoneal injection. Designated carcinogen in ♀ rats and mice, non-carcinogen in ♂ rats and mice (5).
Significantly increased incidence of lung tumours in ♂, ♀ mice after intraperitoneal injection over 8 wk of 5 doses totalling 1.3 g kg^{-1} or 24 doses totalling 0.45-1.125 g kg^{-1} (6).
Increased incidence of malignant lymphoma in ♀ mice given 20 mg kg^{-1} intraperitoneally 3 × wk^{-1} for 52 wk (7).
In two studies involving subcutaneous injection of 0.2-2.0 mg $mouse^{-1}$ to ♀ NZB/NZW mice, one found significantly increased incidence of neoplasms , whereas the other study produced negative results (8,9).

Teratogenicity and reproductive effects

Increased rate of resorption, growth retardation and incidence of hydrocephalus, micromelia, adactyly, syndactyly, kidney ectopia and delayed ossification in mice given 20 mg kg^{-1} intraperitoneally on day-11 of pregnancy; growth retardation alone occurred at 10 mg kg^{-1} (10).

Metabolism and toxicokinetics

In humans, clearance after a single intravenous bolus is biphasic, with mean terminal elimination $t_{1/2}$ 15 hr. Clearance from plasma after repeated, lower doses is monoexponential with $t_{1/2}$ 7 hr. It is extensively metabolised in the liver to active metabolites; metabolism appears saturated at higher doses. It is excreted largely in urine as unchanged drug and metabolites (11).

It is rapidly metabolised in many animal species, in a similar way to cyclophosphamide, to acrolein and, in dogs, the carboxy derivative and 4-ketoisophosphamide (12).

Metabolic activation in humans may be like cyclophosphamide, with ring hydroxylation to isophosphamide mustard and acrolein. An intravenous dose is excreted in urine as one or both dechloroethylated metabolite (50%), intact drug (20%) and carboxyisophosphamide (2%); there is wide inter-individual variation (13,14).

In humans, plasma pharmacokinetics of high doses is biphasic with a secondary $t_{1/2}$ 15 hr, but monophasic with $t_{1/2}$ 7 hr with lower doses (15).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with metabolic activation positive (16,17).

Dose-dependent increase in chromosomal aberrations in Chinese hamster bone marrow cells after intraperitoneal administration (18).

Drosophila melanogaster sex-linked recessive lethal test positive (19).

Other effects

Other adverse effects (human)

Toxic effects of treatment involve urinary tract, kidney and central nervous system. Kidney damage is irreversible. Central nervous system effects include encephalopathy, with EEG abnormalities, disorientation, confusion, catatonia, coma and occasionally death from central nervous system depression and circulatory collapse. Incidence of encephalopathy is greater after oral than intravenous administration, and the contributory role of mesna, with which it is given, is unclear but may be due to chelating properties (11).

Urinary tract toxicity, characterised by signs of cystitis, limits therapeutic doses to 50 mg kg^{-1}. Less important side-effects are myelosuppression, nausea, vomiting, alopecia, lethargy, confusion and reversible glycosuria (20).

Any other adverse effects

Results in rats suggest renal damage may be due to formation of toxic metabolites in the kidney. Central nervous system toxicity may also be due to a metabolite (11).

Other comments

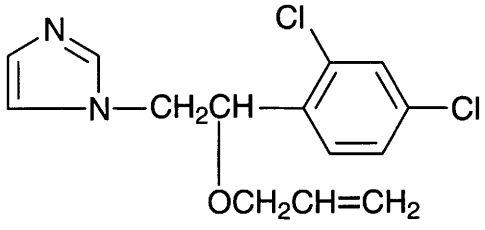
Pharmacology and toxicity reviewed (21).

References

1. *Kiso to Rinsho* 1982, **16**, 431.
2. *US Patent* 3732340, U. S. Patent Office, Box 9, Washington, DC, USA.
3. *Arzneim.-Forsch.* 1974, **24**, 1149.
4. *IARC Monograph* 1987, **Suppl. 7**, 65.
5. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-032, NIEHS, Research Triangle Park, NC, USA.
6. Stoner, G. D. et al *Cancer Res.* 1973, **33**, 3069-3085.
7. *NCI Carcinog. Tech. Rep. Ser.* 1977, No. 32.
8. Mitron, P. S. et al *Arzneim.-Forsch.* 1979, **29**, 483-488.
9. Mitron, P. S. et al *Arzneim.-Forsch.* 1979, **29**, 662-667.
10. Bus, J. S. et al *Proc. Soc. Exp. Biol. Med.* 1973, **143**, 965-970.

11. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
12. Hill, D. L. et al *Cancer Res.* 1973, **33**, 1016-1022.
13. Norporth, K. *Cancer Treat. Rep.* 1976, **60**, 437-443.
14. Goren, M. P. *J. Chromatogr.* 1991, **570**(2), 351-359.
15. Nelson, R. L. et al *Clin. Pharmacol. Ther.* 1976, **19**, 365-370.
16. Benedict, W. F. et al *Cancer Res.* 1977, **37**, 2209-2213.
17. Matney, T. S. et al *Teratog., Carcinog., Mutagen.* 1985, **5**, 319-328.
18. Rohrborn, G. et al *Arch. Toxicol.* 1977, **38**, 35-43.
19. *Environ. Mol. Mutagen.* 1986, **8**(6), 849-865.
20. van Dyk, J. et al *Cancer Res.* 1972, **32**, 921-924.
21. Zalupski, M. et al *J. Natl. Cancer Inst.* 1988, **80**(8), 556-566

I4 imazalil



$C_{14}H_{14}Cl_2N_2O$ **Mol. Wt.** 297.18 **CAS Registry No.** 35554-44-0

Synonyms 1-[2-(2,4-dichlorophenyl)-2-(2-propenyloxy)ethyl]-1*H*-imidazole; Enilconazole; Florasan; Fungaflor; Fungazil; R23979; Bromazil; Citrashine; Deccosil

EINECS No. 252-615-0

Uses Disinfectant of kennel and stable equipment. Fungicide.

Physical properties

M. Pt. 52.7°C **B. Pt.** Decomposes on distillation at >340°C **Specific gravity** 1.243 at 23°C
Partition coefficient log P_{ow} 3.89 **Volatility** v.p. 1.18×10^{-6} mmHg at 20°C
Solubility Water: 0.18 g l^{-1} at 20°C and pH 7.6. Organic solvents: acetone, dichloromethane, hexane, isopropanol, methanol, toluene

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to the eyes (R22, R36)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (duration unspecified) rainbow trout 2.5 mg l^{-1} (1).
LC_{50} (duration unspecified) bluegill sunfish 3.2 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} *Daphnia* 3.2 mg l^{-1} (1).
LC_{50} (48 hr) earthworm, contact 12.8 μg cm^{-3} and (14 day) artificial soil test 541 μg g^{-1}. Survival in soil test >90% even at levels of 1000 μg g^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral ring-necked pheasant 2000 mg kg^{-1} (1).
LD_{50} oral rat 227 mg kg^{-1} (3).
LC_{50} (4 hr) inhalation rat 16 mg l^{-1} air (with 200 g l^{-1} emulsifiable concentrate) (1).
LD_{50} dermal rat 4200-4880 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 155 mg kg^{-1} (3).

Sub-acute and sub-chronic data

LC_{50} (8 day) mallard duck 2510 mg kg^{-1} body weight (1).
Oral (8 wk) bobwhite quail 0-1000 mg kg^{-1} in feed. Liver weight, hepatic microsomal protein content, induction of cytochrome P_{450}, NADPH-cytochrome c reductive activity were unaffected. 7-Ethoxyresorufin or 7-ethoxycoumarin *O*-deethylase activities in liver microsomes were neither induced nor inhibited. At high doses, increased aniline hydroxylase activity was observed, which normalised after a drug-free wk (4).

Metabolism and toxicokinetics

Oral rat, 90% eliminated in metabolised form within 4 days (5).

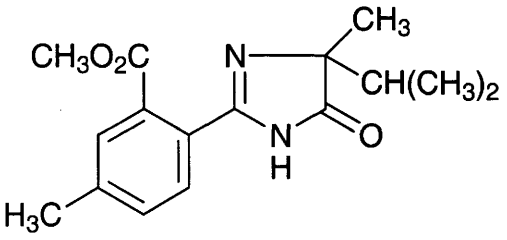
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (8).
WHO Toxicity Class II (9).
EPA Toxicity Class II (formulation) (1).
ADI 0.03 mg kg^{-1} (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Van Laemput, L. et al *Ecotoxicol. Environ. Saf.* 1989, **18**(3), 313-320.
3. *Arzneim.-Forsch.* 1981, **31**, 309.
4. Lavrijsen, K. et al *Pestic. Sci.* 1990, **29**(1), 47-56.
5. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
9. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

15 imazamethabenz-methyl



$C_{16}H_{20}N_2O_3$ **Mol. Wt.** 288.35 **CAS Registry No.** 81405-85-8

Synonyms 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-4(or 5)-methylbenzoic acid, methyl ester; Imazamethabenz; AC222293; Assert; Dagger; Imifen

RTECS No. DG 8576140

Uses Herbicide.

Physical properties

M. Pt. 113-153°C **Flash point** >93°C (closed cup) **Specific gravity** 0.3 (20°C)
Partition coefficient log P_{ow} 1.54 (*p*-isomer), log P_{ow} 1.82 (*m*-isomer) (1) **Volatility** v.p. 1.125×10^{-8} mmHg (25°C)
Solubility Water: 857 mg l^{-1} (*m*-isomer), 1370 mg l^{-1} (*p*-isomer). Organic solvents: acetone, dimethylformamide, dimethyl sulfoxide, isopropanol alcohol, methylene chloride, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout >100 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* >100 mg l^{-1} (2).
LD_{50} contact >100 μg bee^{-1} (2).

Environmental fate

Degradation studies
Slowly degraded to free acids in sandy loam and clay loam soils under both aerobic and anaerobic conditions (3). In tank experiments, herbicide activity persisted longer in sandy loam than in clay soil in fallow system. Under cropped conditions, persistence was reduced in sandy loam and unaffected in clay soil (3).

Abiotic removal
Photolytic degradation occurs in water and on soil surfaces. $t_{1/2}$ of residues in the soil is ca. 30-276 days with no accumulation of acid metabolites. Hydrolysis increases with increasing pH (3).

Adsorption and retention
In arable-soil field experiments at recommended and 2 × recommended doses, persistence times ranged from 4 to >10 months. Leaching down to 5-15 cm occurred in all trials and to 15-25 cm in several trials (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail, mallard duck >2150 mg kg^{-1} (2).
LD_{50} oral rat >5000 mg kg^{-1} (2).
LC_{50} (duration unspecified) inhalation rat >5.8 mg l^{-1} (2).
LD_{50} dermal rabbit >2000 mg kg^{-1} (2).

Sub-acute and sub-chronic data

LC_{50} (8 day) oral bobwhite quail, mallard duck >5000 mg kg^{-1} in diet (2).

Metabolism and toxicokinetics

Oral rat excreted 77% in urine and 13-19% in the faeces within 24 hr. After 48 hr, blood and tissue residue levels were <0.05 mg kg^{-1}. Milk/tissue and egg/tissue residue levels were low in lactating goats and laying hens, respectively (2).

Irritancy

Non-irritating to skin; reversible rabbit eye irritant (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
WHO Toxicity Class Table 5 (7).
EPA Toxicity Class IV (2).
ADI 0.0625 mg kg^{-1} body weight (2).

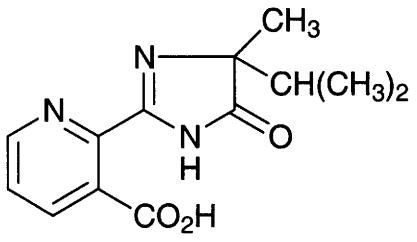
Other comments

A mixture of *m*- and *p*-isomers (2).
Biology reviewed (8).
Tested against OECD species, wheat and oilseed rape, with the former tolerant (9).
Metabolic pathways reviewed (10).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Allen, R. et al *Proc. Br. Crop. Prot. Conf. – Weeds* 1987, 569-576.
4. Nilsson, H. et al *Swed. Crop Prot. Sci.* 1989, **30**(2), 270-277.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No.472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
8. Los, M. *Pestic. Sci. Biochnol., Proc. Int. Congr. Pestic. Chem., 6th* 1987, 35-42.
9. Richardson, W. G. et al *Tests Agrochem. Cultiv.* 1985, **6**, 148-149.
10. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

16 imazapyr



$C_{13}H_{15}N_3O_3$ **Mol. Wt.** 261.28 **CAS Registry No.** 81334-34-1

Synonyms 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid; 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-3-pyridinecarboxylic acid; AC243997; Arsenal; Assault; Chopper; Pivot; Claymore; Contain

RTECS No. US 5682500

Uses Herbicide.

Physical properties

M. Pt. 169-173°C **Partition coefficient** log P_{ow} 0.113 **Volatility** v.p. 0.20×10^{-6} mmHg at 45°C
Solubility Water: 10-15 g l^{-1} at 25°C

Occupational exposure

Supply classification irritant
Risk phrases Irritating to eyes – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R36, R52/53)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S26, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish, channel catfish >100 mg l^{-1} (1).
LC_{50} (24, 48, 72, 96 hr) Nile tilapia 4.67, 4.63, 4.61, 4.36 ppm, respectively, in static bioassay (2).
LC_{50} (96 hr) silver barb 2.71 ppm static bioassay (2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* >100 mg l^{-1} (1).
LD_{50} contact honeybee >100 μg bee^{-1} (1).

Environmental fate

Abiotic removal
Photolytic degradation occurs in aqueous media in sunlight (1).
Residual soil activity ranges from 6 months to 2 yr in temperate climates and 3 to 6 months in the tropics. The major soil residue is the parent compound (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail, mallard duck >2150 mg kg^{-1} (1).
LD_{50} oral ♀ mouse, ♂ ♀ rabbit, ♂ and ♀ rats >2000, 4800, >5000 mg kg^{-1}, respectively (1).

LC_{50} (duration unspecified) inhalation rat >1.3 mg l^{-1} (1).
LD_{50} dermal rat, rabbit >2000 mg kg^{-1} (1).
LD_{50} intraperitoneal ♂ rat 2500 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail, mallard duck >5000 mg kg^{-1} in diet (1).
In 21-day dermal study with rabbits, no indications at 400 mg kg^{-1} day^{-1} of systemic toxicity (1).
In 13-wk feeding study with rats, no-effect dose was 10,000 mg kg^{-1} (highest tested) (1).

Teratogenicity and reproductive effects
At 1000 mg kg^{-1} in rats or 400 mg kg^{-1} in rabbits (highest doses tested), no teratogenic effects observed (1).

Metabolism and toxicokinetics
Oral rats 87% excreted within 24 hr. Residual levels in liver and kidney were 0.03 and 0.02 mg kg^{-1}, respectively, at 24 hr and <0.01 ppm in both at 192 hr. In muscle, fat tissue and blood residues were <0.01 mg kg^{-1} at both times (1).

Irritancy
Rabbit eye irritant, mild rabbit skin irritant (doses and durations unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class Table 5 (5).
EPA Toxicity Class IV (formulation) (1).

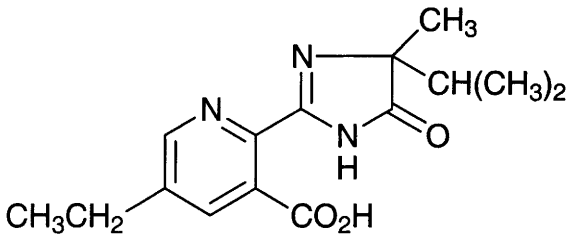
Other comments

Metabolic pathways reviewed (6).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Supamataya, K. et al *Warasan Songkhla Nakkharin* 1987, **9**(3), 309-313 (Thai.) (*Chem. Abstr.* **110**, 207524j).
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
6. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

17 imazethapyr



$C_{15}H_{19}N_3O_3$ **Mol. Wt.** 289.33 **CAS Registry No.** 81335-77-5

Synonyms (*RS*)-5-ethyl-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid; (±)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-5-ethyl-3-pyridinecarboxylic acid; AC263,499; Event; Pivot; Pursuit; Hammer; Overtop

RTECS No. US 5682900

Uses Herbicide.

Physical properties

M. Pt. 169-173°C **Partition coefficient** log P_{ow} 1.49 at pH 7, 25°C **Volatility** v.p. $<1.01 \times 10^{-7}$ mmHg at 60°C **Solubility** Water: 1.4 g l^{-1} at 25°C. Organic solvents: acetone, dichloromethane, dimethyl sulfoxide, isopropanol, methanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 420 mg l^{-1} (1).

LC_{50} (96 hr) rainbow trout 340 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} contact honeybee >0.1 mg bee^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil 1-3 months (1).

In vitro ^{14}C-label experiments showed 95% unaltered after 12 wk incubation in sterilised soil. In unsterilised soil the major degradation product was $^{14}CO_2$ and adsorption was negatively correlated with degradation (2).

Abiotic removal

$t_{1/2}$ ~3 day in sunlight (1).

In ^{14}C-label experiments volatilisation losses for soil were <2%. Photodecomposition losses of up to 8% occurred from soil. The total $^{14}CO_2$ evolved from soils ranged from 2.4 to 3.6% of total applied. However, as detected by high performance liquid chromatography, 62-82% had been degraded (3).

Adsorption and retention

In laboratory and greenhouse experiments lower pH reduced effectiveness and mobility and increased adsorption. Adsorption was greatest in silty clay loam and least in sandy loam soil (4-6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, ♀ mouse >5000 mg kg^{-1} (1).

LD_{50} oral bobwhite quail, mallard duck >2150 mg kg^{-1} (1).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
In 28-day feeding study with rats no-effect dose was 10,000 mg kg^{-1} (highest tested) (1).

Metabolism and toxicokinetics
Oral rat 92% excreted in urine and 5% in faeces within 24 hr. Residues in liver, kidney, muscle, fat tissue and blood were <0.01 ppm after 48 hr (1).

Irritancy
Mild skin irritation, reversible eye irritation in rabbit (1).

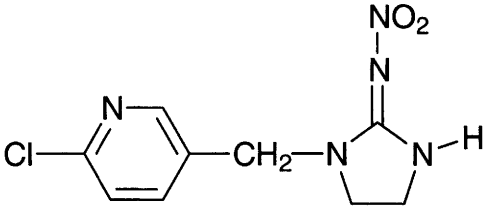
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).
WHO Toxicity Class Table 5 (9).
EPA Toxicity Class III (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Cantwell, J. R. et al *Weed Sci.* 1989, **37**(6), 815-819.
3. Goetz, A. J. et al *Weed Sci.* 1990, **38**(4-5), 421-428.
4. Stougaard, R. N. et al *Weed Sci.* 1990, **38**(1), 63-73.
5. Loux, M. M. et al *Weed Sci.* 1989, **37**(5), 712-718.
6. Loux, M. M. et al *Weed Sci.* 1989, **37**(2), 259-267.
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
9. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

I8 imidacloprid



$C_9H_{10}ClN_5O_2$ **Mol. Wt.** 255.66 **CAS Registry No.** 138261-41-3

Synonyms 1-(6-chloro-3-pyridylmethyl)-*N*-nitroimidazolidin-2-ylideneamine; 1-[(6-chloro-3-pyridinyl)-methyl]-*N*-nitro-2-imidazolidinimine; Admire; Confidor; Gaucho; Merit; Premier; Premise; Provado
Uses Insecticide used in the control of sucking insects. Effective also against soil insects, termites and some species of biting insects. Used as a seed dressing, as soil treatment and as foliar treatment in crops.

Physical properties

M. Pt. 144°C **Specific gravity** 1.54 (20°C) **Partition coefficient** log P_{ow} 0.57 at 22°C
Volatility v.p. 4×10^{-7} mPa at 20°C
Solubility Water: 0.61 g l^{-1} at 20°C. Organic solvents: dichloromethane

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) golden orfe, rainbow trout 237, 211 mg^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 85 mg l^{-1} (1).
Harmful to bees by foliar application (1).
LC_{50} *Eisenia foetida* 10.7 mg kg^{-1} dry soil (1).

Environmental fate

Degradation studies

The authors of a study of the soil metabolism of imidacloprid in sugar beet fields concluded that imidacloprid was progressively transformed into non-toxic and common compounds (2).
The most important metabolic steps in the degradation of imidacloprid in soil and water (with and without vegetation) are oxidation at the imidazolidine ring, reduction or loss of the nitro group, hydrolysis to 6-chloronicotinic acid and mineralisation. These processes are greatly accelerated by vegetation (1).

Adsorption and retention

The adsorption coefficient of imidacloprid was greater on vegetable crop soils which had been treated with organic fertilizers than on the soils of the organic fertilizer control plots. This was related to the slowing down of the biodegradation of the insecticide in soils treated with organic fertilizers, relative to the organic fertilizer untreated control plots. Repetition in the past of the organic fertilizer treatments generally did not increase these effects, which suggests that it is the young soil organic matter which is the most able to adsorb the insecticide and slow down its soil biodegradation (3).
Column leaching tests with imidacloprid (with prior ageing) indicate that the pesticide and its metabolites developing in the soil are immobile. As long as the pesticide is used as recommended it is not expected to leach into deeper soil layers (1).

Mammalian & avian toxicity

Acute data

LD_{50} and Japanese quail, bobwhite quail 31, 152 mg kg^{-1}, respectively (1).
LD_{50} oral rats, mice *c.* 450, *c.* 150 mg kg^{-1}, respectively (1).
LC_{50} (4hr) inhalation rat >69 mg m^{-3} air (aerosol) (1).
LD_{50} (24 hr) dermal rat >5000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No-observed-effect level (2 yr) ♂ rats, ♀ rats, mice and dogs (1 yr) 100, 300, 330 and 500 mg kg^{-1}, respectively (1).

Metabolism and toxicokinetics

Methylene-^{14}C- and 4,5-imidazolidine-^{14}C-labelled imadacloprid administered orally to rats was rapidly and almost completely absorbed from the gastro-intestinal tract and was eliminated quickly (96% of the administered dose within 48 hr). Of this, 70 to 80% was eliminated via the urine, the rest via the faeces. Only about 15% was eliminated via urine and faeces as unchanged parent compound; most was metabolised. Hydroxylation at the imidazoline ring, hydrolysis to 6-chloronicotinic acid, and loss of the nitro group with formation of the guanidine and conjugation of the 6-chloronicotinic acid with glycine were the major metabolic steps (4).

Irritancy

Non-irritating to eyes and skin of rabbits (1).

Genotoxicity

Metabolites of imidacloprid were obtained enzymatically using aroclor-induced rat liver S9 fraction, in an NADPH generating system, and were reacted with calf thymus DNA. Nuclease P1 enrichment resulted in an increased number of DNA-adducts compared to the level of adducts in control DNA, indicating pesticide genotoxicity in this *in vitro* system (4).

Legislation

WHO Toxicity Class II (5).
EPA Toxicity Class II (1).
Under the Federal Food, Drug, and Cosmetic Act, a tolerance is established for residues of the insecticide imidacloprid and its metabolites of 0.05 ppm in or on canola seed, and 3.5 ppm in or on leafy green vegetables. A time-limited tolerance of 0.2 ppm is established for indirect or inadvertent combined residues resulting from crop rotational practices in or on the raw agricultural commodities in the cucurbit vegetables crop group (6-8).
The US Environmental Protection Agency is establishing permanent tolerances for residues of the insecticide imidacloprid and its metabolites in or on cottonseed (6.0 ppm) and cotton gin by-products (4.0 ppm), revoking the existing feed additive tolerance for imidacloprid on cotton meal, and establishing a maximum residue limit for imidacloprid on cottonseed meal (8.0 ppm) (9).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticide: maximum admissible concentration 0.1 μgl^{-1} (10).
Included in schedule 6 (Release onto Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (11).
ADI 0.057 mg kg^{-1} body weight (1).

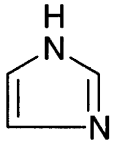
Other comments

Stable to hydrolysis at pH 5-11 (1).
Non-phytotoxic when used as directed (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Rouchard, J. et al *Bull. Environ. Contam. Toxicol.* 1996, **56**(1), 29-36.
3. Rouchard, J. et al *Meded.-Fac. Landbouwkd. Toegepaste Biol. Wet. (Univ. Gent)* 1995, **60**(2b, Proceedings, 47th International Symposium on Crop Protection, Pt. 2, 1995), 585-592.
4. Shah, R.G. et al *Mol. Cell. Biochem.* 1997, **169**(1-2), 177-184.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
6. *Fed. Regist.* 1996, **61**(31), 4714-4716.
7. *Fed. Regist.* 1996, **61**(114), 29674-29676.
8. *Fed. Regist.* 1996, **61**(31), 5711-5712.
9. *Fed. Regist.* 1996, **61**(41), 7734-7736.
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

19 imidazole



$C_3H_4N_2$ **Mol. Wt.** 68.08 **CAS Registry No.** 288-32-4

Synonyms 1*H*-imidazole; 1,3-diazole; Imutex; Miazole; Glyoxaline

EINECS No. 206-019-2 **RTECS No.** NI 3325000

Physical properties

M. Pt. 90-91°C **B. Pt.** 257°C **Flash point** 145°C
Solubility Water: freely soluble. Organic solvents: chloroform, diethyl ether, ethanol, pyridine

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 231 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1880 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 817 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 610 mg kg^{-1} (2).

LD_{50} intravenous mouse 475 mg kg^{-1} (4).

Other comments

In vitro 19-day-old Sprague-Dawley rat foetus brain cells incubated for 3 days then exposed for a further 3 days to 140 mg l^{-1} showed no cytoxic effects (5).

Reviews on experimental toxicology, human health effects, workplace experience listed (6).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Nishie et al *Toxicol. Appl. Pharmacol.* 1969, **14**, 301.
3. *J. Pharmacol. Exp. Ther.* 1957, **119**, 444.
4. *Arzneim.-Forsch.* 1983, **33**, 716.
5. Khera, K. S. et al *Toxicol. In Vitro* 1988, **2**(4), 257-273.
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I10 iminoctadine

$$H_2NC(=NH)NH(CH_2)_8NH(CH_2)_8NHC(=NH)NH_2$$

$C_{18}H_{41}N_7$ **Mol. Wt.** 355.57 **CAS Registry No.** 13516-27-3 (base); 39202-40-9 (triacetate)

Synonyms 1,1′-iminodi(octamethylene)diguanidinium triacetae; Befran

EINECS No. 236-855-3 **RTECS No.** MF 3624100

Uses Fungicide.

Physical properties

M. Pt. 143.0-144.2 **Volatility** v.p. $<3.0 \times 10^{-6}$ mmHg at 23°C

Solubility Water: 764 g l^{-1}. Organic solvents: ethanol, methanol

Occupational exposure

Supply classification harmful

Supply classification dangerous for the environment

Risk phrases Harmful in contact with skin and if swallowed – Irritating to eyes and skin – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21/22, R36/38, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S36/37, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (triacetate, 96 hr) carp 200 mg l^{-1} (1).
LC_{50} (triacetate, 96 hr) rainbow trout 36 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (triacetate, 48 hr) *Daphnia* 2.1 mg l^{-1} (1).
LD_{50} (triacetate) oral and contact >0.1 mg bee^{-1} (1).

Environmental fate

Nitrification inhibition
Slight inhibitory effect on nitrification (2).

Degradation studies
$t_{1/2}$ (triacetate): diluvial sandy loam, 90 day; volcanic ash loamy upland soil, 122 day; colluvial clayey loamy upland soil, 75 day; volcanic ash loamy upland soil, 28 day (1).
Effects on soil microorganisms studied (2).

Mammalian & avian toxicity

Acute data
LD_{50} (triacetate) oral mallard duck 985 mg kg^{-1} (1).
LD_{50} (triacetate) oral rat, mouse 300, 400 mg kg^{-1}, respectively (1).
LC_{50} (triacetate, 4 hr) inhalation rat 0.073 mg l air^{-1} (for 25% liquid) (1).
LD_{50} (triacetate) dermal rat 1500 mg kg^{-1} (1).

Teratogenicity and reproductive effects
Non-toxic to embryos (species unspecified) at 8 mg kg^{-1} (1).

Irritancy
Triacetate is a mild skin and eye irritant (rats) (1).

Sensitisation
Triacetate is not a skin sensitiser (rats) (1).

Genotoxicity

Triacetate is not mutagenic in Ames and Rec tests (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class II (for iminoctadine base) (5).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Torstensson, L. *Vaextskyddsrapp., Jordbruk* 1988, **49**, 165-172 (Swed.).
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

I11 iminodiacetic acid

$$NH(CH_2CO_2H)_2$$

$C_4H_7NO_4$ **Mol. Wt.** 133.10 **CAS Registry No.** 142-73-4

Synonyms *N*-(carboxymethyl)glycine; aminodiacetic acid; diglycine; diglykokoll; IDA; iminobis(acetic acid)

EINECS No. 205-555-4 **RTECS No.** AI 2975000

Physical properties

M. Pt. 243°C (decomp.)

Solubility Water: 2.43 g 100 ml^{-1}

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 250 mg kg^{-1} (1).

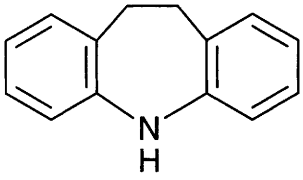
Other comments

As a chelating agent for human serum albumin-bound copper(II) the reaction followed a process involving intermediate tertiary complexes (2).

References

1. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
2. Gao, L. et al *J. Inorg. Biochem.* 1989, **36**(2), 83-92

I12 iminodibenzyl



$C_{14}H_{13}N$ **Mol. Wt.** 195.26 **CAS Registry No.** 494-19-9

Synonyms 10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine; RP 23669

EINECS No. 207-787-1 **RTECS No.** HN 8950000

Physical properties

M. Pt. 105-108°C

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 320 mg kg^{-1} (1).

Irritancy
100 mg instilled into rabbit eye caused well-defined erythema and slight oedema (2).

References

1. U.S. Army Armament Research and Development Command *Report NX No. 01352* Chemical Systems Laboratory, Aberdeen Proving Ground, MD, USA.
2. *Food Chem. Toxicol.* 1982, **20**, 573

I13 3,3′-iminodipropionitrile

$$NH(CH_2CH_2CN)_2$$

$C_6H_9N_3$ **Mol. Wt.** 123.16 **CAS Registry No.** 111-94-4

Synonyms 3,3′-iminobis(propanenitrile); BBCE; bis(cyanoethyl)amine; IDPN; β,β′-iminodipropionitrile

EINECS No. 203-922-3 **RTECS No.** UG 2975000

Physical properties

M. Pt. –5.5°C **B. Pt.** 173°C **Specific gravity** 1.0165 at 30°C **Volatility** v.den. 3.3

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2700 mg kg^{-1} (1).
LD_{50} dermal rabbit 2520 mg kg^{-1} (2).

Sub-acute and sub-chronic data
Subcutaneous Sprague-Dawley rat neonates 100 mg kg^{-1} on postnatal days 2, 4, and 6. Neurobehavioural testing was carried out and the animals were killed at 101 days of age. The righting reflex was impaired and forepaw suspension times were decreased. The spinal cord content of norepinephrine, serotonin, and 5-hydroxyindoleacetic acid was elevated in ♀s. In ♂'s serotonin and 5-hydroxyindoleacetic acid levels were elevated. The monoamine content of the cerebellum, mediobasal hypothalamus, and hippocampus was altered in both sexes. The authors conclude that neonatal exposure to 3,3′-iminodi(propanenitrile) results in permanent changes in adult neurochemistry that may be related to reorganisational effects induced by toxin-mediated neuroplasticity in developing neurones (3).
Gavage (5 wk) Sprague-Dawley rats 50 or 125 mg kg^{-1} day^{-1} for 7 days wk^{-1} affected body weight, weight gain, food consumption, general activity, muscle tone, urination, motor reflexes, posture and gait. The ♂ in particular suffered significant sex effects. Minimal to moderately severe axonal swelling was observed in the brainstem and the cervical and lumbar regions of the spinal cord. This was most pronounced in the ♂. An increased incidence of chronic progressive nephropathy also occurred (4).
Mice that received 1 g kg^{-1} (route unspecified) 3 × wk^{-1} for 6 wk showed an increase in locomotor acitivity in wk 1 and 2, a decrease in acetylcholinesterase activity in the central nervous system, decreased diameter of neuronal cell bodies and an accumulation of bundles of 10 nm neurofilaments in the proximal axons (5).

Metabolism and toxicokinetics
3,3′-iminobis(propanenitrile) is metabolised to *N*-hydroxy-3,3′-iminodipropionitrile (a neurotoxin) in rats. This conversion to the toxic metabolite is inhibited by methimazole, suggesting that flavin-containing monooxygenase-mediated metabolism is required for the auditory and vestibular neurotoxicity of 3,3′-iminobis(propanenitrile) to be observed (6).

Other effects

Any other adverse effects

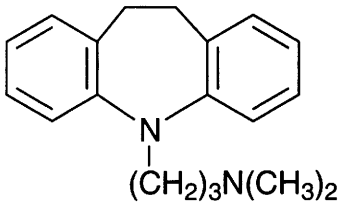
Cat (5 wk) exhibited neurotoxic effects including swellings in intraparenchymal spinal axons and clumping of neurofilaments in some motor neurones (7).

A mechanism for neurotoxicity involving cyanoethenylation of amino groups is described (8).

References

1. *J. Ind. Hyg. Toxicol.* 1949, **31**, 60.
2. *Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
3. Dawson, R., Jr. et al *Neurotoxicol. Teratol.* 1998, **20**(2), 181-192.
4. Schulze, G. E. et al *Fundam. Appl. Toxicol.* 1991, **16**(3), 602-615.
5. Yano, I. et al *Wakayama Med. Rep.* 1990, **32**(1), 1-9.
6. Nace, C. G. et al *Fundam. Appl. Toxicol.* 1997, **37**(2), 131-140.
7. Fiori, M. G. et al *Cytol. Pathol.* 1988, **20**(1), 137-146.
8. Jacobson, A. R. et al *Mol. Toxicol.* 1987, **1**(1), 17-34

I14 imipramine



$C_{19}H_{24}N_2$ **Mol. Wt.** 280.41 **CAS Registry No.** 50-49-7

Synonyms 10,11-dihydro-*N*,*N*-dimethyl-5*H*-dibenz[*b*,*f*]azepine-5-propanamine; 5-[3-(dimethylamino) propyl]-10,11-dihydro-5*H*-dibenz[*b*,*f*] azepine; Antideprin; Prazepine

EINECS No. 200-042-1 **RTECS No.** HO 1575000

Uses Antidepressant drug.

Physical properties

M. Pt. 173-175°C **B. Pt.** 160°C at 0.1 mmHg

Mammalian & avian toxicity

Acute data

LD_{Lo} oral human 30-40 mg kg^{-1} (1,2).

LD_{50} oral mouse, rat 188, 250 mg kg^{-1}, respectively (3).

LD_{50} intravenous rat, mouse 16, 21 mg kg^{-1}, respectively (4,5).

LD_{50} intraperitoneal mouse, rat 52, 79 mg kg^{-1}, respectively (6-8).

LD_{50} subcutaneous mouse 195 μg kg^{-1} (7).

LD_{50} subcutaneous rat 250 mg kg^{-1} (8).

Teratogenicity and reproductive effects

Negative developmental toxicity for primate, rat and mouse. Equivocal in rabbit (9).

Subcutaneous pregnant rats 3, 5, 10 mg kg^{-1} day^{-1} on days 8-20 of pregnancy. There were no dose-related

differences in offspring body weights, but maternal weight gain declined in a dose-related fashion. The functional development of the central adrenergic systems was altered in a complicated way (10).

Metabolism and toxicokinetics

In a study of the biliary excretion of the compound and its metabolites, desipramine, 2-OH-imipramine and 2-OH-desipramine, rats were given an intraperitoneal daily dose of 10 mg kg^{-1} over 13 days. An inhibition of imipramine demethylation and hydroxylation and acceleration of desipramine hydroxylation was suggested (11).
Oral rat (2 wk) 20 mg kg^{-1} day^{-1} decreased imipramine hydroxylase activity and slightly reduced imipramine demethylase activity. Desipramine competitively inhibited imipramine metabolism (12).
Dermal hairless mice were administered 2 mg in distilled water followed by rapid evaporation of the water. After 1, 2, 4 or 6 hr the highest levels were recorded in the lung and the lowest in the heart and liver. Levels in blood were similar to low therapeutic to toxic concentrations in humans, whereas solid tissue levels were much lower than those observed in human overdose (13).

Sensitisation

Urticaria, angioedema and other allergic skin reactions and photosensitisation reported in humans (14-16).
Agranulocytosis, particularly affecting the elderly, occurred 4 to 8 wk after starting treatment (17,18).

Genotoxicity

In vivo polychromatic erythrocytes 1.87 and 2.81 mg $mouse^{-1}$ induced dose-related increase in frequency of micronuclei (19).
Drosophila melanogaster fed oral dose for 48 hr in Somatic Mutation and Recombination Test, positive for concentrations >280 mg (20).
In vitro human lymphocyte cells (24, 48, 72 hr) 25, 500 and 5000 ng ml^{-1} gave a significant increase in chromosome damage at the upper plasma level and at higher concentrations. Only at levels higher than the plasma level (5 µg ml^{-1}) were sister chromatid exchanges significantly increased. At no concentration was the mitotic index affected (21).

Other effects

Other adverse effects (human)

Volunteers given 100 and 40 mg, orally, on separate occasions displayed dose-related rises in blood pressure and resting heart rate. No appreciable effect was exhibited by heart rate response to Valsalva's manoeuvre, respiratory sinus arrhythmia or the responses to exercise (22).
Patients without prior cardiovascular disease given therapeutic doses showed significant cardiovascular side-effects of orthostatic hypotension and tachycardia (23,24).
Oral ♂ human 100 mg increased circulating levels of cortisol, prolactin and growth hormone. A dose of 40 mg had no effect on hormone release (25).

Any other adverse effects

In intravenous rat decreased mean arterial blood pressure and heart rate and caused electrocardiogram rhythm and conduction changes (26).

Other comments

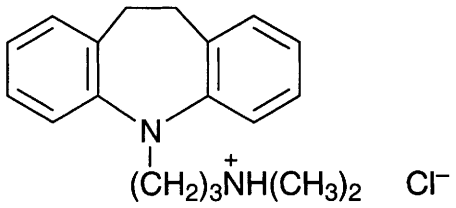
Sexual dysfunction reviewed (27-29).
Teratogenicity, metabolism and pharmacokinetics reviewed (30-32).

References

1. *Handb. Exp. Pharmacol.* 1980, **55**, 527.
2. *Proc. Eur. Soc. Study Drug Toxicol.* 1965, **6**, 171.
3. *Pharm. Chem. J. (Engl. Transl.)* 1980, **14**, 773.
4. *Arzneim.-Forsch.* 1979, **29**, 193.
5. *Arch. Int. Pharmacodyn. Ther.* 1980, **245**, 283.
6. *British Patent Document No.1460700.*

7. *Pharm. Chem. J. (Engl. Transl.)* 1981, **15**, 412.
8. *Arch. Int. Pharmacodyn. Ther.* 1964, **148**, 560.
9. Jelovsek, F. R. et al *Obstet. Gynecol. (N. Y.)* 1989, **74**(4), 624-636.
10. Ali, S. F. et al *Neurotoxicology* 1986, **7**(2), 365-380.
11. Melzacka, M. et al *Pol. J. Pharmacol. Pharm.* 1987, **39**(4), 379-386.
12. Wladyslawa, D. et al *Pol. J. Pharmacol. Pharm.* 1987, **39**(2), 135-141.
13. Bailey, D. N. *J. Anal. Toxicol.* 1990, **14**(4), 217-218.
14. Almeyda, J. *Br. J. Dermatol.* 1971, **84**, 298-299.
15. Quitkin, F. *JAMA, J. Am. Med. Assoc.* 1979, **241**, 1625.
16. Smith, A. G. *Adverse Drug React. Bull.* 1989, **136**, 508-511.
17. Heimpel, H. *Med. Toxicol.* 1988, **3**, 449-462.
18. Albertini, R. S. et al *J. Clin. Psychiatry* 1978, **39**, 483-485.
19. Shaheen, S. et al *IRCS Med. Sci.* 1986, **14**(11), 1129-1130.
20. Van Schaik, N. et al *Mutat. Res.* 1991, **260**(1), 99-104.
21. Saxena, R. et al *Environ. Mol. Mutagen.* 1988, **12**(4), 421-430.
22. Middleton, H. C. et al *Hum. Psychopharmacol.* 1988, **3**(3), 181-190.
23. Glassman, A. H. *Annu. Rev. Med.* 1984, **35** 503-511.
24. Mortensen, S. A. *Practitioner* 1984, 288, 1180-1183.
25. Nutt, D. et al *Psychoneuroendocrinology (Oxford)* 1987, **12**(5), 367-375.
26. Balcioglu, A. et al *Arch. Int. Pharmacodyn. Ther.* 1991, **309**, 64-74.
27. Beeley, L. *Adverse Drug React. Poisoning Rev.* 1984, **3**, 23-42.
28. *Med. Lett. Drugs Ther.* 1987, **29**, 65-70.
29. Shen, W. W. et al *J. Reprod. Med.* 1983, **28**, 497-499.
30. De Vane, C. L. et al *Psychopharmacol. Ser.* 1987, **3**, 174-178.
31. Sallee, F. R. et al *Clin. Pharmacokinet.* 1990, **18**(5), 346-364.
32. Gram, L. F. *Acta Psychiatr. Scand. Suppl.* 1988, **345**, 81-84

I15 imipramine hydrochloride



$C_{19}H_{25}ClN_2$ **Mol. Wt.** 316.87 **CAS Registry No.** 113-52-0

Synonyms Berkomine; Deprinol; Tofranil; Pryleugau; Janimine

EINECS No. 204-030-7 **RTECS No.** HO 1925000

Uses Antidepressant drug.

Physical properties

M. Pt. 174-175°C

Solubility Water: freely soluble. Organic solvents: acetone, chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 275, 305 mg kg^{-1}, respectively (1,2).

LD_{Lo} oral child 15 mg kg^{-1} (3).

LD_{50} intraperitoneal rat, guinea pig, mouse 72-104 mg kg^{-1} (4-6).
LD_{Lo} intravenous monkey 25 mg kg^{-1} (7).

Teratogenicity and reproductive effects
Gavage ICR/SIM mouse on gestation days 8-12 non-teratogenic (8).

Metabolism and toxicokinetics
Readily absorbed from the human small intestine. Considerably demethylated by first-pass metabolism in the liver to desipramine, the primary active metabolite. The metabolic pathways include hydroxylation and *N*-oxidation. Excretion occurs via the urine, mainly as free or conjugated metabolites. Distributed throughout the body and extensively bound to plasma and tissue protein. Elimination $t_{1/2}$ 9-28 hr (higher in overdose). Can cross the blood-brain and placental barriers and is excreted in breast-milk (9).
As a suppository, bioavailability in rabbit was 25% compared to intravenous injection. When tested on three inpatients the plasma level and clinical efficiency were in the same range as reported in literature for oral administration (10).

Other effects

Other adverse effects (human)
Agranulocytosis reported (11).
Orthostatic hypotension and tachycardia are the significant cardiovascular side effects (12,13).
Sexual function effects, including painful ejaculation and anorgasmia or delayed orgasm in women reported (14-16).
Some panic disorder patients exhibit symptoms of insomnia, jitteriness and irritability (17).
Cold and blue hands and feet reported for a woman at dose of 150 mg daily (18).

Other comments

Pharmacokinetics reviewed (19).

References

1. *Therapie* 1965, **20**, 67.
2. *Toxicol. Appl. Pharmacol.* 1971, **18**, 185.
3. *Br. Med. J.* 1974, **1**, 261.
4. *Arzneim.-Forsch.* 1971, **21**, 391.
5. *Pharmazie* 1983, **38**, 749.
6. *Arzneim.-Forsch.* 1974, **24**, 166.
7. *Indian J. Exp. Biol.* 1984, **22**, 539.
8. Seidenberg, J. M. et al *Teratog., Carcinog., Mutagen.* 1987, **7**, 17-28.
9. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
10. Chaumeil, J. C. et al *Drug Dev. Ind. Pharm.* 1988, **14**(15-17), 2225-2239.
11. Heimpel, H. *Med. Toxicol.* 1988, **3**, 449-462.
12. Glassman, A. H. *Annu. Rev. Med.* 1984, **35**, 503-511.
13. Mortensen, S. A. *Practitioner* 1984, **228**, 1180-1183.
14. Beeley, L. *Adverse Drug React. Acute Poisoning Rev.* 1984, **3**, 23-42.
15. *Med. Lett. Drugs Ther.* 1987, **29**, 65-70.
16. Shen, W. W. et al *J. Report. Med.* 1983, **28**, 497-499.
17. Yeragani, V. K. et al *Br. Med. J.* 1986, **292**, 1529.
18. Appelbaum, P. S. et al *Am. J. Psychiatry* 1983, **140**, 913-915.
19. Task Force on the Use of Laboratory Tests in Psychiatry *Am. J. Psychiatry* 1985, **142**, 155-162

I16 improsulfan hydrochloride

$$(CH_3SO_3CH_2CH_2CH_2)_2NH_2^+Cl^-$$

$C_8H_{20}ClNO_6S_2$ **Mol. Wt.** 325.83 **CAS Registry No.** 3458-22-8

Synonyms 3,3'-iminobis(1-propanol) dimethanesulfonate hydrochloride; Compound 864; Yoshi 864

RTECS No. UB 6620000

Uses Chemotherapeutic agent.

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat 75 mg kg^{-1} (1).

LD_{10} intraperitoneal mouse 170 mg kg^{-1} (2).

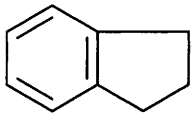
Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via intraperitoneal injection. Equivocal evidence of carcinogenicity (3).

References

1. *Arzneim.-Forsch.* 1974, **24**, 1139.
2. *J. Med. Chem.* 1977, **20**, 515.
3. *National Toxicology Program Research and Testing Division* 1992, Report No.TR-018, NIEHS, Research Triangle Park, NC, USA

I17 indan



C_9H_{10} **Mol. Wt.** 118.18 **CAS Registry No.** 496-11-7

Synonyms 2,3-dihydro-1*H*-indene; benzocyclopentane; hydrindene; hydrindonaphthene

EINECS No. 207-814-7 **RTECS No.** NK 3750000

Uses Component of fuels, solvents and varnishes.

Occurrence In coal tar. Water pollutant (1).

Physical properties

M. Pt. –51.4°C **B. Pt.** 176.5°C **Flash point** 50°C **Specific gravity** 0.9639 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 3.33

Solubility Organic solvents: miscible in ethanol, diethyl ether

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Intragastric Fischer 344 rat (dose unspecified) alternate days for 14 days. In ♂ rats toxic injury shown by increased cytoplasmic hyaline droplets in proximal convoluted tubular epithelial cells. ♀ rats showed no renal damage (2).

Metabolism and toxicokinetics
In ♂ Fischer 344 rats metabolised to 1-, 2- and 5-indanol, 1- and 2-indanone, 2- and 3-hydroxy-1-indanone and *cis*- and *trans*-indan-1,2-diol (3,4).

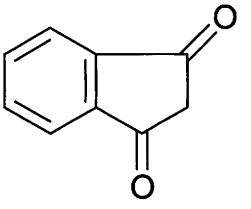
Other effects

Any other adverse effects
♂, but not ♀, Fischer 344 rats, exhibit lesions to the kidney typical of cyclic hydrocarbons (3,4).

References

1. Wang, Y. et al *Beijing Daxue Xuebao Ziran Kexueban* 1988, **24**(2), 163-166 (Ch.) (*Chem. Abstr.* **109**, 79296b).
2. Serve, M. P. *Gov. Rep. Announce. Index (U. S.)* 1989, **89**(19), Abstr. No.952, 011.
3. Serve, M. P. et al *J. Toxicol. Environ. Health* 1990, **29**(4), 409-416.
4. Yu, K. O. et al *Biomed. Environ. Mass Spectrom.* 1987, **14**(11), 649-651

I18 1,3-indandione



$C_9H_6O_2$ **Mol. Wt.** 146.15 **CAS Registry No.** 606-23-5

Synonyms 1*H*-indene-1,3(2*H*)-dione; 1,3-diketohydrindene

EINECS No. 210-109-7 **RTECS No.** NK 5070000

Physical properties

M. Pt. 129-131°C **Specific gravity** 1.37 at 21°C
Solubility Organic solvents: benzene, hot ethanol

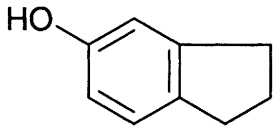
Mammalian & avian toxicity

Acute data
LD_{Lo} intraperitoneal mouse 100 mg kg^{-1} (1).

References

1. *Arch. Toxicol.* 1975, **33**, 191

I19 5-indanol



$C_9H_{10}O$ **Mol. Wt.** 134.18 **CAS Registry No.** 1470-94-6

Synonyms 2,3-dihydro-1*H*-inden-5-ol; 5-hydroxyhydrindene; 5-hydroxyindan

EINECS No. 216-006-3 **RTECS No.** NK 7525000

Physical properties

M. Pt. 51-53°C **B. Pt.** 255°C **Flash point** >110°C

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2811

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3250 mg kg^{-1} (1).

LD_{50} dermal rabbit 450 mg kg^{-1} (1).

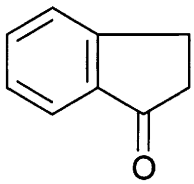
Other comments

A urinary metabolite of indan (2,3).

References

1. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
2. Yu, K. et al *Biomed. Environ. Mass. Spectrom.* 1987, **14**(11), 649-651.
3. Serve, M. P. et al *J. Toxicol. Environ. Health* 1990, **29**(4), 409-416

I20 1-indanone



C_9H_8O **Mol. Wt.** 132.16 **CAS Registry No.** 83-33-0

Synonyms 1-hydrindone; indone; oxohydrindene; α-indanone; indanone; α-hydrindone; 1-indone; 2,3-dihydro-1*H*-indene-1-one

EINECS No. 201-470-1

Uses Catalyst. Chemical intermediate.

Physical properties

M. Pt. 40-42°C **B. Pt.** 243-245°C **Flash point** 111°C **Specific gravity** 1.1028 at 40°C with respect to water at 40°C
Solubility Water: miscible. Organic solvents: acetone, chloroform, diethyl ether, ethanol, lignoin

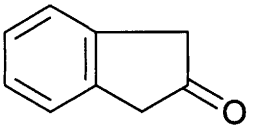
Other comments

Groundwater pollutant from coal and petroleum gasification plants (1).
Residues have been identified in forest soil (2).
Biodegradation product of linear dodecylbenzene sulfonates (3).
Contaminant in river, potable and rain waters. Occurs in gas oil, diesel exhaust and cigarette smoke emissions.

References

1. Turney, G. L. et al *Ground Water Monit. Rev.* 1990, **10**(3), 187-198.
2. Hempling, R. et al *Org. Geochem.* 1990, **15**(2), 131-145.
3. Kubodera, T. et al *Yukagaku* 1978, **27**(12), 838 (*Chem. Abstr.* **90**, 109402m)

I21 2-indanone



C_9H_8O **Mol. Wt.** 132.16 **CAS Registry No.** 615-13-4
Synonyms 1,3-dihydro-1*H*-inden-2-one; β-hydrindone
EINECS No. 210-410-3 **RTECS No.** NK 7535500
Uses Chemical intermediate.
Occurrence Contaminant in river, potable and rain waters. Occurs in gas oil, diesel exhaust and cigarette smoke emissions. Metabolite of indan.

Physical properties

M. Pt. 54-56°C **B. Pt.** 218°C **Flash point** 100°C **Specific gravity** 1.0712 at 69°C with respect to water at 4°C
Solubility Organic solvents: acetone, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

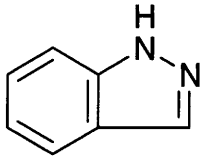
Acute data
LD_{50} intravenous mouse 56 mg kg^{-1} (1).

Metabolism and toxicokinetics
Gavage or subcutaneous routes to rabbits and rats. Metabolised to *cis*-indone-1,2-diol and to a lesser degree to *trans*-indone-1,2-diol, both metabolites were excreted in urine (2).

References

1. U.S. Army Armament Res. and Dev. Command, Chemical Systems Lab., NIOSH Exchange Chemicals, NX 08390, Aberdeen Proving Ground, MD, USA.
2. Lewis, D. A. *Nature (London)* 1966, **210**, 1046

I22 indazole



$C_7H_6N_2$ **Mol. Wt.** 118.14 **CAS Registry No.** 271-44-3

Synonyms 1*H*-indazole; 2-azaindole; 1*H*-benzopyrazole; 1,2-diazaindene; isoindazole

EINECS No. 205-978-4 **RTECS No.** NK 7745000

Physical properties

M. Pt. 147-149°C **B. Pt.** 267-270°C at 743 mmHg

Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

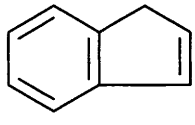
Acute data

LD_{50} intraperitoneal mouse 440 mg kg^{-1} (1).

References

1. *J. Med. Chem.* 1963, **6**, 480

I23 indene



C_9H_8 **Mol. Wt.** 116.16 **CAS Registry No.** 95-13-6

Synonyms 1*H*-indene; indonaphthene; inden

EINECS No. 202-393-6 **RTECS No.** NK 8225000

Uses In paint and coating manufacture. In tile manufacture. Chemicals synthesis intermediate. In the production of coumarin-indene resins.

Occurrence From tars of coal, lignite and crude petroleum.

Physical properties

M. Pt. –1.8°C **B. Pt.** 181.6°C **Flash point** 58°C **Specific gravity** 0.9968 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 2.92

Occupational exposure

FR-VME 10 ppm (45 mg m^{-3})

UK-LTEL 10 ppm (48 mg m^{-3}) **UK-STEL** 15 ppm (72 mg m^{-3})

US-TWA 10 ppm (48 mg m^{-3})

Ecotoxicity

Fish toxicity

LC_{50} (1 hr) fathead minnow 39 mg l^{-1} static bioassay in Lake Superior water at 18-22°C (1).

LC_{50} (24-96 hr) fathead minnow 14 mg l^{-1} static bioassay in Lake Superior water at 18-22°C (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycylic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (2).

Other comments

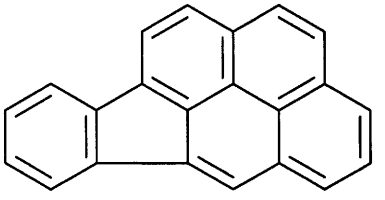
Study of oil- and creosote-associated compounds under aerobic and anaerobic biodegradation showed that polycyclic aromatic hydrocarbons with ≥4 aromatic rings are degraded slowly (3).

Reviews on experimental toxicology and human health effects listed (4).

References

1. Mattson, V. R. et al *Acute Toxicity of Selected Organic Compounds to Fathead Minnows* 1976, EPA-600/3-76-097.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. Arvin, E. et al *Int. Conf. Physiochemical Biol. Detoxif. Hazard. Wastes* 1989, **2**, 828-847.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

124 indeno[1,2,3-*cd*]pyrene



$C_{22}H_{12}$ **Mol. Wt.** 276.34 **CAS Registry No.** 193-39-5

Synonyms *o*-phenylenepyrene; 1,10-(*o*-phenylene)pyrene

EINECS No. 205-893-2 **RTECS No.** NK 9300000

Physical properties

M. Pt. 160-163°C **B. Pt.** 536°C **Volatility** v.p. 1.0×10^{-10} mmHg at 20°C

Solubility Water: 62 μg l^{-1}

Ecotoxicity

Bioaccumulation

Levels of 160, 13 and 1.5 ng g dry wt^{-1} in seston, *Mytilus edulis* soft parts and eider duck gallbladder, respectively, from the Baltic Sea. Concentration in eider duck: gall bladder >adipose tissue >liver; on lipid weight basis: gall bladder ≥liver >adipose tissue (1).

Environmental fate

Degradation studies

$t_{1/2}$ 224-408 day in sandy loam soil (2).
$t_{1/2}$ at 10, 20, 30°C, respectively, 600, 730, 630 days in unacclimated agricultural sandy loam soil (3).
1.9 μg ml^{-1} contaminated groundwater from creosote works site inoculated with indigenous adapted microorganisms sampled at 1, 3, 5, 8 and 14 days gave levels of 1.3, 1.4, 1.4, 1.2 and 0.9 μg ml^{-1}, respectively (4).

Abiotic removal

Anaerobic sludge digestion, batch incubation with and without NaN_3 to arrest biological activity. Significant removal observed over 32 days. Removal was concluded to be non-biological (5).
After 48-hr incubation in sandy loam soil 11.5-13.5% removal by abiotic means. Volatilisation was negligible (2).
Following two-stages (powdered and granular) activated carbon treatment 98% removal from river water (60.4 ng l^{-1}) giving a concentration of 1.2 ng l^{-1} in the drinking water (6).

Mammalian & avian toxicity

Acute data

Yolks of chicken eggs preincubated for 4 days were injected with 2.0 and 0.5 mg kg egg^{-1} single dose and the mortality measured 2 wk later was 17/20 and 2/20, respectively (7).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (8).
Dermal mice administered total initiating dose of 1 mg induced a 72% incidence of skin tumours (9).
At a total dose ranging from 0.14 to 0.58 mg $mouse^{-1}$ no tumorigenic effects were observed in newborn CD-1 mice (route unspecified) (10).

Teratogenicity and reproductive effects

Single-dose injection of 2.0 mg kg egg^{-1} caused abnormalities to the chicken embryo including degenerative hepatic lesions, pericardial oedema, subcutaneous oedema and microphthalmia (7).

Metabolism and toxicokinetics

Metabolised *in vivo* by mouse skin. The major metabolites were 8-hydroxyindeno[1,2,3-*cd*]pyrene, 9-hydroxyindeno[1,2,3-*cd*]pyrene, and *trans*-1,2-dihydro-1,2-dihydroxyindeno[1,2,3-*cd*]pyrene. Minor metabolites identified included *trans*-1,2-dihydro-1,2,8-trihydroxyindeno[1,2,3-*cd*] pyrene, *trans*-1,2-dihydro-1,2,9-trihydroxyindeno[1,2,3*cd*]pyrene, indeno[1,2,3-*cd*]pyrene-1,2-dione, and 10-hydroxyindeno[1,2,3-*cd*]pyrene. Two metabolites, *trans*-1,2-dihydro-1,2-dihydroxyindeno[1,2,3-*cd*]pyrene and 1,2-dihydro-1,2-epoxyindeno-[1,2,3-*cd*]pyrene both produced an 80% incidence of tumours at a total initiating dose of 1.0 mg. 8-Hydroxyindeno-[1,2,3-*cd*] pyrene, which is mutagenic when assayed in the presence of a microsomal activation system, exhibited only weak tumour-initiating activity (11).
In vitro rodent liver metabolised to hydroxy, dihydrodiol and quinone metabolites (12).

Genotoxicity

As a component of PAH fraction of airborne pollutants, *Salmonella typhimurium* TA100 with metabolic activation positive (13).
As a component of a diesel exhaust fraction, *Salmonella typhimurium* TA98 with and without metabolic activation positive (direct acting); TA100 with metabolic activation weakly positive and without metabolic activation negative (14).
In vivo ♀ CD-1 mice single topical application (unspecified), single major DNA adduct detected (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (16).

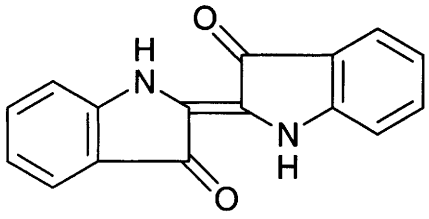
Other comments

In fresh motor oil 0.03 mg kg^{-1}, used motor oil after 10,000 km 46.7-83.2 mg kg^{-1} and petrol 0.04-0.18 mg kg^{-1} (17).
In exhaust gases of petrol-engine cars 11-87 μg m^{-3} (18).
In coke oven emissions 101.5 μg g $sample^{-1}$ (19).
Cigarette smoke 0.4 μg 100 $cigarettes^{-1}$ (20).
In groundwater 0.2-1.8 μg m^{-3} and tapwater 0.9-3.0 μg m^{-3} from man-made sources (21).
Effects of exposure to PAHs in road workers in New Zealand were investigated. In general the exposures were within permissible limits for these materials, and the health hazards were slight. The possible effects of exposure were mitigated by the work pattern (22).
PAHs pose a considerable occupational hazard to evaporative pattern casting process workers in metal industry (23).
PAHs are known to leach from pipe and storage tank linings. Potential cancer risks in drinking water discussed (24).
Environment monitoring of the mutagenic/carcinogenic hazard associated with bitumen fumes showed occupational exposures to these agents was low (25).
The relationship between exposure to environmental carcinogens (PAHs) and lung cancer discussed (26).
Median air concentration of 0.2 μg m^{-3} (SD 144%) from tar bitumen in road works. Over an 8-hr working shift varied by a factor of 30. The study concludes that there is a considerable risk to health (27).
Reviews on experimental toxicology, environmental effects and human health effects listed (28).

References

1. Broman, D. et al *Environ. Toxicol. Chem.* 1990, **9**(4), 429-442.
2. Park, K. S. et al *Environ. Chem.* 1990, **9**, 187-195.
3. Coover, M. P. et al *Hazard. Waste Hazard. Mater.* 1987, **4**(1), 69-82.
4. Mueller, J. G. et al *Appl. Environ. Microbiol.* 1991, **57**(5), 1277-1285.
5. Kirk, P. W. W. et al *Environ. Technol.* 1991, **12**(1), 13-20.
6. Harrison, R. et al *Environ. Sci. Technol.* 1976, **10**(12), 1151-1156.
7. Brunstrom, B. et al *Environ. Pollut.* 1990, **67**(2), 133-143.
8. *IARC Monograph* 1987, **Suppl. 7**, 64.
9. Rice, J. E. et al *Carcinogenesis (London)* 1990, **11**(11), 1971-1974.
10. Lavoie, E. J. et al *Cancer Lett. (Shannon, Irel.)* 1987, **34**(1), 15-20.
11. Rice, J. E. et al *Carcinogenesis (London)* 1986, **7**(10), 1761-1764.
12. Rice, J. E. et al *Polynuclear Aromatic Hydrocarbons (Pap. Int. Symp.)* 8th ed., 1985, Battelle Press, Columbus, OH, USA.
13. Motykiewicz, G. et al *Mutat. Res.* 1989, **223**(2), 243-251.
14. Ball, J. C. et al *Environ. Sci. Technol.* 1990, **24**, 890-894.
15. Weyand, E. H. et al *Cancer Lett. (Shannon, Irel.)* 1987, **37**(3), 257-266.
16. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
17. *Influence of engine/driving-conditions and operating time of engine oil on the emission of polycyclic aromatic hydrocarbons from gasoline passenger cars: 1. Emissions* 1977, German Soc. for Petroleum Sciences and Coal Chem., Hamburg, Germany.
18. Schrodter, W. P. et al *Erdoel Kohle, Erdgas, Petrochem.* 1976, **294**.
19. Coon, R. et al *Toxicol. Appl. Pharmacol.* 1970, **16**, 646.
20. Wynder et al *Tobacco and Tobacco Smoke* 1967, Academic Press, New York, NY, USA.
21. Borneff, J. et al *Arch. Hyg.* 1969, **153**(3), 220-229.
22. Darby, F. W. et al *Ann. Occup. Hyg.* 1986, **30**(4), 445-454.
23. Gressel, M. G. et al *Appl. Ind. Hyg.* 1988, **3**(1), 11-17.
24. Olori, L. et al *Rapp. ISTISAN* 1989, ISTISAN 89/28 (Ital.) (*Chem. Abstr.* **113**, 120439y).
25. Monarca, S. et al *Int. Arch. Occup. Environ. Health* 1987, **59**(4), 393-402.
26. Galassi, G. *AES* 1988, **10**(6), 9-10 (Ital.) (*Chem. Abstr.* **110**, 81633y).
27. Knecht, U. et al *Br. J. Ind. Med.* 1989, **46**(1), 24-30.
28. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

125 Indigo



$C_{16}H_{10}N_2O_2$ **Mol. Wt.** 262.27 **CAS Registry No.** 482-89-3

Synonyms 2-(1,3-dihydro-3-oxo-2*H*-indol-2-ylidene)-1,2-dihydro-3*H*-indol-3-one; C.I. 73000; Indigo Blue; Lithosol Deep Blue B; Vat Blue 1; Vynamon Blue A; Nacco

EINECS No. 207-586-9 **RTECS No.** DU 2988400

Uses Textile dye.

Occurrence *Indigofera* of the Leguminosae.

Physical properties

M. Pt. 390-392°C **Specific gravity** 1.35 **Volatility** v.p. 47 mmHg at 430°C

Solubility Organic solvents: aniline, chloroform, glacial acetic acid, nitrobenzene

Ecotoxicity

Bioaccumulation

Confirmed to be non-accumulative or low accumulative (1).

Mammalian & avian toxicity

Sensitisation

The allergic potential of 13 pharmaceutical dyes including indigo was investigated by sensitising guinea pig skin with a series of intradermal applications. Intradermally, all dyes elicited an allergenic response; epidermally only indigo gave an allergenic response (2).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation (3-methylcholanthrene induced) positive (3).

Other effects

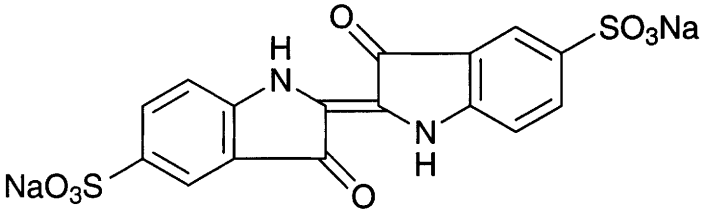
Other adverse effects (human)

A man accidently splashed a 7% alkaline solution of the reduced form in his eyes. The conjunctiva appeared blue several hr later, this cleared within 10 days. The cornea was turbid but not stained (4).

References

1. *The list of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* Chemicals Inspection and Testing Institute, Japan.
2. Maurer, T. *Acta Pharm. Technol.* 1979, **Suppl. 8**, 37.
3. Jongen, W. M. F. *Carcinogenesis (London)* 1982, **3**(11), 1321-1323.
4. Grant, W. M. *Toxicology of the Eye* 2nd ed., 1974, 577, C. C. Thomas, Springfield, IL, USA

I26 Indigo Carmine



$C_{16}H_8N_2Na_2O_8S_2$ **Mol. Wt.** 466.36 **CAS Registry No.** 860-22-0

Synonyms 2-(1,3-dihydro-3-oxo-5-sulfo-2*H*-indol-2-ylidene)-2,3-dihydro-3-oxo-1*H*-indole-5-sulfonic acid, disodium salt; Acid Blue 74; Amacid Brilliant Blue; Intense Blue; C.I. 73015; C.I. 75781; FD&C Blue No. 2

EINECS No. 212-728-8 **RTECS No.** DU 3000000

Uses Dye. Reagent for detection of chlorate and nitrate. In testing milk. In test for renal function. Clinical marker dye, particularly in urological procedures. Food colour.

Physical properties

Solubility Water: 1 g ~100 ml^{-1} at 25°C

Environmental fate

Abiotic removal

In a wastewater treatment plant using activated carbon with pore radius $<2 \times 10^{-8}$ m; a filling correlation between the amount absorbed and pore size was obtained (1).

At 25°C adsorption rate by activated carbon was ~1.7 to 6.5×10^9 cm^2 s^{-1} (2).

Carbon-mineral adsorbents obtained from mixtures of waste carbonaceous materials and montmorillonite, attapulgite and polygoroskite were more effective than activated carbon in removal from wastewater (3).

Adsorption and retention

Uptake to give monolayer coverage for kaolinite is greater than that for chlorite (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2000, 2500 mg kg^{-1}, respectively (5).

LD_{50} intravenous rat 93 mg kg^{-1} (6).

LD_{50} subcutaneous mouse 405 mg kg^{-1} (5).

Teratogenicity and reproductive effects

Gavage Charles River CD rats 25, 75 or 250 mg kg^{-1} day^{-1} on days 6-15 of gestation. Dutch belted rabbits received the same dose on days 6-18 of gestation. No teratogenicity was observed (7).

Sensitisation

Occasionally skin rash, pruritus and bronchoconstriction in humans (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (9).

In vitro mouse lymphoma tk+/tk– with metabolic activation indeterminate (9).

Oral mouse in diet increased bone marrow chromosomal aberrations (10).

Allium cepa showed significant increase in polyploid cells and at high doses chromosome breaks and micronucleus formation occurred (11).

Other effects

Other adverse effects (human)

May cause vomiting, hypertension, nausea and bradycardia. Discoloured skin has occurred following a large parenteral dose (8).

Two elderly patients, both with a history of asthmatic bronchitis, suffered total cardiac arrest following 80 mg intravenously (12).

Any other adverse effects

No inhibition of *in vitro* rabbit renal medulla prostaglandin synthetase activity at 117 mg l^{-1} (13).

Legislation

Estimated acceptable daily intake: up to 2.5 mg kg body $weight^{-1}$ (8).

References

1. Tamura, T. et al *Environ. Technol. Lett.* 1988, **9**(4), 281-286.
2. Tamura, T. et al *Tokushima J. Exp. Med.* 1987, **34**(3-4), 97-100.
3. Tarasevich, Y. I. et al *Khim. Tekhnol. Vody* 1988, **10**(4), 315-317 (Russ.) (*Chem. Abstr.* **109**, 155525t).
4. Awal, K. P. *J. Nepal Chem. Soc.* 1988, **8**, 1-5.
5. *Scientia Pharmaceutica* 1979, **47**, 39.
6. *Drugs in Japan. Ethical Drugs* 6th ed., 1982, Japan Pharmaceutical Information Centre, Yakugyo Jiho Co., Ltd., Tokyo, Japan.
7. Borzelleca, J. F. et al *Food Chem. Toxicol.* 1987, **25**(7), 495-497.
8. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
9. Cameron, T. P. et al *Mutat. Res.* 1987, **189**(3), 223-261.
10. Das, S. K. et al *Cytobios* 1988, **53**(216), 25-29.
11. Roychondhury, A. et al *Mutat. Res.* 1989, **223**(3), 313-319.
12. Voiry, A. M. et al *Ann. Med. Nancy* 1976, **15**, 413-419.
13. Yoshihira, K. et al *J. Pharmacobio-Dyn.* 1991, **14**(6), 327-334

127 indium

In

In **Mol. Wt.** 114.82 **CAS Registry No.** 7440-74-6

EINECS No. 231-180-0 **RTECS No.** NL 1050000

Uses In bearing and dental alloys; as a thin film on moving metallic surfaces. In nuclear reactor control rods. In semi-conductor research.

Occurrence In Earth's crust 1×10^{-5}%.

Physical properties

M. Pt. 155°C **B. Pt.** 2000°C **Specific gravity** 7.3 at 20°C

Occupational exposure

SE-LEVL 0.1 mg m^{-3}

UK-LTEL 0.1 mg m^{-3} **UK-STEL** 0.3 mg m^{-3}

US-TWA 0.1 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{Lo} (calculated as indium) subcutaneous mouse 10 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Inhalation rat (9 month) 80 mg Pb-Zn dust containing trace amounts of indium, 9-month exposure, impaired liver function (2).

Teratogenicity and reproductive effects

Chick egg injected with the trichloride salt 1-100 μg egg^{-1} on day-2 of incubation. Gross malformations observed included twisted limbs, haemorrhage, everted viscera and reduced body weight (2).

Other effects

Any other adverse effects

Intravenous Japanese quail (dose and duration unspecified) 32% ^{114}In radiolabel accumulates in kidney of estradiol-treated ♂ and 37% in growing oocytes plus ova (3).

Injury to blood, heart, liver and kidneys in experimental animals. As sulfate relatively non-toxic when administered orally, but highly toxic when administered subcutaneously or intravenously as citrate (1).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

Uses, physical and chemical properties, acute/chronic toxicity, metabolism and exposure limits reviewed (5,6). Reviews on experimental toxicology, human health effects and workplace experience listed (7).

References

1. Browning, E. *Toxicity of Industrial Metals* 2nd ed., 1969, 164-168, Appleton-Century-Crofts, New York, NY, USA.
2. Burkhanov, A. I. et al *Gig. Sanit.* 1987, (2), 90-91 (Russ.) (*Chem. Abstr.* **106**, 133362y).
3. Robinson, G. A. et al *Poult. Sci.* 1990, **69**(2), 300-306.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. Horiguchi, S. et al *Jinrui Idengaku Zasshi* 1988, **33**(4), 120-137 (Japan.) (*Chem. Abstr.* **110**, 226636p).
6. Horiguchi, S. et al *Sumitomo Sangyo Eisei* 1987, **23**(4), 120-137 (Japan.) (*Chem. Abstr.* **111**, 128332n).
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

128 indium phosphide

InP

InP **Mol. Wt.** 145.79 **CAS Registry No.** 22398-80-7

EINECS No. 244-959-5 **RTECS No.** NL 1800000

Uses Used in semiconductor devices, injector lasers, experimental solar cells.

Physical properties

M. Pt. 1070°C **Specific gravity** 4.81

Solubility Water: insoluble

Occupational exposure

SE-LEVL 0.1 mg m^{-3} (as In)
UK-LTEL 0.1 mg m^{-3} (as In) **UK-STEL** 0.3 mg m^{-3} (as In)
US-TWA 0.1 mg m^{-3} (as In)

Mammalian & avian toxicity

Sub-acute and sub-chronic data

♂ Fischer 344 rats were intratracheally instilled with 0, 1.2, 6.0, or 62.0 μg kg^{-1} indium phosphide particles and the effects examined on the following day and on day-8. Pulmonary inflammation and epithelial cell damage occurred up to 8 days following the 62.0 μg kg^{-1} dose. No significant effects were seen in rats dosed with 6.0 μg kg^{-1} or below (1).

♂ Syrian golden hamsters instilled intratracheally with indium phosphide 1 × wk^{-1} for 15 wk (total dose 7.5 mg phosphorus). Cumulative body weight gain over total life span was not significantly different between dosed and control hamsters. Severe damage occurred to the lungs of dosed hamsters as indicated by increased incidence rates of proteinosis-like lesions, alveolar or bronchiolar cell hyperplasia, pneumonia, emphysema, and metaplastic ossification (2).

Metabolism and toxicokinetics

Intratracheal ♂ Fischer 344 rats received a single dose of indium phosphide particles (0-100 mg kg^{-1}) and were observed on days 1 and 7 after instillation. Serum indium was detected in the group given 100 mg kg^{-1}. Indium was detected in the liver and spleen and increased in a dose-related manner on days 1 and 7. Phagocytosed indium phosphide particles were seen in lung macrophages. Migration of neutrophils in lung alveoli was observed. No histopathological changes were detected in the liver or spleen and a haematological study did not reveal significant findings. Pulmonary inflammation was observed. The authors suggest that phagocytosis by macrophages may contribute to the dispersal of intratracheally installed indium phosphide particles to the liver and spleen (3).

Intraperitoneal or oral ♂ ICR mice 0-500 mg kg^{-1}. No mice died during the 2-wk observation period. In intraperitoneally treated mice there were dose-dependent increases in serum indium concentration, lung and spleen weights. Accumulation of indium occurred mainly in the lungs and liver. Black granules of indium phosphide were deposited in the lymph nodes, spleen, lungs and liver. Extramedullary granulopoiesis was observed. Eosinophilic exudates and mononuclear cells were seen in the pulmonary alveoli. An increase in the proportion of blood stem cells and monocytes was seen in mice dosed intraperitoneally with 5000 mg kg^{-1}. In mice administered indium phosphide orally there was no clear relationship between dose and biological effects (4).

Poorly absorbed from gastro-intestinal tract of rats in both single or multiple oral doses (totalling 10 mg kg^{-1}). Upon absorption, relatively evenly distributed among major organs (liver, kidney, lung, spleen, testes). By 96 hr after oral dosing <0.11% of the dose of indium was recoved from tissues in the single- or multipe-dose experiments. At 96 hr after a single intratracheal instillation (10 mg kg^{-1}), retention in the body was ~0.36% of dose (except for lung). The major route for indium elimination following oral or intratracheal dosing was via faeces. Because of poor absorption it seems unlikely that indium will accumulate in the body following exposure to indium phosphide (5).

Irritancy

May cause irritation to the skin, mucous membranes and respiratory tract in man (6).

Other effects

Other adverse effects (human)

Inhalation exposure may cause damage to the lungs, liver, kidneys and heart (6).

Other comments

Indium phosphide is clearly soluble in synthetic gastric fluid and insoluble in saline or synthetic lung fluid (4).
Adequate precautions must be taken during the handling and processing of indium phosphide to prevent the production of acutely toxic gaseous phosphine (2).
Non-combustible solid, incompatible with strong oxidising agents, sulfur, and strong acids.

References

1. Oda, K. *Ind. Health* 1997, **35**(1), 61-68.
2. Mosovsky, J. A. et al *Appl. Occup. Environ. Hyg.* 1992, **7**(6), 375-384.
3. Uemura, T. et al *J. Occup. Health* 1997, **39**(3), 205-210.
4. Kabe, I. et al *J. Occup. Health* 1996, **38**(1), 6-12.
5. Zheng, W. et al *J. Toxicol. Environ. Health* 1994, **43**(4), 483-494.
6. *Draft Report: Laboratory Health and Safety Review of Indium Phosphide* 1988, National Toxicology Program, National Institutes of Health, Building 31, Room 2B-55, Bethesda, Maryland 20205, USA

129 indium trichloride

$InCl_3$

$InCl_3$ **Mol. Wt.** 221.18 **CAS Registry No.** 10025-82-8

Synonyms Indium chloride ($InCl_3$); trichloroindium

EINECS No. 233-043-0 **RTECS No.** NL 1400000

Uses In electroplating.

Physical properties

M. Pt. 586°C **Specific gravity** 4.0

Solubility Water: freely soluble

Occupational exposure

SE-LEVL 0.1 mg m^{-3} (as In)

UK-LTEL 0.1 mg m^{-3} (as In) **UK-STEL** 0.3 mg m^{-3} (as In)

US-TWA 0.1 mg m^{-3} (as In)

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rabbit 2350 μg kg^{-1} (1).

LD_{Lo} subcutaneous rat, mouse 10, 60 mg kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal mouse 9500 μg kg^{-1} (3).

LD_{50} chicken egg 121 μg egg^{-1} (4).

Teratogenicity and reproductive effects

Chick egg injected with 1-100 μg egg^{-1} on day-2 of incubation. Gross malformations observed included twisted limbs, haemorrhage, everted viscera and reduced body weight (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides: guide level 25 mg l^{-1} (5).

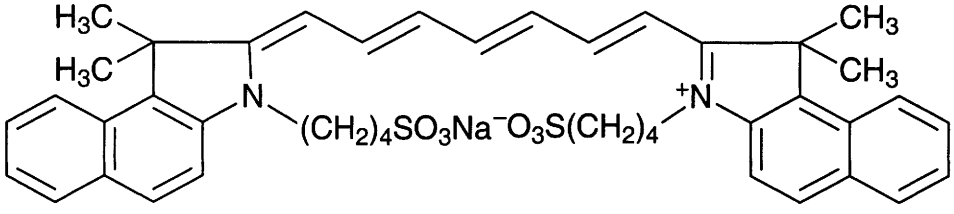
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

References

1. *Environ. Qual. Saf., Suppl.* 1975, **1**, 1.
2. *J. Ind. Hyg. Toxicol.* 1942, **24**, 243.
3. *C. R. Hebd. Seances Acad. Sci.* 1963, **256**, 1043.

4. Gilani, S. H. et al *J. Toxicol. Environ. Health* 1990, **30**(1), 23-31.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

I30 Indocyanine Green



$C_{43}H_{47}N_2NaO_6S_2$ **Mol. Wt.** 774.98 **CAS Registry No.** 3599-32-4

Synonyms 2-[7-[1,3-dihydro-1,1-dimethyl-3-(4-sulfobutyl)-2*H*-benz[*e*]indol-2-ylindene]-1,3,5-heptatrienyl]-1,1-dimethyl-3-(4-sulfobutyl)-1*H*-benz[*e*]indolium, hydroxide, inner salt, sodium salt; 4,5-benzoindotricarbocyanine; Cardio Green; Ujoviridin; Wofaverdin

EINECS No. 222-751-5 **RTECS No.** DE 1500000

Uses Dye in infra-red photography. In preparation of Wratten filters. Aid for blood volume determination, hepatic function and cardiac output.

Physical properties

Solubility Organic solvents: methanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse, rat 400, 700 mg kg^{-1}, respectively (1).
LD_{50} intravenous mouse 60 mg kg^{-1} (2).

Metabolism and toxicokinetics

Bound to plasma protein following intravenous injection. Rapidly taken up by the liver and is excreted unmodified into the bile (3).
Intravenous Sprague-Dawley rat 46 mg l^{-1} kg^{-1} maximum biliary secretory rate of 108 μg l^{-1} kg^{-1} min^{-1} (metabolism by the liver was inhibited by administration of diethyl maleate) (4).

Other effects

Other adverse effects (human)

Anaphylactoid reactions reported (5).

Any other adverse effects

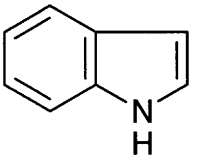
In Sprague-Dawley rats 14 mg^{-1} kg^{-1} inhibited the maximum biliary secretory rate of intravenously administered amaranth (181 mg^{-1} kg^{-1}) by 50% and 39 mg kg^{-1} inhibited liver ADP-stimulated O_2 consumption by 20-30% (4).

References

1. *Toxicol. Appl. Pharmacol.* 1973, **24**, 37.

2. *Toxicol. Appl. Pharmacol.* 1978, **44**, 225.
3. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
4. Varga, F. et al *Arch. Toxicol., Suppl.* 1989, **13**, 309-311.
5. Speich, R. et al *Ann. Intern. Med.* 1988, **109**, 345-346

I31 indole



C_8H_7N **Mol. Wt.** 117.15 **CAS Registry No.** 120-72-9

Synonyms 1*H*-indole; 1-azaindene; ketole; 2,3-benzopyrrole

EINECS No. 204-420-7 **RTECS No.** NL 2450000

Uses In perfume (in highly dilute solution).
Occurrence Coal tar. Faeces. Cigarette smoke.

Physical properties

M. Pt. 52°C **B. Pt.** 253°C **Flash point** 110°C **Specific gravity** 1.22 **Partition coefficient** log P_{ow} 2.14
Solubility Organic solvents: benzene, diethyl ether, hot ethanol

Ecotoxicity

Fish toxicity
5 ppm killed trout, bluegill sunfish and goldfish within 4, 5 and 5 hr, respectively. 1 ppm had no effect. Test conditions: pH 7.0; dissolved oxygen, 7.5 ppm; total hardness (soap method), 300 ppm; methyl orange alkalinity, 310 ppm; free carbon dioxide, 5 ppm; and 12.8°C (1).
At 10 mg l^{-1} death occurred at 0-2 and 12-21 hr of exposure for the steelhead trout and bridgelip sucker, respectively. At 5 mg l^{-1} the trout died between 2 and 6 hr. Test conditions: total hardness, 0-17 mg l^{-1}; methyl orange alkalinity, 14 mg l^{-1}; pH 7.6; or total hardness, 67-120 mg l^{-1}; methyl orange alkalinity, 151-183 mg l^{-1}; total dissolved solids, 160-175 mg l^{-1}; pH 7.1 (2).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 2.39 ppm Microtox test (3).

Environmental fate

Nitrification inhibition
Depending on soil type 1.2, 12 and 59 μg l^{-1} g^{-1} caused, respectively, 0, 1-5 and 3-6% inhibition of nitrification of ammonium in soil (4).

Degradation studies
Oxindole accumulation under methanogenic, but not under denitrifying, conditions is caused by differences between relative rates of oxindole production and destruction (5).
With an inoculum of sewage sludge and incubation under methanogenic conditions, metabolism occurred within 10 days. Oxindole was the temporary intermediate formed. Almost complete mineralisation occurred (6).
The rate of transformation to oxindole and its subsequent disappearance was dependent on the concentration of inoculum and indole and the temperature. The dominant process was methanogenesis. Sulfate reducers

predominated over methanogens in the mixed culture of anaerobic bacteria. 75% of the substrate was mineralised to CO_2 (7).
BOD_5 2.07 using the standard dilution technique with normal sewage as seed material (8).
COD, 2.460 mg l^{-1} O_2 (9).
ThOD, 2.46 (10).
BOD_5, 84% of ThOD (11).
Degradation time in groundwater from a gasoline-contaminated aquifer 310 hr. Initial concentration 0.2-1 mg l^{-1}, temperature 10°C (12,13).

Mammalian & avian toxicity

Acute data
LD_{50} (estimated) redwing blackbird >100 mg kg^{-1} (14).
LD_{50} oral rat 1000 mg kg^{-1} (15).
LD_{50} dermal rabbit 790 mg kg^{-1} (15).
LD_{50} intraperitoneal mouse 117 mg kg^{-1} (16).
LD_{50} subcutaneous mouse 225 mg kg^{-1} (17).
Oral pony 0.1 or 0.2 g kg^{-1} caused intravascular haemolysis and haemoglobinuria. Heinz body formation was observed in the higher dosed animals. Plasma indole levels increased. Death of some higher-dosed ponies occurred between 24 and 72 hr after dose. At necropsy all body fat, elastic tissue and mucous membrane was stained yellow. The most prominent microscopic lesion was haemoglobinuric nephrosis (18).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (after nitrite treatment). Showed mutagenic precursor activity (19).

Other effects

Any other adverse effects
Intraperitoneal rat 5 mg kg^{-1} reduced oxygen consumption significantly. *In vitro* rat diaphragm or liver showed no influence on respiration (20).

Other comments

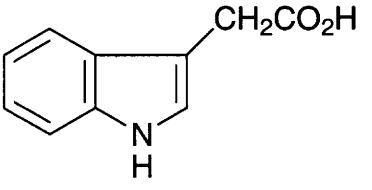
Major metabolite of orally administered tryptophan in ponies (21).
0.25 µg l^{-1} found in domestic sewage (22).
Metabolism and hazards reviewed (23,24).
Intense faecal odour.

References

1. US EPA *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, Washington, DC, USA.
2. US EPA *Fish Toxicity Screening Data* 1989, EPA 560/6-89-001, Washington, DC, USA.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. McCarty, G. W. et al *Biol. Fertil. Soils* 1989, **8**, 204-211.
5. Madsen, E. L. et al *Appl. Environ. Microbiol.* 1988, **54**(1), 74-78.
6. Berry, D. F. et al *Appl. Environ. Microbiol.* 1987, **53**(1), 180-182.
7. Shanker, R. et al *Microb. Ecol.* 1990, **20**(2), 171-183.
8. Mills, E. J. et al *Proc. 8th Purdue Ind. Waste Conf.* 1953, 492.
9. Chudoba, J. et al *Water Res.* 1973, **7**, 663-668.
10. Meinck, F. et al *Les Eaux Residuaires Industrielles* 1970.
11. Wolters, N. *unterschiedliche Bestimmungsmethoden zur Erfassung der organischen Substanz in einer Verbindung* Lehrauftrag Wasserbiologie a.d., Technischen Hochschule, Darmstadt, Germany.
12. Arvin, E. et al *Proc. Pap. Int. Symp. Groundwater Microbiol., Probl. Biol. Treat.* 1987, Kuopio, Finland.
13. Arvin, E. et al *Water Sci. Technol.* 1988, **20**(3), 109-118.
14. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.

15. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
16. *Yakugaku Zasshi* 1974, **94**, 1620.
17. *Klin. Wochenschr.* 1957, **35**, 504.
18. Paradis, M. R. et al *Am. J. Vet. Res.* 1991, **52**(5), 748-753.
19. Ochiai, M. et al *Mutat. Res.* 1986, **172**(3), 189-197.
20. Hohenegger, M. et al *Nephron* 1988, **48**(2), 154-158.
21. Paradis, M. R. et al *Am. J. Vet. Res.* 1991, **52**(5), 742-747.
22. Faust, S. J. et al *Organic Compounds in Aquatic Environment* Marcel Dekker, New York, NY, USA.
23. Subramanian, V. et al *Biol. Oxid. Syst., [Proc. Symp.] 1989* 1990, **1**, 417-429.
24. *Dangerous Prop. Ind. Mater. Rep.* 1988, **8**(3), 63-67

I32 indole-3-acetic acid



$C_{10}H_9NO_2$ **Mol. Wt.** 175.19 **CAS Registry No.** 87-51-4

Synonyms indol-3-ylacetic acid; indoleacetic acid; 1*H*-indole-3-acetic acid; heteroauxin; IAA; Rhizopin; heteroauxin

EINECS No. 201-748-2 **RTECS No.** NL 3150000

Uses Plant growth regulator.
Occurrence In all plants. In bacteria and fungi.

Physical properties

M. Pt. 168-170°C **Volatility** v.p. 0.15×10^{-6} mmHg at 60°C
Solubility Water: 1.5 g l^{-1} at 20°C. Organic solvents: acetone, chloroform, diethyl ether, ethanol

Environmental fate

Nitrification inhibition
Growth, dinitrogen fixation and heterocyst frequency of *Anabaena* PCC7119 and *Nodularia* sp. were investigated. Concentrations higher than 1.75×10^{-2} g l^{-1} were inhibitory to growth. Lower concentrations did not alter the growth of *Anabaena* (1).

Degradation studies
Degraded by the fungi *Aspergillus niger*, *Paecilomyces varioti* and *Penicillium oxalicum*, but in *Chaetomium cupreum* and *C. globosum* growth was totally inhibited. There was no positive correlation between degradation and vegetative growth or pH of the medium (2).
Degrades rapidly in soil (3).

Abiotic removal
Unstable to light (3).

Mammalian & avian toxicity

Acute data
LD_{50} dermal mouse 1000 mg kg^{-1} (3).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1538 histidine revertants with and without metabolic activation negative (4).

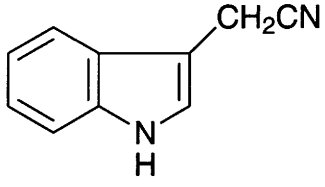
Other comments

Occurs in secondary domestic sewage plant effluent 0.013 mg l^{-1} (5).
Metabolised in *Vicia faba* via biosynthetic pathway to indole-3-acetylaspartic acid, 3- hydroxy-2-indolone-3-acetylaspartic acid and 3-(*O*-β-glucosyl-2-indolone-3-acetylaspartic acid (6).
Plant biochemistry reviewed (7).
Metabolic pathways reviewed (8).

References

1. Leganes, F. et al *Plant Cell Physiol.* 1987, **28**(3), 529-533.
2. Reddy, V. K. et al *Indian J. Mycol. Plant Pathol.* 1987, **17**(1), 75-77.
3. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
4. Kappas, A. *Mutat. Res.* 1988, **204**(4), 615-621.
5. Wilson Pitt, W. et al *Environ. Sci. Technol.* 1975, **9**(12), 1068-1073.
6. Tsurumi, S. *Shokubutsu no Kagaku Chosetsu* 1986, **21**(2), 126-133 (Japan.) (*Chem. Abstr.* **107**, 112734b).
7. Nonhebel, H. M. et al *Plant Growth Subst. 1988, (International Conference on Plant Growth Substances)* 1990, 333-340, Springer, Berlin, Germany.
8. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

133 indole-3-acetonitrile



$C_{10}H_8N_2$ **Mol. Wt.** 156.19 **CAS Registry No.** 771-51-7

Synonyms 3-indoleacetonitrile; 1*H*-indole-3-acetonitrile; 3-(cyanomethyl)indole; IAN; indoleacetonitrile; 3-indolylacetonitrile

EINECS No. 212-232-1 **RTECS No.** AM 0700000

Physical properties

M. Pt. 35-37°C **B. Pt.** 157-160°C at 0.2 mmHg **Flash point** >110°C

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rat 255 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (2).

Other effects

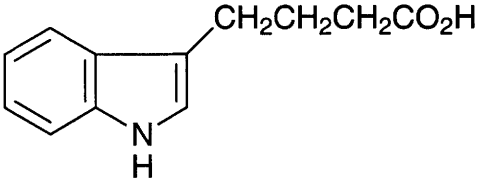
Any other adverse effects

In vitro primary chick embryo hepatocytes 35 μg ml^{-1} gave 1.6-fold increase in ethoxyresorufin-*O*-deethylase and a 2-fold increase in ethoxycoumarin-*O*-deethylase activities. Has a protective effect against benzo[*a*]pyrene genotoxicity (3,4).

References

1. *Food Cosmet. Toxicol.* 1980, **18**, 159.
2. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
3. Jongen, W. M. F. et al *Mutat. Res.* 1989, **222**(3), 263-269.
4. Jongen, W. M. F. et al *Toxicol. In Vitro* 1987, **1**(2), 105-110

134 indole-3-butyric acid



$C_{12}H_{13}NO_2$ **Mol. Wt.** 203.24 **CAS Registry No.** 133-32-4

Synonyms 3-indolebutyric acid; 1*H*-indole-3-butanoic acid; Hormex; Hormodiu; IBA; β-indolylbutyric acid; Seradix; 4-(indol-3-yl)butyric acid

EINECS No. 205-101-5 **RTECS No.** NL 5250000

Uses Promoter/accelerator of roots from plant-cuttings.

Physical properties

M. Pt. 123-125°C **Volatility** v.p. $<8 \times 10^{-8}$ at 60°C

Solubility Water: 250 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

Trout, bluegill sunfish, goldfish (24 hr) 5 ppm non-toxic. Test conditions: pH 7; dissolved oxygen, 7.5 ppm; total hardness (soap method), 300 ppm; methyl orange alkalinity, 310 ppm; free carbon dioxide, 5 ppm; and 12.8°C (1).

Invertebrate toxicity

Not toxic to bees (2).

Environmental fate

Degradation studies

Degrades rapidly in soil (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 100 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 100 mg kg^{-1} (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1538 histidine revertants with and without metabolic activation negative (5).

Legislation

EPA Toxicity Class III (formulation) (2).

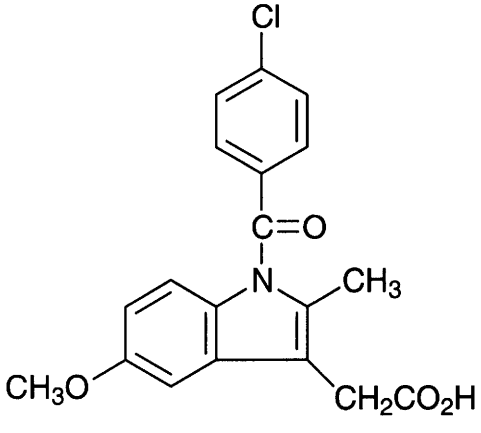
Other comments

Metabolic pathways reviewed (6).

References

1. Wood, E. M. *The Toxicity of 3400 chemicals to fish* 1987, EPA report 560/6-87-002, Washington, DC, USA.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Thompson, W. T. *Agricultural Chemicals* Book 3, 1976/77, 76, Thompson Publications, Fresno, CA, USA.
4. Anderson et al *Proc. Soc. Exp. Biol. Med.* 1936, **34**, 138.
5. Kappas, A. *Mutat. Res.* 1988, **204**(4), 615-621.
6. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

135 indomethacin



$C_{19}H_{16}ClNO_4$ **Mol. Wt.** 357.79 **CAS Registry No.** 53-86-1

Synonyms 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indole-3-acetic acid; Amuno; Inacid; Indocin; Indomed; Indomee; Indoptol

EINECS No. 200-186-5 **RTECS No.** NL 3500000

Uses Analgesic, antiflammatory and antihistaminic drug.

Physical properties

M. Pt. ~155 and ~162°C (polymorphic crystals)

Solubility Organic solvents: acetone, castor oil, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 13 mg kg^{-1} (1).
LD_{50} oral dog 160 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse 13, 15 mg kg^{-1}, respectively (3,4).
LD_{50} intravenous mouse, rat 30, 35 mg kg^{-1}, respectively (5,6).

Sub-acute and sub-chronic data

Oral marmoset (4 wk) 0.2, 6, 12 mg kg^{-1} day^{-1}, 100% mortality at highest dose. Intermediate dose induced severe gastro-intestinal toxicity, whereas low dose caused functional and morphological renal alterations (7).
Rats 3.55 mg kg^{-1} day^{-1} (route unspecified) for 3 months caused kidney damage (8).
Three repeat administrations of 0.02 mg kg^{-1} to rat (route unspecified) caused liver damage manifested by increased activities of aminotransferases and alkaline phosphatase activities, a decrease in glutathione levels and disturbance of liver functions (9).
Oral mice 5, 10, 20 mg l^{-1} in drinking water, hepatotoxicity was minimal at 5 mg l^{-1} but higher doses killed (10).

Teratogenicity and reproductive effects

Injection AKR mice on day 13.5 gestation, no teratogenic effect observed (11).
Implant ♂ rat 50% rod adjacent to each epididymis. 1-4 wk after implant fertility was reduced but returned to normal within 5-10 wk (12).
Oral rat maternal administration 1 and 2.5 mg kg^{-1} day^{-1} (days 18 and 21 gestation) caused dose-dependent retardation in structural development in mesenteric lymph nodes of foetuses (13).
Oral pregnant rat 0.7 mg kg^{-1} caused constriction of foetal rat ductus and cardiac failure. Effects were persistent (14).

Metabolism and toxicokinetics

Human single oral dose (concentration unspecified), peak concentrations in blood were observed 1.5-3.5 hr (15).
Dermal rat single application 2.5 mg, plasma concentration peaked at 8-9 hr, muscle concentration maximal levels after 8 hr. Dermal muscle/plasma concentration ratio was higher than when administered orally (16).
99% bound to plasma proteins, it is distributed to the synovial fluid, central nervous system, placenta and breast milk. Metabolised to its glucuronide conjugate and to desmethyl-desbenzoylindomethacin, desbenzoylindomethacin, desmethylindomethacin, and to their glucuronides. Some *N*-deacylation occurs. Undergoes enterohepatic circulation. Metabolites excreted chiefly in the urine (17,18).

Irritancy

100 mg placed into ♀ rabbit eye minimal irritation, recovery within 24 hr (19).

Sensitisation

Hypersensitivity reactions, including acute asthma, have occurred in patients with a history of asthma or aspirin sensitivity (20-22).

Genotoxicity

In vivo mice assays for bone marrow micronuclei, abnormal sperm formation, meiotic chromosome abnormalities in spermatocysts positive in concentration range 12-36 mg kg^{-1} (23).

Other effects

Other adverse effects (human)

Nephrotic syndrome, acute renal failure and renal papillary necrosis have been reported (24-26).
Gastro-intestinal lesions, bleeding, ulceration and perforation as well as nausea, vomiting and dyspepsia recorded (27).

Any other adverse effects

Potent prostaglandin synthesis inhibitor (28).
In vitro rat liver microsomes denatured cytochrome P_{450} to cytochrome P_{420}, independent of NADPH and enzymes. Activities of NADH-cytochrome b5 reductase, NADPH cytochrome *c* reductase and epoxide hydratase decreased (29).

Indomethacin is an inhibitor of the cyclooxygenase pathway for arachidonate metabolism in vertebrates (30).

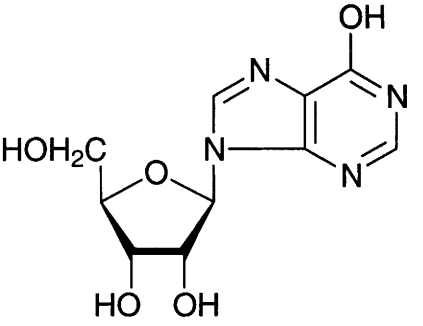
Other comments

Usually administered as the sodium salt (CAS RN 74252-25-8).
Potential use as antiovulatory drug (31).
Cyclo-oxygenase activity inhibitor, reported to be transient and not continuing beyond 20 hr (32,33).
Indomethacin (2.0 or 5.0 mM) totally inhibited the incorporation of ^{32}P into *Tetrahymena*. It influences the lipid cycle and therefore the inositol phosphate cycle in *Tetrahymena* (30).

References

1. *Arzneim.-Forsch.* 1980, **30**, 1398.
2. *Oyo Yakuri* 1968, **2**, 70.
3. Klaassen, C. D. *Toxicol. Appl. Pharmacol.* 1976, **38**, 127.
4. *Eur. J. Med. Chem.* 1989, **24**, 91.
5. *Arzneim.-Forsch.* 1969, **19**, 1198.
6. *Oyo Yakuri* 1973, **7**, 333.
7. Oberto, G. et al *Fundam. Appl. Toxicol.* 1990, **15**(4), 800-813.
8. Grom, V. V. et al *Eksp. Med. (Riga)* 1987, **24**, 67-71 (Russ.) (*Chem. Abstr.* **108**, 68518d).
9. Klimnyuk, E. V. *Farmakol. Toksikol. (Moscow)* 1989, **52**(2), 81-82 (Russ.) (*Chem. Abstr.* **110**, 165775j).
10. Sanjar, S. et al *Jpn. J. Pharmacol.* 1989, **51**(2), 151-160.
11. Montenegro, M. A. et al *J. Craniofacial Genet. Dev. Biol.* 1990, **10**(1), 83-94.
12. Ratnasooriya, W. D. et al *Int. J. Fertil.* 1987, **32**(2), 152-156.
13. Morozova, E. V. *Arkh. Anat., Gistol. Embriol.* 1989, **96**(3), 48-55 (Russ.) (*Chem. Abstr.* **110**, 225204j).
14. *Am. J. Obstet. Gynecol.* 1990, **162**(5), 1304-1310.
15. Wichlinski, L. M. et al *Acta Pol. Pharm.* 1986, **43**(4), 276-282.
16. Yonemitsu, M. et al *Yakuri to Chiryo* 1988, **16**(5), 2027-2032 (Japan.) (*Chem. Abstr.* **109**, 115961a).
17. Lebeders, T. H. et al *Br. J. Clin. Pharmacol.* 1991, **32**, 751-754.
18. Wiest, D. B. et al *Clin. Pharmacol. Ther.* 1991, **49**, 550-557.
19. Sugai, S. et al *J. Toxicol. Sci.* 1990, **15**(4), 245-262.
20. Timperman, J. A. *J. Forensic Med.* 1971, **18**, 30-32.
21. Sheehan, G. J. et al *Ann. Intern. Med.* 1989, **111**, 337-338.
22. Johnson, N. M. et al *Br. Med. J.* 1977, **2**, 1291.
23. Shobha, D. P. et al *Mutat. Res.* 1987, **188**(4), 343-347.
24. Chan, X. *Lancet* 1987, **ii**, 340.
25. Boiskin, I. et al *Ann. Intern. Med.* 1987, **106**, 776-777.
26. Mitchell, H. et al *Lancet* 1982, **ii**, 558-559.
27. Stewart, J. T. et al *Br. Med. J.* 1985, **290**, 787-788.
28. Nagasawa, H. et al *Breast Cancer Res. Treat.* 1986, **8**(3), 249-255.
29. Falzon, M. et al *Biochem. Pharmacol.* 1986, **35**(22), 4019-4024.
30. Kovacs, P. et al *Comp. Biochem. Physiol., C: Pharmacol. Toxicol. Endocrinol.* 1997, **117C**(3), 311-315.
31. Wu, S. et al *Zhongguo Yike Daxue Xuebao* 1989, **18**(Zengkau), 18-20 (Ch.) (*Chem. Abstr.* **113**, 126692x).
32. Raud, J. et al *Proc. Natl. Acad. Sci. U. S. A.* 1988, **85**(7), 2315-2319.
33. Patrick, J. et al *J. Dev. Physiol.* 1987, **9**(3), 295-300

I36 inosine



$C_{10}H_{12}N_4O_5$ **Mol. Wt.** 268.23 **CAS Registry No.** 58-63-9

Synonyms Atorel; hypoxanthine nucleoside; hypoxanthine riboside; hypoxanthosine; Ino; Inosie; Trophicardyl

EINECS No. 200-390-4 **RTECS No.** NM 7460000

Uses Biochemical research. Pharmaceutical preparations and veterinary drugs.
Occurrence Meat. Sugar beet.

Physical properties

M. Pt. 222-226°C (decomp.) **Partition coefficient** log P_{ow} –2.08 (1)
Solubility Water: 1.6 g 100 ml^{-1} at 20°C. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal rat, mouse 2900, 3175 mg kg^{-1}, respectively (2,3).
LD_{50} subcutaneous mouse 5000 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Carcinogenicity under investigation in oral rat 3.0, 30 mg $animal^{-1}$ day^{-1} and subcutaneous 5.0, 50 mg $animal^{-1}$ day^{-1} in long-term study (N. N. Petrov Research Institute of Oncology, Ministry of Public Health, St. Petersburg) (4).

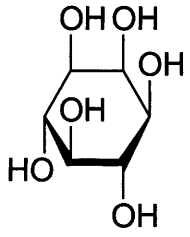
Other comments

Concentrations in primary and secondary domestic sewage plant effluent reported as 0.011-0.050 and 0.020 mg l^{-1}, respectively (5).

References

1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold, New York, NY, USA.
2. *Drugs in Japan. Ethical Drugs* 6th ed., 1982, Japan Pharmaceutical Information Centre, Yakugyo Jiho Co., Ltd., Tokyo, Japan.
3. *Pharm. Chem. J. (Engl. Transl.)* 1986, **20**, 160.
4. IARC *Directory of Agents being tested for Carcinogenicity* 1992, No.15, WHO/IARC, Lyon, France.
5. Wilson Pitt, W. et al *Environ. Sci. Technol.* 1975, **9**(12), 1068-1073

137 inositol



$C_6H_{12}O_6$ **Mol. Wt.** 180.16 **CAS Registry No.** 6917-35-7; 87-89-8 (*myo*-inositol)

Synonyms *myo*-inositol; *cis*-1,2,3,5-*trans*-4,6-cyclohexanehexol; dambose; inosital; meat sugar; mesoinosite

EINECS No. 230-024-9 **RTECS No.** NM 7520800

Occurrence Plants and animals. Growth factor for animals and microorganisms.

Physical properties

M. Pt. 225-227°C **Specific gravity** 1.752

Solubility Water: 14 g 100 ml^{-1} at 25°C. Organic solvents: ethanol (slightly)

Mammalian & avian toxicity

Metabolism and toxicokinetics

Initial take-up *in vitro* by 1210 mouse leukaemia cells is directly proportional to the extracellular concentration. Synthesised from glucose. Levels maintained by a combination of synthesis and uptake by either diffusion or a low-affinity carrier (1).

Accumulation *in vitro* by lens epithelial, kidney endothelial and Chinese hamster ovary cells was stimulated by hypertonic stresses. Reduction in cellular activity and proliferation caused by hypertonic stress was exacerbated by removal from the culture medium. It was suggested that accumulation of the compound has an important role in the acute response to osmotic stress (2).

Other comments

Mutation lessening properties (3).

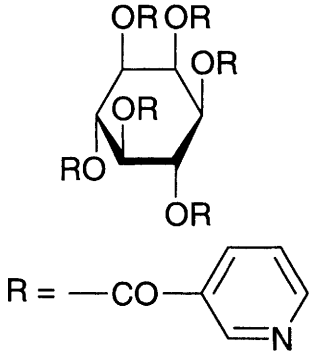
Metabolism reviewed (4-6).

Nine possible stereoisomers; the most common natural form is *cis*-1,2,3,5-*trans*-4,6-cyclohexanehexol.

References

1. Moyer, J. D. et al *Biochem. J.* 1988, **254**(1), 95-100.
2. Hohman, T. C. et al *Int. Congr. Ser. – Excerpta Med.* 1990, **913**, 31-41.
3. Pak, C. H. et al *Han'guk Wonye Hakhoechi* 1987, **28**(3), 277-281 (Korean) (*Chem. Abstr.* **110**, 72647d).
4. Downes, C. P. *FIDIA Res. Ser.* 1989, **20**, 1-14.
5. Lord, J. M. et al *Biochem. Soc. Trans.* 1991, **19**(2), 315-320.
6. Handler, J. S. et al *Colloq. INSERM* 1991, **208**, 473-481

138 inositol niacinate



$C_{42}H_{30}N_6O_{12}$ **Mol. Wt.** 810.73 **CAS Registry No.** 6556-11-2

Synonyms inositol nicotinate; *myo*-inositol hexa-3-pyridinecarboxylate; Dilcit; Esantene; Hexaniat; Linodil; Mesonex; Palohex

EINECS No. 229-485-9 **RTECS No.** NM 7535400

Uses Vasodilator.

Physical properties

M. Pt. 254.3-254.9°C

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat, mouse 268, 345 mg kg^{-1}, respectively (1).

LD_{50} intraperitoneal mouse 6400 mg kg^{-1} (2).

References

1. *Drugs in Japan. Ethical Drugs* 6th ed., 1982, Yakugyo Jiho Co., Ltd., Tokyo, Japan.
2. *Oyo Yakuri* 1973, 7, 149

139 interferon alfa

CAS Registry No. 76543-88-9

Synonyms interferon-α; interferon A; alpha-interferon; alfa-interferon; lymphoblastoid interferon; leukocyte interferon; IFN-α; LeIF; Alferon

Uses As an antiviral and antineoplastic.

Occurrence Produced by peripheral blood leukocytes or lymphoblastoid cells on exposure to live or inactivated virus, bacterial products or double-stranded RNA.

Mammalian & avian toxicity

Carcinogenicity and chronic effects

The National Toxicology Program tested mice via subcutaneous injection; technical report in progress (1).

Metabolism and toxicokinetics
Interferon A is not absorbed from the gastro-intestinal tract; more than 80% of subcutaneously or intramuscularly administered interferon A is absorbed. Peak plasma concentrations of an intramuscular dose are reached within 4 to 6 hr; the plasma half-life may be up to 16 hr. Distribution and elimination are more rapid after intravenous administration. Interferon A is not reported to cross the blood-brain barrier. Urinary excretion is negligible (2).

Other effects

Other adverse effects (human)
Interferon A may cause influenza-like symptoms with fever, chills, headache, malaise, myalgia, arthralgia, nausea, vomiting and diarrhoea. Anorexia, weight loss, alopecia and bone-marrow depression may occur. Altered liver function and liver necrosis have been reported, as have renal failure and nephrotic syndrome. Cardiovascular effects including myocardial infarction and strokes have been reported. At high doses, electrolyte disturbances may occur. Other adverse effects include EEG abnormalities and neurological symptoms, severe fatigue and mental depression, and visual disturbances (2).

Any other adverse effects
Interferon A specifically inhibits the secretion of cortisol from bovine fasciculata cells stimulated by ACTH (3).

References

1. *National Toxicology Program Research and Testing Division* April 1997, Report No. TR-469, NIEHS, Research Triangle Park, NC, USA.
2. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
3. Itoh, K. et al *Iwate Igaku Zasshi* 1997, **49**(3), 229-238

I40 iodine

I_2

I_2 **Mol. Wt.** 253.81 **CAS Registry No.** 7553-56-2

EINECS No. 231-442-4 **RTECS No.** NN 1575000

Uses Manufacture of iodine compounds. In germicides, antiseptics. Catalyst. Analytical chemistry reagent. Antihyperthyroid. In lubricants. In dyestuffs.
Occurrence Igneous rocks. Brine lakes, seawater and seaweed.

Physical properties

M. Pt. 113.60°C **B. Pt.** 185.24°C **Specific gravity** 4.93 (solid) at 20°C **Partition coefficient** log P_{ow} 2.49
Volatility v.p. 0.305 mmHg at 25°C
Solubility Water: 0.16 g l^{-1} at 25°C. Organic solvents: benzene, carbon disulfide, carbon tetrachloride, chloroform, cyclohexane, ethanol, glacial acetic acid

Occupational exposure

DE-MAK 0.1 ppm (1.1 mg m^{-3})
FR-VLE 0.1 ppm (1 mg m^{-3})
JP-OEL 0.1 ppm (1 mg m^{-3})
SE-CEIL 0.1 ppm (1 mg m^{-3})
UK-STEL 0.1 ppm (1.1 mg m^{-3})

US-STEL ceiling limit 0.1 ppm (1 mg m^{-3})
Supply classification harmful
Risk phrases Harmful by inhalation and in contact with skin (R20/21)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour – Avoid contact with the eyes (S2, S23, S25)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) channel catfish 0.44 mg l^{-1} (1).

Bioaccumulation
Soil microorganisms isolated from humus horizons of podzolic and sod-podzolic soils containing iodine at concentrations of 0.12-0.24 mg kg^{-1} dry matter could accumulate ≤315 mg iodine kg^{-1} dry matter and thus possessed an iodine concentration function. Soil bacterial and fungal biomass could bind ≤3.24% of total iodine of the 0-20 cm soil layer. Some strains of *Penicillium chrysogenum* were able to accumulate 4.1% in a medium containing 1%; accumulation at this concentration was higher than at its threshold concentration by 9600 times (2).
^{129}I accumulates within marine algae at 740 times greater than background levels (3).
The average atom ratio of $^{129}I/^{127}I$ in algal samples was 2.5×10^{-4}, compared with 2.2×10^{-12} in the ocean as the general background due to the natural production of ^{129}I. Found in byssal threads of *Mytilus coruscus* (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, rat, mouse 10, 14, 22 g kg^{-1}, respectively (5).
LD_{Lo} oral dog 800 mg kg^{-1} (6).
LC_{Lo} (1 hr) inhalation rat 800 mg m^{-3} (7).
LD_{Lo} intravenous dog 40 mg kg^{-1} (8).
LD_{Lo} subcutaneous rabbit 175 mg kg^{-1} (8).

Teratogenicity and reproductive effects
C57 ♀ mice injected with 20 µl iodised oil were mated 8 days later. Urine content 24 hr^{-1} was 20 times higher than control and 18 times higher 2 months later. Serum T4 values in the progeny were not affected, however T4 levels were depressed. There was no difference between treated animal and control progeny in brain protein, body weight, motility, DNA and learning ability (9).

Metabolism and toxicokinetics
Slight dermal absorption. When ingested converted into iodide and trapped by the thyroid gland. Iodides not trapped are excreted mainly in the urine, with lesser quantities released in the faeces, sweat and saliva. Iodides cross the placenta and also appear in milk (10).

Irritancy
0.1-1.6 ppm reported to cause irritation to eyes with excessive flow of tears, chest tightness, sore throat and headache (11).

Sensitisation
Occupationally exposed workers exhibit allergic dermatoses (12).
With a modified Beuhler's technique weak sensitiser (1/10 guinea pigs) (13).

Genotoxicity

Escherichia coli PQ37 ($uvrB^{-1}$) SOS chromotest without metabolic activation negative (14).

Other effects

Other adverse effects (human)
Workers exposed to vapour had increased frequency of gingivitis, glossitis and stomatitis (15).

Can cause goitre, hypothyroidism and hyperthyroidism. At doses >2 mg day^{-1} thyroid hormone production falls and may produce chronic inhibition of hormone synthesis (16-19).
Acute poisoning by ingestion may lead to death due to circulatory failure, oedema of the glottis resulting in asphyxia, pulmonary oedema or aspiration pneumonia (10).
Several hundred women living downward of a nuclear installation at Handford, Washington, USA were surveyed about their health history by questionnaire. Spontaneous abortions occurred more than twice as frequently in those who had been diagnosed as having hypothyroidism compared with those who had not. Approximately half of the women who responded to the survey had hypothyroidism. The elevated levels of spontaneous abortions were attributed to environmental contamination caused by releases of radioactive iodine (^{131}I) from the nuclear facility (20).

Legislation

Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (21).

Other comments

Accumulation in freshwater invertebrates compared with the soil and water from ecosystems of the forest-steppe zone and tundra studied. Concentrations were the same in different species. Distribution was habitat dependent (22).
Case studies of occupational exposure to vapour causing saturation are reported. Risk of dysthyroidism is discussed and preventive measures suggested (23).
Reviews on experimental toxicology, epidemiology, human health effects, physico-chemical properties and workplace experience listed (24).
Disease, environmental distribution, autoimmune thyroiditis, immunity, risks to infants from milk of iodine-exposed mothers, role in thyroid function and cretinism, toxicological and physiological effects and prophylaxis reviewed (25-33).
Teratogenicity resulting from iodine deficiency reviewed (34).

References

1. Le Valley, M. J. *Bull. Environ. Contam. Toxicol.* 1982, **29**, 7.
2. Letunova, S. V. et al *Mengen – Spurenelem., Arbeitstag.* 1987, **1**, 11-26 (Russ.) (*Chem. Abstr.* **109**, 145929p).
3. Doshi, G. R. et al *Indian J. Mar. Sci.* 1989, **18**(2), 87-90.
4. Ikuta, K. *Kenkyu Hokoku – Miyazaki Daigaku Nogakubu* 1986, **33**(2), 255-264.
5. *Drugs of the Future* 1979, **4**, 876, J. R. Prous SA, International Publishers, Barcelona, Spain.
6. *Abdernalden's Handbuch der Biologischen Arbeitsmethoden* 1935, **4**, 1289.
7. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure* 1982, Centre of International Projects, GKNT, Moscow, USSR.
8. *Handbook of Toxicology* 1959, 5, W. B. Saunders, Philadelphia, PA, USA.
9. Liu, X. L. et al *J. Endocrinol. Invest.* 1988, **11**(6), 399-401.
10. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
11. Health and Safety Executive *Occupational Exposure Limits: Criteria Document Summaries* 1993, HMSO, London, UK.
12. Budina, L. V. et al *Gig. Tr. Prof. Zabol.* 1991, (10), 32-34 (Russ.) (*Chem. Abstr.* **115**, 262347g).
13. Goh, C. L. *Contact Dermatitis* 1989, **21**(3), 166-171.
14. Olivier, P. et al *Mutat. Res.* 1987, **189**(3), 263-269.
15. Polyak, A. L. *Gig. Tr. Prof. Zabol.* 1988, (7), 26-28 (Russ.) (*Chem. Abstr.* **109**, 134321h).
16. Li, M. et al *Lancet* 1987, **ii**, 257-259.
17. Murray, I. P. C. et al *Lancet* 1967, **i**, 922-926.
18. Gomolin, I. H. *Drug Intell. Clin. Pharm.* 1987, **21**, 726-727.
19. Smerdely, P. et al *Lancet* 1989, **ii**, 661-664.
20. Grossman, C. M. et al *Arch. Environ. Health* 1996, **51**(3), 175-176.
21. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
22. Zhulidov, A. V. et al *Gidrobiol. Zh.* 1989, **25**(4), 70-75 (Russ.) (*Chem. Abstr.* **111**, 191775z).
23. Proust, B. et al *Arch. Mal. Prof. Med. Trav. Secur. Soc.* 1987, **48**(3), 207-211 (Fr.) (*Chem. Abstr.* **107**, 120356v).

24. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
25. Tan, J. et al *J. Environ. Sci. (China)* 1989, **1**(1), 107-114.
26. Muramatsu, Y. et al *Hoshasen Kagaku (Tokyo)* 1988, **31**(8), 199-203 (Japan.) (*Chem. Abstr.* **110**, 100752e).
27. Sundick, R. S. *Immunol. Ser.* 1990, **52**, 213-228.
28. Ye, J. *Zhongguo Mianyixue Zazhi* 1987, **3**(5), 312-314 (Ch.) (*Chem. Abstr.* **108**, 148355p).
29. Ythier, H. et al *Med. Infant.* 1987, **94**(1), 55-58 (Fr.) (*Chem. Abstr.* **107**, 32420f).
30. Wang, X. *Xibei Shifan Xueyuan Xuebao, Ziran Kexueban* 1987, (1), 80-85 (Ch.) (*Chem. Abstr.* **107**, 153217d).
31. Polyak, A. L. *Gig. Sanit.* 1988, (2), 67-70 (Russ.) (*Chem. Abstr.* **108**, 155577r).
32. Fuge, R. *Trace Subst. Environ. Health* 1987, **21**, 74-87.
33. Pennington, J. A. T. *NTIS Report* FDA/CFSAN-89/54 order No. PB89-183016, Natl. Tech. Inf. Ser., Springfield, VA, USA.
34. Hollowell, J.G., Jr. et al *Teratology* 1997, **55**(6), 389-405

I41 iodine monochloride

ICl

ClI **Mol. Wt.** 162.36 **CAS Registry No.** 7790-99-0

Synonyms iodine chloride; chlorine iodide; chlorine monoiodide; iodochlorine; Wijs' chloride

EINECS No. 232-236-7 **RTECS No.** NN 1650000

Uses In Wijs' solutions used to determine iodine values of fats and oils. Topical anti-infective.

Physical properties

M. Pt. 27.2°C (α-form), 13.9°C (β-form) **B. Pt.** 97°C (decomp.) **Specific gravity** 3.10 at 29°C with respect to water at 4°C

Solubility Organic solvents: acetic acid, carbon disulfide, diethyl ether, ethanol

Occupational exposure

UN No. 1792 **HAZCHEM Code** 2WE **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 50 mg kg^{-1} (1).

LD_{Lo} dermal rat 500 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides: guide level 25 mg l^{-1} (2). Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *Kodak Company Report* 21 May 1971, Rochester, New York, NY, USA.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

I42 iodoacetic acid

ICH_2CO_2H

$C_2H_3IO_2$ **Mol. Wt.** 185.95 **CAS Registry No.** 64-69-7

Synonyms MIA; monoiodoacetic acid

EINECS No. 200-590-1 **RTECS No.** AI 3500000

Physical properties

M. Pt. 82-83°C

Solubility Organic solvents: ethanol

Occupational exposure

Supply classification toxic, corrosive

Risk phrases Toxic if swallowed – Causes severe burns (R25, R35)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S36/37/39, S45)

Environmental fate

Degradation studies

A stable methanogenic mixed culture was enriched from an industrial environment to utilise iodoacetic acid as the sole carbon and energy source for growth. Dehalogenation was identified as metabolic route and methane, CO_2 and iodide ions as products of metabolism (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 83 mg kg^{-1} (2).

LD_{Lo} (30 min) inhalation rat 94 g m^{-3} (3).

LD_{50} subcutaneous rat, rabbit 60 mg kg^{-1} (4,5).

LD_{50} intravenous dog 45 mg kg^{-1} (6).

Other effects

Any other adverse effects

Hepatocytes isolated from 2-wk-old and adult mice (8-10 wk) were exposed for incubation times up to 24 hr; positive hepatotoxicity was indicated (7).

Intravenous administration destroyed visual cells in the retina of rabbits and caused an initial increase, then decrease of total glucose-6-phosphatase activity in retinal homogenate. Total glucose-6-phosphatase activity in the retinal microsomal fraction was decreased after 5 days (8).

Legislation

Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

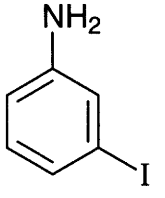
Other comments

Reviews on experimental toxicology, human health effects and physico-chemical properties listed (10).

References

1. Egli, C. et al *Arch. Microbiol.* 1989, **152**(3), 218-223.
2. *J. Pharmacol. Exp. Ther.* 1946, **86**, 336.
3. *Russ. Pharmacol. Toxicol. (Engl. Transl.)* 1978, **41**, 113.
4. *Toxicol. Appl. Pharmacol.* 1973, **26**, 93.
5. *J. Physiol. (London)* 1934, **80**, 360.
6. *J. Natl. Cancer Inst.* 1963, **31**, 297.
7. Adamson, G. M. et al *Biochem. Pharmacol.* 1988, **37**(21), 4183-4190.
8. Durlu, Y. K. et al *Prog. Clin. Biol. Res.* 1989, **314**, 585-600.
9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
10. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

143 3-iodoaniline



C_6H_6IN **Mol. Wt.** 219.02 **CAS Registry No.** 626-01-7

Synonyms *m*-aminoiodobenzene; 3-aminoiodobenzene; *m*-iodoaniline; 3-iodobenzamine

EINECS No. 210-922-7 **RTECS No.** BY 3750000

Physical properties

M. Pt. 25°C **B. Pt.** 145-146°C at 15 mmHg **Flash point** >110°C **Specific gravity** 1.821

Solubility Organic solvents: chloroform, ethanol

Occupational exposure

UN No. 2810

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 100 mg kg^{-1} (1).

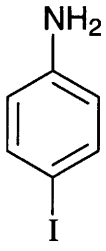
Other comments

Evaluated in 48 hr *Tetrahymena pyriformis* population growth impairment system (2).

References

1. US Army Armament Research and Development Command *Report NX #06766* Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA.
2. Schultz, T. W. et al *Sci. Total. Environ.* 1991, **109-110**, 569-580

144 4-iodoaniline



C_6H_6IN **Mol. Wt.** 219.02 **CAS Registry No.** 540-37-4

Synonyms *p*-iodoaniline; *p*-iodoaminobenzene; 4-aminoiodobenzene; 4-iodobenzamine

EINECS No. 208-743-4 **RTECS No.** BY 3850000

Physical properties

M. Pt. 67-68°C

Solubility Organic solvents: chloroform, ethanol, petroleum ether

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, rat 100, 523 kg^{-1}, respectively (1,2).

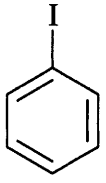
Other comments

Evaluated in 48 hr *Tetrahymena pyriformis* population growth impairment system (3).

References

1. *Toxicol. Appl. Pharmacol.* 1972, **21**, 315.
2. *Cesk. Hyg.* 1978, **23**, 168.
3. Schultz, T. W. et al *Sci. Total Environ.* 1991, **109-110**, 569-580

145 iodobenzene



C_6H_5I **Mol. Wt.** 204.01 **CAS Registry No.** 591-50-4

Synonyms benzene iodide; phenyl iodide

EINECS No. 209-719-6 **RTECS No.** DA 3390000

Physical properties

M. Pt. –30°C **B. Pt.** 188-189°C **Flash point** 74°C **Specific gravity** 1.838 at 15°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.25
Solubility Organic solvents: miscible with chloroform, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 3.23 ppm Microtox test (1).

Other effects

Any other adverse effects
~50% of cultured ♂ Sprague-Dawley rat hepatocytes were killed on addition of 40 g l^{-1} iodobenzene in dimethyl sulfoxide (2).

Legislation

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3). Log P_{ow} exceeds European Union recommended limit of 3.0 (4).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Coleman, J. B. et al *Toxicol. Appl. Pharmacol.* 1990, **105**, 393-402.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK

146 1-iodobutane

$$CH_3CH_2CH_2CH_2I$$

C_4H_9I **Mol. Wt.** 184.02 **CAS Registry No.** 542-69-8
Synonyms *n*-butyliodide; butyl iodide
EINECS No. 208-824-4 **RTECS No.** EK 4400000

Physical properties

M. Pt. –103.0°C **B. Pt.** 130.4°C **Flash point** 36°C **Specific gravity** 1.616 at 20°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) inhalation rat 6100 mg m^{-3} (1).
LD_{50} intraperitoneal mouse, rat 101, 692 mg kg^{-1}, respectively (2).

Carcinogenicity and chronic effects
A slight but significant increase in lung tumours was seen in Strain A mice injected with a total dose of 2.42 g kg^{-1} (3).

Legislation

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

1. Diechmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
2. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
3. Poirier, L. A. et al *Cancer Res.* 1975, **35**, 1411-1415.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991 HMSO, London, UK

147 2-iodobutane

$$CH_3CH_2CHICH_3$$

C_4H_9I **Mol. Wt.** 184.02 **CAS Registry No.** 513-48-4

Synonyms *sec*-butyl iodide; 2-butyl iodide; *sec*-iodobutane

EINECS No. 208-163-1 **RTECS No.** EK 4410000

Physical properties

M. Pt. –104°C **B. Pt.** 120°C **Flash point** 23°C (99% purity) **Specific gravity** 1.592 at 20°C with respect to water at 4°C

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2390 **HAZCHEM Code** 2[illegible]E **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity

EC_{50} (4 hr) *Daphnia pulex* 10.93 mg l^{-1} (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

A slight but significant increase in the number of lung tumours was seen in ♂, ♀ mice injected with a total of 5.99 g kg^{-1} (2).

Genotoxicity

Escherichia coli P3478E without metabolic activation positive (3).

Legislation

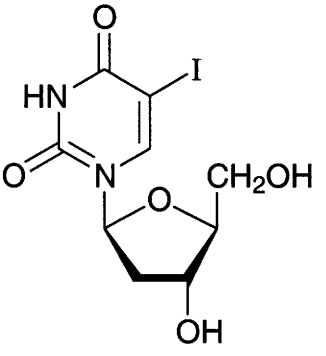
Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

1. Smith, S. B. et al *J. Great Lakes Res.* 1988, **14**(4), 394-404.

2. Poirier, L. A. et al *Cancer Res.* 1975, **35**, 1411-1415.
3. Fluck, E. R. et al *Chem.-Biol. Interact.* 1976, **15**, 219-231.
4. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

148 5-iodo-2′-deoxyuridine



$C_9H_{11}IN_2O_5$ **Mol. Wt.** 354.10 **CAS Registry No.** 54-42-2

Synonyms 2′-deoxy-5-iodouridine; 1-(2-deoxy-β-D-ribofuranosyl)-5-iodouracil; Dendrid; Herplex; Iduridin; Ophthalmadine; Virexen

EINECS No. 200-207-8 **RTECS No.** YU 7700000

Uses Antiviral agent, used in treatment of Herpes simplex keratitis and cutaneous forms of Herpes simplex and zoster.

Physical properties

M. Pt. 194°C

Solubility Water: 2.0 mg ml^{-1} at 25°C. Organic solvents: acetone, chloroform, diethyl ether, 1,4-dioxane, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse, rat 1000, 4000 mg kg^{-1}, respectively (1,2).

Carcinogenicity and chronic effects

Squamous carcinoma observed in one patient associated with topical iododeoxyuridine treatment (3).

Teratogenicity and reproductive effects

Embryotoxic in chick embryotoxicity screening test at >0.3 μg $embryo^{-1}$. Administration on day-2 was followed by various forms of the caudal regression syndrome (4).

Metabolism and toxicokinetics

^{3}H-5-iodo-2′-deoxyuridine (IDU) was detected in rat epidermis but not in circulating blood 60 min after local application of a 40% w/v solution of ^{3}H-IDU in dimethyl sulfoxide (5).

Obeys Michaelis-Menten equation elimination kinetics (6).

Sensitisation

Guinea pig sensitisation studies by the Magnusson and Kligman method showed slight transient erythematous responses in some animals after the first and second challenges (5).

Genotoxicity

In vitro human lymphocyte cells (48 hr) 50 mg l^{-1} and *in vitro* human fibroblasts (72 hr) 50 mg l^{-1} increased frequency of sister chromatid exchanges (7).

Other effects

Other adverse effects (human)

Cytotoxic to cultured human conjunctival cells, thus in clinical ophthalmological applications, concentrations below 100 μg ml^{-1} are recommended (8).

Legislation

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

References

1. *J. Natl. Cancer. Inst.* 1979, **62**, 911.
2. *Adv. Teratol.* 1968, **3**, 181.
3. Koppang, H. S. et al *Br. J. Dermatol.* 1983, **108**, 501-503.
4. Jelinek, R. et al *Folia Morphol. (Prague)* 1987, **35**(4), 374-380.
5. Bravo, M. L. et al *Methods Find. Exp. Clin. Pharmacol.* 1988, **10**(11), 705-709.
6. Wagner, J. G. et al *Sel. Cancer Ther.* 1989, **5**(4), 193-203.
7. Cassiman, J. J. et al *Br. Med. J.* 1981, **283**, 817-818.
8. Ikoma, N. *Kanazawa Ika Daigaku Zasshi* 1990, **15**(2), 121-129, (Japan.) (*Chem. Abstr.* **113**, 224235v).
9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

149 iodoethane

$$CH_3CH_2I$$

C_2H_5I **Mol. Wt.** 155.97 **CAS Registry No.** 75-03-6

Synonyms ethyl iodide; hydriodic ether; monoiodoethane

EINECS No. 200-833-1 **RTECS No.** KI 4750000

Physical properties

M. Pt. –108°C **B. Pt.** 69-73°C **Flash point** >71°C **Specific gravity** 1.950 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} 2.00
Solubility Organic solvents: ethanol

Environmental fate

Degradation studies

Oxidised by *Nitrosomonas europaea* at a rate of 19 nmol min mg $protein^{-1}$. Major product detected was acetic acid (1).

Mammalian & avian toxicity

Acute data

LC_{50} (30 min) inhalation rat 65,000 mg m^{-3} (2).
LD_{50} subcutaneous mouse 1000 mg kg^{-1} (3).
LD_{50} intraperitoneal guinea pig, rat, mouse 322-560 mg kg^{-1} (4).

Genotoxicity

Escherichia coli WP2 uvrA without metabolic activation positive (5).

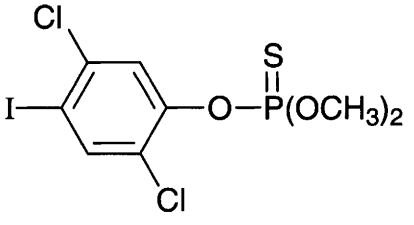
Legislation

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

References

1. Rasche, M. E. et al *J. Bacteriol.* 1990, **172**(9), 5368-5373.
2. *Fiz. Akt. Vesh.* 1975, **7**, 35.
3. *Japan. J. Pharmacol.* 1954, **3**, 99.
4. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
5. Hemminki, K. et al *Arch. Toxicol.* 1980, **46**, 277-285.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

150 iodofenphos



$C_8H_8Cl_2IO_3PS$ **Mol. Wt.** 413.00 **CAS Registry No.** 18181-70-9

Synonyms phosphorothioic acid, *O*-(2,5-dichloro-4-iodophenyl) *O,O*-dimethyl ester; Alfacron; Ciba 9491; iodophos; Monocron 9491; Nuvanol N; OMS 1211; jodfenphos

EINECS No. 242-069-1 **RTECS No.** TF 0175000

Uses Superseded insecticide/acaricide. Used to control flies and ticks on cattle.

Physical properties

M. Pt. 72-73°C

Solubility Water: <2 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, dichloromethane, isopropanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish 0.06-0.10, 0.42-0.75 mg l^{-1} (1).

Toxic to carp at ≥0.01 mg l^{-1}. Changes were observed in the numbers of blood corpuscles, cardiovascular activity and growth rate. Juveniles were more sensitive than adults (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, mouse, dog 2-3 g kg^{-1} (3,4).

LC_{50} (6 hr) inhalation rat >0.246 mg l^{-1} (1).

LD_{50} dermal rabbit, rat 500, 2150 mg kg^{-1}, respectively (4,5).

Sub-acute and sub-chronic data
In 90-day feeding trials, no-effect level for rats was 5 mg kg^{-1} diet and for dogs 15 mg kg^{-1} diet (1).

Metabolism and toxicokinetics
92% of an oral dose in rats was eliminated within 24 hr (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Non-toxic to birds. Toxic to bees (1).

References

1. *The Pesticide Manual* 9th ed., British Crop Protection Council, Farnham, UK.
2. Guseva, S. S. et al *Biol. Nauki (Moscow)* 1988, (1), 53-58 (Russ.) (*Chem. Abstr.* **108**, 145069n).
3. *Guide to the Chemicals Used In Crop Protection* 1968, **5**, 197, Information Canada, 171 Slater St., Ottawa, Ontario, Canada.
4. *Wirksubstanzen der Pflanzenschutz- und Schaedlingsbekaempfungsmittel* 1971-1976, Verlag Paul Parey, Berlin, Germany.
5. *Special Publication of the Entomological Society of America* 1974, **78-1**, 45, 4603 Calvert Rd., College Park, MD, USA.
6. Johanssen, F. R. et al *J. Econ. Entomol.* 1970, **63**, 693-697.
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

151 iodoform

$$CHI_3$$

CHI_3 **Mol. Wt.** 393.73 **CAS Registry No.** 75-47-8

Synonyms carbon triiodide; triiodomethane

EINECS No. 200-874-5 **RTECS No.** PB 7000000

Uses Topical anti-infective.

Physical properties

M. Pt. 120-123°C **Specific gravity** 4.008
Solubility Organic solvents: acetone, benzene, carbon disulfide, chloroform, diethyl ether, ethanol, glycerol, olive oil

Occupational exposure

FR-VME 0.6 ppm (10 mg m^{-3})
UK-LTEL 0.6 ppm (9.8 mg m^{-3}) **UK-STEL** 1.0 ppm (16 mg m^{-3})
US-TWA 0.6 ppm (10 mg m^{-3})

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) minnow 1.2 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (24 hr) *Daphnia* 0.1 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, mouse 355, 450, 810 mg kg^{-1}, respectively (2).

LC_{50} (7 hr) inhalation rat 165 ppm (3).

LD_{50} dermal rat 1184 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 630 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Judged non-carcinogenic in studies of ♂ and ♀ Fischer 344 or Osborne-Mendel rats and $B6C3F_1$ mice by the National Cancer Institute and National Toxicology Program (5).

Teratogenicity and reproductive effects

Minimum toxic concentration for rat spermatozoa exposed for 35 day was 2 mg kg^{-1} and for rat embryos was 25 mg kg^{-1}. No mutagenic or teratogenic effects were observed in rats (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with and without metabolic activation positive, TA1537 with metabolic activation negative (5).

Induced unscheduled DNA synthesis. Exposure of Syrian hamster embryo cells for 18-20 hr produced a significant level of sister chromatid exchanges (6).

Treatment of V-79 cells with iodoform caused reduced growth at 30 μg ml^{-1} for 24 or 48 hr, complete inhibition of growth at 100 μg ml^{-1} for 24 or 48 hr and no inhibitory effect on survival at 10-30 μg ml^{-1} for 2-24 hr (7).

Other effects

Any other adverse effects

Induced lipid peroxidation and inactivation of cytochrome P_{450} in rat liver microsomes at oxygen partial pressures of 0-1 mmHg (8).

0.39 g l^{-1} in dimethyl sulfoxide incubated with rat red blood cells for 2 hr did not significantly change the content of oxyhaemoglobin or methaemoglobin relative to untreated cells (9).

Morphological transformation was induced in Syrian hamster embryo cells by treatment with iodoform for 48 hr (6).

Legislation

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (11).

References

1. Khristov, K. T. *Gig. Sanit.* 1987, (11), 74-75 (Russ.) (*Chem. Abstr.* **108**, 50831r).
2. *Zdravookhr. Kaz.* 1983, **27**(5), 9.
3. *J. Toxicol. Environ. Health* 1981, **8**, 59.
4. *Toxicol. Appl. Pharmacol.* 1962, **4**, 354.
5. Zeiger, E. et al *Cancer Res.* 1987, **47**, 1287-1296.
6. Suzuki, H. *Shigaku* 1987, **74**(6), 1385-1403.
7. Bae, R. D. et al *Shigaku* 1987, **75**(5), 997-1004 (Japan.) (*Chem. Abstr.* **108** 126050h).
8. DeGroot, H. et al *Toxicol. Appl. Pharmacol.* 1989, **97**(3), 530-537.
9. Hidalgo, F. J. et al *Toxicol. Lett.* 1990, **52**, 191-199.

10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

152 iodomethane

CH_3I

CH_3I **Mol. Wt.** 141.94 **CAS Registry No.** 74-88-4

Synonyms methyl iodide

EINECS No. 200-819-5 **RTECS No.** PA 9450000

Uses In methylations. Used in microscopy because of its high refractive index. Used in testing for pyridine.
Occurrence Produced by various marine organisms.

Physical properties

M. Pt. –66.5°C **B. Pt.** 42.5°C **Specific gravity** 2.28 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.51 **Volatility** v.p. 400 mm Hg at 25.3°C ; v.den. 4.89
Solubility Water: 14 g l^{-1} at 20°C. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

FR-VME 2 ppm (12 mg m^{-3})
SE-LEVL 1 ppm (6 mg m^{-3}) **SE-STEL** 5 ppm (30 mg m^{-3})
UK-LTEL MEL 2 ppm (12 mg m^{-3})
US-TWA 2 ppm (12 mg m^{-3})

UN No. 2644 **HAZCHEM Code** 2XE **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Harmful in contact with skin – Toxic by inhalation and if swallowed – Irritating to respiratory system and skin – Possible risk of irreversible effects (R21, R23/25, R37/38, R40)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S38, S45)

Ecotoxicity

Bioaccumulation
Concentrated in *Modialus modiolus*: 10 ng g^{-1} in digestive tissue, 188 ng g^{-1} in mantle. In coalfish: 4 ng g^{-1} in muscle and 166 ng g^{-1} in brain. Enrichment was 2-25 times greater on dry weight basis compared with seawater concentrations (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 76 mg kg^{-1} (2).
LC_{50} (4 hr) inhalation rat 1300 mg kg^{-1} (3).
LD_{Lo} dermal rat 800 mg kg^{-1} (4).
LD_{50} subcutaneous mouse 110 mg kg^{-1} (5).
LD_{50} intraperitoneal guinea pig, rat, mouse 51-172 mg kg^{-1} (6).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (7).

Subcutaneous sarcomas were observed in 9/12 and 6/6 rats injected with 10 and 20 mg kg^{-1}, respectively, for 1 yr and in 4/14 in rats injected once with 50 mg kg^{-1}. Local fibrosarcomas and sarcomas were seen more than 1 yr after the first injection (8).

Lung tumours were reported in 6/29, 4/19, 6/20 and 5/11 A/He mice treated with 0, 8.5, 21.3 and 44.0 mg kg^{-1}, respectively (9).

Metabolism and toxicokinetics

Rats administered orally with 76 mg kg^{-1} exhaled 1% unchanged within 30 min (2).

Urinary metabolites in rats injected with 50 mg kg^{-1} originated from *S*-methyl glutathione and included *S*-methylcysteine, *N*-acetyl-*S*-methylcysteine, *S*-methyl thioacetic acid and *N*-(methythioacetyl)glycine (10).

Disappearance of methyl iodide in the presence of glutathione was catalysed by liver and kidney homogenates (11).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation weakly positive (12).

Salmonella typhimurium TA1535, TA1538 with and without metabolic activation positive and negative, respectively (13).

Escherichia coli pol A without metabolic activation positive (13).

In vitro mouse lymphoma L5178Y tk^+/tk^- positive (14).

Other effects

Other adverse effects (human)

A worker manufacturing methyl iodide exhibited severe neurological symptoms before death. Autopsy showed congested organs (15).

Workers poisoned non-fatally during the manufacture of methyl iodide suffered neurological disturbances such as vertigo, visual disturbances and weakness, followed by psychological disturbances and intellectual impairment (16).

Two workers at a plant producing methyl iodide were exposed to vapours at different times due to inadequate protective clothing. Both patients developed symptoms of cerebellar lesions and damage to the cranial nerve pathways, and showed late psychiatric disorders. Spinal cord lesions resulting in motor and sensory disturbances were present in one subject, who was repeatedly overdosed with methyl iodide (17).

Legislation

Regulated under the OSHA Air Contaminants Standard 1989 (18).

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (19).

Other comments

Induced chromatid aberrations in *Vicia faba* root-tip meristems (20).

Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology and workplace experience listed (21).

References

1. Dickson, A. G. et al *Mar. Pollut. Bull.* 1976, 7(9), Sept.
2. Johnson, M. K. *Biochem. J.* 1966, **98**, 38-43.
3. Diechmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
4. *Kodak Company Reports* No 21, May 1971.
5. *Toxicol. Appl. Pharmacol.* 1962, **4**, 354.
6. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.

7. *IARC Monograph* 1987, **Suppl. 7**, 66.
8. Druckrey, H. et al *Z. Krebsforsch.* 1970, **74**, 241-273 (Ger.).
9. Poirier et al *Cancer Res.* 1975, **35**, 1411-1415.
10. Barnsley, E. A. et al *Biochem. J.* 1965, **95**, 77-81.
11. Johnson, M. K. *Biochem. J.* 1966, **98**, 44-56.
12. McCann, J. et al *Proc. Natl. Acad. Sci. U. S. A.* 1975, **72**(12), 5135-5139.
13. Rozenkranz, H. S. et al *J. Natl. Cancer Inst.* 1979, **62**, 873-892.
14. Moore, M. M. et al *Mutat. Res.* 1985, **151**, 147-159.
15. Garland, A. et al *Br. J. Ind. Med.* 1945, **2**, 209-211.
16. Appel, G. B. et al *Ann. Intern. Med.* 1975, **82**, 534-536.
17. Hermonet, C. et al *Am. J. Ind. Med.* 1996, **30**(6), 759-764.
18. Paxman, D. G. et al *Regul. Toxicol. Pharmacol.* 1990, **12**, (3, Pt.1), 296.
19. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
20. Rieger, R. et al *Mutat. Res.* 1988, **208**(2), 101-104.
21. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

153 1-iodo-2-methylpropane

$$CH_3CH(CH_3)CH_2I$$

C_4H_9I **Mol. Wt.** 184.02 **CAS Registry No.** 513-38-2

Synonyms isobutyl iodide

EINECS No. 208-160-5 **RTECS No.** TZ 4250000

Physical properties

M. Pt. –93°C **B. Pt.** 120°C **Flash point** 12°C (97% purity) **Specific gravity** 1.605 at 20°C
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 2391 **HAZCHEM Code** 2[illegible]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) 6700 mg m^{-3} (1).
LD_{50} intraperitoneal mouse 549 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 1241 mg kg^{-1} (1).

Legislation

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. Diechmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, NY, USA.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

154 2-iodo-2-methylpropane

$(H_3C)_3CI$

C_4H_9I **Mol. Wt.** 184.02 **CAS Registry No.** 558-17-8

Synonyms propane,2-iodo-2-methyl-; *tert*-butyl iodide; trimethyliodomethane

EINECS No. 209-190-1 **RTECS No.** TZ 4251000

Physical properties

M. Pt. –38°C **B. Pt.** 99-100°C **Flash point** 7°C **Specific gravity** 1.544

Occupational exposure

UN No. 2391 **HAZCHEM Code** 2[illegible]E **Conveyance classification** flammable liquid

Genotoxicity

Escherichia coli P3478 without metabolic activation positive (1).

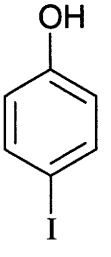
Legislation

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. Fluck, E. R. et al *Chem.-Biol. Interact.* 1976, **15**, 219-231.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

155 4-iodophenol



C_6H_5IO **Mol. Wt.** 220.01 **CAS Registry No.** 540-38-5

Synonyms *p*-iodophenol

EINECS No. 208-745-5 **RTECS No.** SL 5600000

Physical properties

M. Pt. 93-94°C **B. Pt.** 138°C at 5 mmHg **Specific gravity** 1.857 **Partition coefficient** log P_{ow} 2.91 (1)
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 700 mg kg^{-1} (2).

Carcinogenicity and chronic effects

The skin of 32 ♀ Sutter mice was treated with 25 µl of a solution of 0.3% 7, 12-dimethylbenz[*a*]anthracene in benzene followed by 1 drop of 25 µl of a solution of 20% 4-iodophenol in benzene 2 × wk^{-1} for 18 wk. Application to the back of the mouse resulted in papillomas in 35% of the 31 survivors (3).

Teratogenicity and reproductive effects

Chernoff/Kavlock assay performed on Sprague-Dawley rats exposed on day-11 of gestation to 0, 100, 333, 667, 1000 mg kg^{-1}. 333 mg kg^{-1} decreased maternal body weight by 1 g at 24 hr. Calculated concentrations which would decrease the total litter weight by 60% day-6 post natal was >5000 mg kg^{-1}. Categorised as inactive in developmental potency category (4).

Metabolism and toxicokinetics

4 µg cm^{-2} was applied to full-thickness hairless mouse skin. 46% was absorbed after 6 hr, 65% after 12 hr and 81% after 24 hr (5).

Other effects

Any other adverse effects

p-Halogenated phenols induced the release of K^+ from mitochondria decreasing the respiratory control index (6).

References

1. Leo, A. et al *Chem. Res.* 1971, **71**, 525-616.
2. *J. Pharm. Sci.* 1978, **67**, 1154.
3. Boutwell, R. K. et al *Cancer Res.* 1959, **19**, 413-424.
4. Kavlock, R. J. *Teratology* 1990, **41**, 43-59.
5. Hinz, R. S. et al *Fundam. Appl. Toxicol.* 1991, **17**, 575-583.
6. Izushi, F. et al *Acta. Med. Okayama* 1988, **42**(1), 7-14

156 6,3-ionene

$$[\text{-}(CH_3)_2N(CH_2)_3N(CH_3)_2(CH_2)_6\text{-}]_n\ ^{2+}\cdot 2Br^-$$

CAS Registry No. 28728-55-4

Synonyms poly[(dimethylimino)hexamethylene(dimethylimino)trimethylene]dibromide; hexadimethrine bromide; Polybrene; COP1

RTECS No. TQ 2655000

Uses Heparin antagonist.

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 30 mg kg^{-1} (1).

LD_{50} intravenous rat, mouse 20, 28 mg kg^{-1}, respectively (2).

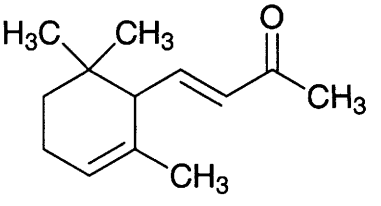
Legislation

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *Russ. Pharmacol. Toxicol. (Engl. Transl.)* 1974, **37**, 267.
2. *United States Patent Document* No.4013507, Commissioner of Patents and Trademarks, Washington, DC, USA.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

157 α-ionone



$C_{13}H_{20}O$ **Mol. Wt.** 192.30 **CAS Registry No.** 127-41-3

Synonyms 3-buten-2-one, 4-(2,6,6-trimethyl-2-cyclohexen-l-yl)-, (*E*)-; α-cyclocitrylideneacetone; (*E*)-α-ionone; *trans*-α-ionone

RTECS No. EN 0525000

Physical properties

B. Pt. 131°C at 13 mmHg **Flash point** >104°C **Specific gravity** 0.930

Environmental fate

Degradation studies

Converted by *Aspergillus niger* JTS191 into *cis*-3-hydroxy-α-ionone, *trans*-3-hydroxy-α-ionone, 3-oxo-α-ionone, 2,3-dehydro-α-ionone, 3,4-dehydro-β-ionone, and 1-(6,6-dimethyl-2-methylene-3-cyclohexenyl)-buten-3-one (1).

Mammalian & avian toxicity

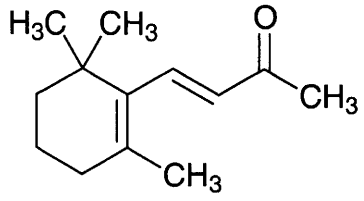
Acute data

LD_{50} oral rat 4590 mg kg^{-1} (2).

References

1. Yamazaki, Y. et al *Appl. Environ. Microbiol.* 1988, **54**(10), 2354-2360.
2. *Food Cosmet. Toxicol.* 1964, **2**, 327

158 β-ionone



$C_{13}H_{20}O$ **Mol. Wt.** 192.30 **CAS Registry No.** 79-77-6; 14901-07-6

Synonyms 4-(2,6,6-trimethyl-1-cyclohexenyl)-3-buten-2-one

EINECS No. 238-969-9 **RTECS No.** EN 0350000

Uses Key intermediate in the synthesis of vitamin A.

Physical properties

B. Pt. 126-128°C at 12 mmHg **Flash point** 110°C **Specific gravity** 0.945

Solubility Water: very slightly soluble. Organic solvents: benzene, chloroform, ether, 70% ethanol

Mammalian & avian toxicity

Acute data

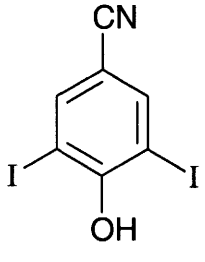
LD_{50} oral redwing blackbird 562 mg kg^{-1} (1).

LD_{50} oral rat 4590 mg kg^{-1} (2).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *Food Cosmet. Toxicol.* 1964, **2**, 327

159 ioxynil



$C_7H_3I_2NO$ **Mol. Wt.** 370.92 **CAS Registry No.** 1689-83-4

Synonyms 4-hydroxy-3,5-diiodobenzonitrile; 2,6-diiodo-4-cyanophenol; Actril; Bentrol; CA69-15; Certrol; Actrilawn; Caraz; Cipotril

EINECS No. 216-881-1 **RTECS No.** DI 4025000

Uses Herbicide.

Physical properties

M. Pt. 212-214°C **Volatility** v.p. $<7.52 \times 10^{-6}$ mmHg
Solubility Water: 50 mg l^{-1}. Organic solvents: acetone, carbon tetrachloride, chloroform, cyclohexanone, dimethylformamide, ethanol, methanol, tetrahydrofuran

Occupational exposure

Supply classification toxic
Risk phrases Harmful in contact with skin – Toxic if swallowed – Possible risk of harm to the unborn child (R21, R25, R63)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) harlequin fish 3.3 mg l^{-1} (ioxynil-sodium) (1).

Bioaccumulation
The sorption kinetics in the unicellular microalgae *Ankistrodesmus braunii* are independent of the herbicide concentration. Sorption is influenced by environmental factors including light, temperature, pH and oxygen concentration. Thus, the response of the target cells to environmental factors is at least as important for sorption in the cells and the prediction of accumulation can only be partially deduced from the properties of the pesticide molecule (2).

Environmental fate

Degradation studies
In soil $t_{1/2}$ ~10 days. Degraded to less toxic compounds such as hydroxybenzoic acid by deiodination and hydrolysis (3).

Abiotic removal
Decomposed by UV light (3).

Adsorption and retention
Highly mobile and resisted degradation in groundwater under treated ploughed land (4).

Mammalian & avian toxicity

Acute data
LD_{50} pheasant, chicken 75, 200 mg kg^{-1} (1).
LD_{50} oral cat, rabbit, rat, mouse, 75-230 mg kg^{-1} (3,5,6).
LD_{Lo} oral human 28 mg kg^{-1} (7).
LC_{50} (6 hr) inhalation rat >3 mg l^{-1} (3).
LD_{Lo} dermal rat 210 μg kg^{-1} (8).
LD_{50} intravenous mouse 56 mg kg^{-1} (9).

Sub-acute and sub-chronic data
In 90-day feeding trials, no-effect level for rats was 5.5 mg kg^{-1} day^{-1} (sodium salt) and 4 mg kg^{-1} day^{-1} (octanoate) (3).

Other effects

Any other adverse effects
In vitro ID_{50} (72 hr) 3T3-L1 cell culture 47±1 μg ml^{-1} FRAME kenacid blue assay (10).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (12).
WHO Toxicity Class II (13).
EPA Toxicity Class II (1).

Other comments

Reviews on experimental toxicology, human health effects, physico-chemical properties listed (14).
Metabolic pathways listed (15).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Neumann, W. et al *Pestic. Biochem. Physiol.* 1987, **27**(2), 189-200.
3. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
4. Vavra, J. *Agrochemia (Bratislava)* 1987, **27**(3), 82-84.
5. *World Rev. Pest Control* 1970, **9**, 119.
6. Klimmer, O. R. *Pflanzenschutz-und Schaedlingsbekaempfungsmittel: Abriss einer Toxikologie und Therape von Vergiftungen* 2nd ed., 1971, Hattingen, Germany (Ger.).
7. *Arch. Toxicol.* 1977, **37**, 241.
8. Information Canada *Guide to the Chemicals used in Crop Protection* 1973, **6**, 304.
9. *US Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals*, Report No.02818, Aberdeen Proving Ground, MD, USA.
10. Riddell, R. J. et al *ATLA, Altern. Lab. Anim.* 1986, **14**(2), 86-92.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
13. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
14. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
15. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

I60 ipecacuanha

CAS Registry No. 8012-96-2

Synonyms *Cartagena ipecacuanha*; *Cephaelis ipecacuanha*; ipecac, *C. ipecacuanha*; *Uragoga ipecacuanha*; ipecac syrup

EINECS No. 232-385-8 **RTECS No.** NO 1700000

Uses Emetic. Used as expectorant. Ruminatoric aid and antihistomonad for veterinary purposes.
Occurrence Dried rhizome and roots of Rio or Brazilian ipecac. Contains emetine, cephaeline, emetamine, ipecacuanic acid, protoemetrine psychotrine, methyl psychotrine and resin (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 7800 mg kg^{-1} (2).
LD_{Lo} oral human 70 mg kg^{-1} (3).
LD_{Lo} oral dog 5000 mg kg^{-1} (2).

Sensitisation
Packers of ipecacuanha tablets suffered allergic reactions, characterised by rhinitis, conjunctivitis and chest tightness due to inhalation (4).

Other effects

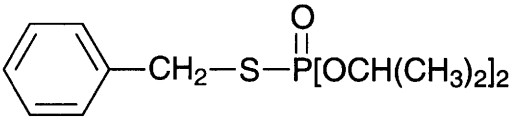
Other adverse effects (human)
A 26-yr-old woman experienced tachycardia, hypotension, dyspnoea and finally death after drinking 3-4 bottles of ipecac syrup a day for 3 months to induce vomiting in order to lose weight (5).
Humans dosed orally with 7.5 ml (syrup) experienced severe nausea, vomiting and headache (3).

Any other adverse effects
0.5 ml kg^{-1} was effective but not drastically toxic to dogs (3).

References

1. Lewis, R. J. Sax's *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
2. Rumaćk, B. H. et al (Ed.) *Management of the Poisoned Patient* 1977, Science Press, Princetown, NJ, USA.
3. Goldenberg, M. M. et al *J. Pharm. Sci.* 1976, **65**, 1398-1400.
4. Luczynska, C. M. et al *Clin. Allergy* 1984, **14**, 169-175.
5. Adler, A. G. et al *JAMA, J. Am. Med. Soc.* 1980, **243**, 1927-1928

I61 iprobenfos



$C_{13}H_{21}O_3PS$ **Mol. Wt.** 288.35 **CAS Registry No.** 26087-47-8

Synonyms phosphorothioic acid, *O,O*-bis(1-methylethyl) *S*-(phenylmethyl) ester; phosphorothioic acid, *S*-benzyl *O,O*-diisopropyl ester; IBP; Kitazin L; Ricid II

EINECS No. 247-449-0 **RTECS No.** TE 6550000

Uses Systemic fungicide used to control leaf and ear blast, stem rot and sheath blight.

Physical properties

B. Pt. 126°C at 0.04 mmHg **Specific gravity** 1.103 at 20°C **Partition coefficient** log P_{ow} 3.21 (1)
Solubility Water: 430 mg l^{-1} at 20°C. Organic solvents: acetone, acetonitrile, methanol, xylene

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) carp 3.7 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} oral 2nd day of 5th instar of silkworm larvae ~6.5 μg g^{-1} (3).
LC_{50} 3rd instar silkworm larvae 1.742 ppm in feed (3).

Bioaccumulation

Average bioconcentration factor in whole body of willow shiner was 33.2. The excretion rate constant was 0.0017 g ng^{-1} hr^{-1} assuming 2nd-order kinetics (4).
Average bioconcentration factors in carp were 4.3-26.7 in various organs. The excretion rate constants were between 0.002-0.024 (all g ng^{-1} hr^{-1}) for muscle, 0.001-0.020 for liver, 0.0004-0.004 for kidney and 0.002-0.023 for gallbladder (5).

Environmental fate

Degradation studies

Degradation in soil was affected by soil temperature, flooding, addition of rice straw and treatment with mixed fertiliser. No degradation was observed in sterile soil, indicating degradation was due to microorganisms (6).

Abiotic removal

A 5000 mg l^{-1} solution of NaOCl was added to 10 mg l^{-1} of iprobenfos in water to give a Cl^{-1} concentration of 50 mg l^{-1}. Iprobenfos was degraded to various products (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 490 mg kg^{-1} (8).
LD_{50} oral mouse 1760 mg kg^{-1} (8).
LC_{50} (4 hr) inhalation ♀, ♂ rat 0.34, 1.12 mg l^{-1}, respectively (1).
LD_{50} dermal mouse 5000 mg kg^{-1} (8).
Oral intoxication in guinea pigs, mice and rats (dose, duration unspecified) affected the liver by inhibiting blood cholinesterase, causing changes to amino transferase and alkaline phosphatase activities, the weakening of antitoxic function of the liver and increasing vital staining of the hepatic parenchyma (9).

Carcinogenicity and chronic effects

In 2-yr feeding trials, no-effect level for ♂ rats 0.036, ♀ rats 0.45 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics

Detected in heart, liver, spleen, lungs, kidney, fatty tissue and stomach wall of rats administered 53 mg kg^{-1} orally after 3 hr. After 1-2 days the heart, kidneys, stomach wall and fat contained 0.47, 0.38, 0.225 and 2.7 mg kg^{-1}, respectively. $t_{1/2}$ in the body was 2 days (10).

Sensitisation

No sensitisation observed in guinea pigs treated orally, but shock was observed after an intracardiac injection of $1:1 \times 10^{-5}$ dilution (11).

Legislation

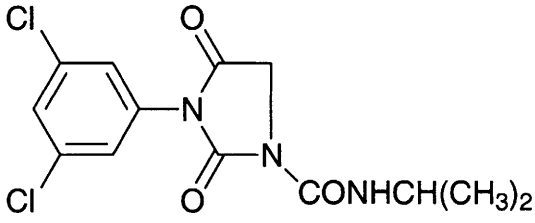
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (12).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).
Log P_{ow} exceeds the European Union recommended limit of 3.0 (14).
WHO Toxicity Class III (15).
EPA Toxicity Class II (formulation) (16).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Hashimoto, E. et al *J. Pestic. Sci.* 1982, **7**, 457.
3. Kuribayashi, S. *JARQ* 1988, **21**(4), 274-283.

4. Tsuda, T. et al *Toxicol. Environ. Chem.* 1989, **24**(3), 185-190.
5. Tsuda, T. et al *Comp. Biochem. Physiol., C: Comp. Pharmacol. Toxicol.* 1990, **96C**, (1), 23-26.
6. Moon, Y. H. *Han'guk Nonghwa Hakhoechi* 1990, **33**(2), 133-137 (Korean) (*Chem. Abstr.* **114**, 160461b).
7. Imanishi, K. et al *Nara-ken Eisei Kenkyusho Nenpo* 1989 (Publ. 1990), (24), 52-55 (Japan.) (*Chem. Abstr.* **114**, 234671u).
8. *Farm Chemicals Handbook* 1991, Meister Publ. Co., Willoughby, OH, USA.
9. Chura, D. A. *Hyg. Sanit.* 1988, (3), 70 (Russ.) (*Chem. Abstr.* **108**, 199834b).
10. Chura, D. A. et al *Gig. Tr. Prof. Zabol.* 1986, (11), 53-54 (Russ.) (*Chem. Abstr.* **106**, 28684g).
11. Petrus, V. S. et al *Gig. Tr. Prof. Zabol.* 1987, (4), 38-39 (Russ.) (*Chem. Abstr.* **107**, 34499n).
12. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
13. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
14. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
15. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
16. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

I62 iprodione



$C_{13}H_{13}Cl_2N_3O_3$ **Mol. Wt.** 330.17 **CAS Registry No.** 36734-19-7

Synonyms 3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imadazolidinecarboxamide; Borial; Escal; Iprodial; Kidan; Rovral; Verisan

EINECS No. 253-178-9 **RTECS No.** NI 8870000

Uses Fungicide used on pome and stone fruit, vegetables, ornamentals, cereals, potatoes, cotton, sunflowers, etc. Can be used as a post-harvest dip or seed treatment.

Physical properties

M. Pt. ~134°C **Specific gravity** 1.00 at 20°C **Partition coefficient** log P_{ow} 2.99 (pH 3); 3.00 (pH 5)
Solubility Water: 13 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, ethanol, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout 3.7, 4.1 mg l^{-1}, respectively (1).

Invertebrate toxicity
9.9 mg l^{-1} inhibited respiration in *Saccharomyces cerevisiae* by 9.6% with a glucose substrate and 8.3% with an ethanol substrate (2).
LD_{50} contact, >0.4 mg bee^{-1} (3).

Environmental fate

Degradation studies

25% was recovered in a plot 4 wk after treatment, with one application of 5 kg active ingredient ha^{-1}, but none was recovered in plots treated with two and three applications of 5 kg active ingredient ha^{-1} 16 and 10 days after treatment, respectively, implying rapid breakdown after repeated application (4).
Degradation occurred faster at pH 6.5 than pH 5.7 and little occurred at pH 4.3 (5).
Rapidly metabolised in soil, forming carbon dioxide. $t_{1/2}$ 20-160 days (1).
Iprodione added to vineyard soil underwent 90% degradation in 35 days (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 4000, 4400 mg kg^{-1}, respectively (7).
LC_{50} (4 hr) inhalation rat >3.3 mg l^{-1} (3).
LD_{50} dermal rabbit, rat >1000, 2500 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects

In 18-month feeding trials, rats receiving 1000 mg kg^{-1} diet and dogs receiving 2400 mg kg^{-1} day^{-1} showed no ill-effects (1).

Teratogenicity and reproductive effects

The lowest-observable-effect levels for ovarian effects (ovarian stromal cell tumours, sex cord tumours, luteomas) in lifetime studies on mice administered iprodione was 600 kg^{-1} day^{-1} (8).

Other effects

Any other adverse effects

♂ rats injected intraperitoneally with 0.13 or 0.33 g kg^{-1} resulted in only minor or no alterations in the renal function parameters measured and renal morphology (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
WHO Toxicity Class Table 5 (12).
EPA Toxicity Class IV (formulation) (3).
ADI 0.06 mg kg^{-1} (3).

Other comments

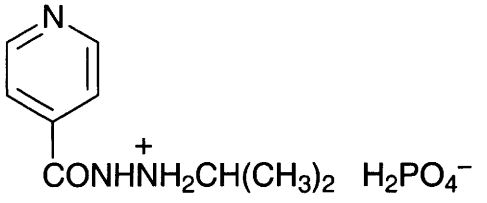
Attributed endocrine disruption effects in wildlife. Altered bird behaviour, reduced egg production, reduced hatchling weight; mysid reproduction impaired (13).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Chiba, M. et al *Can. J. Microbiol.* 1987, **33**(2), 157-161.
3. *The Pesticide Manual* 11th ed., 1997, British Crop Protection Council, Farnham, UK.
4. Duah-Yentumi, S. et al *Soil Biol. Biochem.* 1986, **18**(6), 629-635.
5. Walker, A. *Pestic Sci.* 1987, **21**(3), 219-231.
6. Garcia-Cazorla, J. et al *J. Agric. Food Chem.* 1998, **46**(7), 2845-2850.
7. *The Farm Chemicals Handbook* 1991, Meister Publ. Co., Willoughby, OH, USA.
8. *US Environmental Protection Agency, Office of Pesticide Programs* OPP database files MRID#42825002 and 42637801, HED Doc#010570.
9. Rankin, G. O. et al *Toxicology* 1989, **56**(3), 263-272.

10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
13. *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* 1997, EPA/630/R-96/012, Risk Assessment Forum, US Environmental Agency, Washington, DC 20460, USA

I63 iproniazid phosphate



$C_9H_{16}N_3O_5P$ **Mol. Wt.** 277.22 **CAS Registry No.** 305-33-9

Synonyms 4-pyridinecarboxylic acid, 2-(1-methylethyl)hydrazide, phosphate; isonicotinic acid, 2-isopropylhydrazide, phosphate; iproniazid dihydrogen phosphate; Marailid phosphate

EINECS No. 206-164-1 **RTECS No.** NS 1950000

Uses Antidepressant.

Physical properties

M. Pt. 180-182°C

Mammalian & avian toxicity

Acute data

LD_{50} dermal guinea pig 730 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 442 mg kg^{-1} (2).

Teratogenicity and reproductive effects

♀ Wistar rats single injection of 30 mg kg^{-1} on day 15 of pregnancy or sub-chronically with 10 mg kg^{-1} day^{-1} from day-10 to delivery. No change in neonatal reflexes of pups was observed after acute treatment, but increased numbers of pups showed active avoidance responses including cliff aversion, righting, barholding but not forelimb placing or grasping. Sexual activity was unimpaired (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (4).
In vivo mouse bone marrow cells significant increase in sister chromatid exchange frequency (4).
Escherichia coli WP2, WP2 *uvrA*, WP67, CM871, TM1080 without metabolic activation negative (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. *Arch. Int. Pharmacodyn. Ther.* 1962, **137**, 375.

2. *Acta Biol. Med. Germanica* 1967, **18**, 617.
3. Drago, F. et al *Neurobehav. Toxicol. Teratol.* 1985, **7**, 493-497.
4. Brambilla, G. et al *J. Toxicol. Environ. Health* 1982, **9**, 287-303.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

164 iridium

Ir

Ir **Mol. Wt.** 192.22 **CAS Registry No.** 7439-88-5

Synonyms Iridium Black

EINECS No. 231-095-9

Occurrence Occurs in earth's crust at 0.001 ppm. Found in nature combined with osmium, platinum or gold ores.

Physical properties

M. Pt. 2450°C **B. Pt.** 4500°C **Specific gravity** 22.65 at 20°C with respect to water at 4°C

Ecotoxicity

Invertebrate toxicity

1.0-3.0 ppm iridium salts added to *Tetrahymena pyriformis* in peptone-glucose culture medium stimulated cell proliferation but was inhibitory at >20 ppm (1).

Bioaccumulation

2.1 μg g^{-1} dry weight detected in gut contents of yellow perch from an acidic lake (2).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Tang, R. et al *Yingyang Xuebao* 1986, **8**(3), 224-229 (Ch.) (*Chem. Abstr.* **106**, 15661x).
2. Heit, M. et al *Water, Air, Soil Pollut.* 1989, **44**, 9-30.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

165 iridium tetrachloride

$IrCl_4$

Cl_4Ir **Mol. Wt.** 334.03 **CAS Registry No.** 10025-97-5

Synonyms iridium chloride

EINECS No. 233-048-8 **RTECS No.** NO 3610000

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 8115 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides guide level 25 mg l^{-1} (2). Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *Gig. Tr. Prof. Zabol.* 1977, **21**(7), 55.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

I66 iron

Fe

Fe **Mol. Wt.** 55.85 **CAS Registry No.** 7439-89-6

EINECS No. 231-096-4 **RTECS No.** NO 4565500

Uses Alloyed with carbon, manganese, chromium and nickel and other elements to form steels.

Occurrence About 5% of Earth's crust. Occurs in haematite, magnetite, limonite and siderite. Human body weight contains ~60-70 μg g^{-1} (1).

Physical properties

M. Pt. 1535°C **B. Pt.** 3000°C **Specific gravity** 7.86 (pure)

Occupational exposure

UK-LTEL MEL 10 mg m^{-3} (total inhalable dust); 4 mg m^{-3} (respirable dust)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) starry flounder, bleak, perch 75-230 mg l^{-1} (iron salts) (2).

Juvenile African catfish (*Clarias gariepinus*) fed (5 wk) a ration of 2% body weight day^{-1} containing 664 or 6354 mg iron kg^{-1} dry diet (as $FeSO_4.7H_2O$) suffered suppression of growth at the higher dose. Tissue levels of iron in muscle, liver, and plasma and haemocrit values were not significantly different between the two treatments, but evidence of heightened oxidative stress (increased concentrations of the lipid peroxidation product malondialdehyde in liver and heart and depleted levels of the antioxidant vitamin E in liver) was found in fish receiving the higher dietary iron ration (3).

Invertebrate toxicity

Maximum concentration of iron not toxic to sludge microorganisms in wastewater treatment is 5.2 mg l^{-1} (4).

EC_{50} (21 day) *Daphnia magna* 5.2 mg l^{-1} (iron salts) (5).

LC_{50} (48 hr, 96 hr) *Asellus aquaticus* Fe(III) 183, 124 mg l^{-1}, respectively (6).

Bioaccumulation

Iron salts accumulate in fish (7).

Crayfish injected with 0.05-0.5 mg iron salts selectively stored iron in metal-containing vacuoles of R- and F-cells in the hepatopancreatic cells at levels toxic to cells. High doses caused alterations in the ultrastructural morphology of the antennal gland cells although no accumulation was apparent (8).

Environmental fate

Nitrification inhibition

Carbon and nitrogen fixation increased fourfold in *Anabaena* with increased iron salt nutrition from 5.58×10^{-7} – 5.58×10^{-5} g l^{-1}. Iron salts may be the limiting factor in ocean nitrogen fixation (9).

Anaerobic effects

Anaerobic bacteria in an iron-rich environment formed magnetite at high pHs and free Fe^{2+} or siderite at low pHs (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 30 g kg^{-1} (form unspecified) (11).

LD_{Lo} intraperitoneal rat 20 mg kg^{-1} (form unspecified) (12).

Average human lethal oral dose is 200-300 mg elemental iron kg^{-1} body weight. Toxic manifestations include severe haemorrhagic necrosis of the stomach and small intestine, metabolic derangements and effects on the liver, cardiovascular system and central nervous system (13).

Sub-acute and sub-chronic data

Iron overload causes inhibition of hepatic uroporphyrinogen decarboxylase and uroporphyria in C57BL/10ScSn but not DB A/2 mice. Studies of inbred mice 25 wk after treatment with 600 mg kg^{-1} iron showed no correlation between Ah locus, microsomal enzyme activities associated with cytochrome P_{450} or administration of 5-aminolevulinic acid in drinking water, with the propensity of strains to develop porphyria. Comparison with the congenic A2G-hr/+ strain, which carries the recessive hr gene showed a modulating influence associated with the hr locus (14).

Carcinogenicity and chronic effects

Iron^{III} administered subcutaneously (as iron sulfate, 50 μmol kg^{-1}, 2 × wk^{-1} for 53 wk) to ♀ Sprague Dawley rats subsequent to dimethylbenz[*a*]anthracene-initiation greatly accelerated mammary carcinogenesis, implying its promoting activity for mammary tissue of ♀ rats (15).

Metabolism and toxicokinetics

Absorbed from the gut and enters plasma attached to the protein transferrin. Transferrin enters cells by endocytosis and iron is released as pH drops and is used in synthesis of intracellular protein. Excess iron is stored in protein ferritin (16).

Incorporation into ferritin of bone marrow, liver and spleen mediated by ATP and ascorbic acid. Iron is stored in bone marrow as non-haeme iron (100 μg g^{-1} in humans) and to a lesser extent in liver and kidney (17).

0.03-0.05 mg day^{-1} excreted from normal humans in bile, faeces and urine (1).

Genotoxicity

Salmonella typhimurium TA98, TA102, TA1535, TA1537 with and without metabolic activation negative (17).

In vitro cultured mouse splenocytes dose-dependent increase in micronuclei (18).

Other effects

Other adverse effects (human)

Cases of iron salt overload may occur in patients receiving repeated blood transfusions (19), oral preparations for real or supposed anaemia (20) and food fortified with iron salts (21).

Anaemia may increase the risk of oral cancer (22).

Iron-depleted women, but not men, showed a lower risk of lung cancer (23).
Those occupationally exposed to iron, or who work in iron foundries, seem to be at increased risk of lung cancer (24).
South African Bantu siderosis caused by iron in cooking pots and home brewed beer stored in drums. 81% of subjects, both ♂ and ♀, had excessive haemosiderin-like deposits at autopsy (25).
Acute oral poisoning from iron tablets common in children. The average lethal dose for a 2-yr-old is 3 g (equivalent to ~50 tablets). 600 mg reported fatal to one small child (26).

Any other adverse effects

Animals (species unspecified) treated with a single intraperitoneal injection of 7.5 mg kg^{-1} ferric nitrilotriacetate showed transient changes in liver function and evidence for lipid peroxidation in liver homoganates (27).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron guide level 50 $\mu g\ l^{-1}$, maximum admissible concentration 200 $\mu g\ l^{-1}$ (28).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (29).

Other comments

Lack of body iron is common in cancer patients and is often associated with complications (30).
Toxic action reviewed (31).
Metabolism reviewed (32,33).
Magnetic.

References

1. Abdel-Mageed, A. B. et al *Vet. Hum. Toxicol.* 1990, **32**(4), 324-328.
2. Bagge et al *Ferrosulfaatin ja sitae sisaeltuevien jaeteresien akuutista myrkylisyydestae murtovedessae* 1975, **Meri 3**, 46-64.
3. Baker, R. T. M. et al *Aquat. Toxicol.* 1997, **40**(1), 51-61.
4. Boldyrev, A. I. et al *Vopr. Khim. Khim. Tekhnol.* 1986, **82**, 54-57 (Russ.) (*Chem. Abstr.* **108**, 43278n).
5. Biesinger, K. E. et al *J. Fish. Res. Board Can.* 1972, **29**, 1691-1700.
6. Martin, T. R. et al *Water Res.* 1986, **20**(9), 1137-1147.
7. Munshi, J. S. D. et al *Environ. Ecol.* 1989, **7**(4), 790-792.
8. Roldan, B. M. et al *Comp. Biochem. Physiol., C. Comp. Pharmacol. Toxicol.* 1987, **86C**(1), 201-214.
9. Rueter, J. G. *J. Phycol.* 1988, **24**(2), 249-254.
10. Bell, P. E. et al *App. Environ. Microbiol.* 1987, **53**(11), 2610-2616.
11. *Indian J. Pharm.* 1951, **13**, 240.
12. *NTIS Report* PB158508, Natl. Tech. Inf. Ser., Springfield, VA, USA.
13. Aiser, P. et al *Int. Rev. Exp. Pathol.* 1990, **31**, 1-46.
14. Smith, A. G. et al *Biochem. J.* 1993, **291**, 29-35.
15. Diwan, B. A. et al *Carcinogenesis* 1997, **18**(9), 1757-1762.
16. Halliwell, B. et al *ISI Atlas Sci.: Biochem.* 1988, **1**(1), 48-52.
17. Wang, P. K. *Bull. Environ. Contam. Toxicol.* 1988, **40**(4), 597-603.
18. Dreosti, I. E. et al *Mutat. Res.* 1990, **244**(4), 337-343.
19. Cohen, A. et al *Ann. N. Y. Acad. Sci.* 1985, **445**, 274.
20. Hennigar, G. R. et al *Am. J. Pathol.* 1979, **96**, 611.
21. Crosby, W. H. *N. Engl. J. Med.* 1977, **297**, 543.
22. Altini, M. et al *S. Afr. Med. J.* 1989, Suppl., 6-10.
23. Selby, J. V. et al *Int. J. Cancer* 1988, **41**, 677-682.
24. Perera, F. F. et al *Cancer Res.* 1988, **48**, 2288-2291.
25. Jacobs, A. et al (Eds.) *Iron in Biochemistry and Medicine* 1981, **2**, 427-459, Academic Press, London, UK.
26. Arena, J. M. (Ed.) *Poisoning* 1977, 431-436, Thomas, Springfield, IL, USA.
27. Yamanoi, Y. et al *Acta Haematol. Jpn.* 1982, **45**, 1229.
28. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
29. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.

30. Harju, E. *Met. Ions. Biol. Med., Proc. Int. Symp. 1st* 1990, 45-48.
31. Anke, M. et al *Trace Elem., Anal. Chem. Med. Biol., Proc. Int. Workshop, 4th* 1986 (Publ. 1987), 201-236.
32. Lerner, A. et al *Front. Gastrointest. Res.* 1988, 14 (Prog. Diet Nutr.) 117-134.
33. Flanagan, P. R. *Iron Transp. Storage* 1990, 247-261

167 iron(II) ammonium sulfate

$$Fe(NH_4)_2(SO_4)_2$$

$FeH_8N_2O_8S_2$ **Mol. Wt.** 284.05 **CAS Registry No.** 10045-89-3

Synonyms sulfuric acid, ammonium iron (2+) salt; ammonium ferrous sulfate; ferrous ammonium sulfate; ferrous diammonium disulfate; Mohr's Salt

EINECS No. 233-151-8 **RTECS No.** WS 5890000

Physical properties

Specific gravity 1.86 at 20°C with respect to water at 4°C
Solubility Water: soluble

Occupational exposure

UK-LTEL 1 mg m^{-3} (as Fe) **UK-STEL** 2 mg m^{-3} (as Fe)
US-TWA 1 mg m^{-3} (as Fe)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3.25 g kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sulfates guide level 25 mg l^{-1}, maximum admissible concentration 250 mg l^{-1}; ammonium guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1}; iron guide level 50 μg l^{-1}, maximum admissible concentration 200 μg l^{-1} (2).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Smyth, H. F. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed processes and Substances) Regulations* 1991, HMSO, London, UK

168 iron(II) chloride

$FeCl_2$

Cl_2Fe **Mol. Wt.** 126.75 **CAS Registry No.** 7758-94-3

Synonyms fero 66; ferrous chloride; ferrous dichloride; iron dichloride; iron protochloride

EINECS No. 231-843-4 **RTECS No.** NO 5400000

Uses Reducing agent in metallurgy. Used in pharmaceutical preparations and as mordant in dyeing.

Occurrence Occurs in nature as the mineral lawrencite.

Physical properties

M. Pt. 674°C **B. Pt.** 1023°C **Specific gravity** 3.16 at 25°C

Solubility Water: very soluble

Occupational exposure

UK-LTEL 1 mg m^{-3} (as Fe) **UK-STEL** 2 mg m^{-3} (as Fe)

US-TWA 1 mg m^{-3} (as Fe)

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 59 mg kg^{-1} (1).

Genotoxicity

Escherichia coli WP2S (λ) without metabolic activation positive (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron guide level 50 μg l^{-1}, maximum admissible concentration 200 μg l^{-1}. Chlorides guide level 25 mg l^{-1} (3).

Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

1. *Naunyn-Schmiedeberg's Arch. Exp. Pathol. Pharmakol.* 1962, **244**, 17.
2. Rossman, T. G. et al *Mutat. Res.* 1991, **260**(4), 349-367.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

169 iron(III) chloride

$FeCl_3$

Cl_3Fe **Mol. Wt.** 162.21 **CAS Registry No.** 7705-08-0

Synonyms ferric chloride; ferric trichloride; flores martis; iron chloride; iron perchloride; iron trichloride

EINECS No. 231-729-4 **RTECS No.** LJ 9100000

Uses Photography, ink. Catalyst for organic reactions. Purification and deodorisation of factory effluents and sewage.

Occurrence As mineral (molysite).

Physical properties

M. Pt. ~300°C (volatilises) **B. Pt.** ~316°C **Specific gravity** 2.90 at 25°C

Solubility Water: soluble. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

UK-LTEL 1 mg m^{-3} (as Fe) **UK-STEL** 2 mg m^{-3} (as Fe)

US-TWA 1 mg m^{-3} (as Fe)

UN No. 1773

UN No. 2582 (solution) **HAZCHEM Code** 2X **HAZCHEM Code** 2Z (solution)

Conveyance classification corrosive substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (2 and 4 day) *Asellus aquaticus* 183 and 124 mg l^{-1}, respectively (1).

EC_{50} (2 and 4 day) *Crangonyx pseudogracilis* 160 and 120 mg l^{-1}, respectively (1).

Environmental fate

Carbonaceous inhibition

Respirometry data indicate that iron(III) chloride does not have toxic effects on the biomass of an activated sludge process when concentrations of <100 mg l^{-1} are used; the pH does not vary significantly at these concentrations. Progressive inhibition of biomass occurs at iron(III) chloride concentrations of 500 mg l^{-1}, due to pH decrease (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1280 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 68 mg kg^{-1}, respectively (3).

LD_{50} intravenous mouse 142 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Oral Fischer 344 rat (2 yr) 0.25 or 0.5% in drinking water under investigation (4).

Irritancy

2% topical patch test: response graded at 48 hr, 72 hr and 5-7 day, erythema and oedema was reported in 3 of 17 subjects tested (5).

Genotoxicity

Escherichia coli PQ37 SOS chromotest without metabolic activation negative (6).
Escherichia coli WP2s(λ) without metabolic activation, weakly positive (7).
Salmonella typhimurium without metabolic activation positive (7).
In vitro mouse lymphoma L51787 tk^+/tk^- cell forward mutation assay negative (8).
In vitro human cells (cell type unspecified), DNA damage negative (9).
In vivo mouse bone marrow induced micronuclei (10).

Other effects

Any other adverse effects
In fasting mice induced a dose-dependent increase in nuclear aberrations in the stomach tissue. In normal feeding animals no increase in the nuclear aberrations was seen. It is concluded that iron compounds have an intrinsic cellular toxicity when not administered with food, but do not have any genotoxic potential for the gastro-intestinal tract (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron guide level: 50 μg l^{-1}, maximum admissible concentration 200 μg l^{-1}; chloride guide level 25 mg l^{-1}, approximate concentration at which effects might occur 200 mg l^{-1} (12).

References

1. Martin, T. R. et al *Water Res.* 1986, **20**(9), 1137-1147.
2. Broglio *Inquinamento* 1987, **29**(3), 112-114 (Ital.) (*Chem Abstr.* **107**, 140280u).
3. Lewis, M. A. et al *Registry of Toxic Effects of Chemical Substances* 1984, National Institute for Occupational Safety and Health, No. 83-107-4.
4. *Directory of Agents Being Tested for Carcinogenicity No. 15* 1992, IARC, Lyon, France.
5. Namikoshi, T. et al *J. Oral Rehabil.* 1990, **17**, 377-381.
6. Olivier et al *Mutat. Res.* 1987, **189**(3), 263-269.
7. Rossman, T. G. *Mutat. Res.* 1991, **260**(4), 349-367.
8. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **12**(1), 85-154.
9. Sumiko *Cancer Res.* 1987, **47**(24), 6522-6527.
10. Liao, M. et al *Weisheng Dulixe Zazhi* 1988, **2**(2), 83-86 (Ch.) (*Chem Abstr.* **112**, 134189h).
11. Bianchini et al *J. Appl. Toxicol.* 1988, **8**(3), 179-183.
12. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

170 iron(III) dextran

CAS Registry No. 9004-66-4

Synonyms Imferon; A100; Chinofer; ferric dextran; ferroglucin; Imposil; Myofer

RTECS No. NI 2200000

Physical properties

M. Pt. decomp.

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1 g (Fe) kg^{-1} (1).

LD_{50} intraperitoneal rat 3 g (Fe) kg^{-1} (2).

LD_{50} intravenous mouse 460 mg (Fe) kg^{-1} (3).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (4).

A woman who had multiple injections of iron-dextran complex developed an undifferentiated soft tissue sarcoma (5).

Only 1/9 malignancies in 5 reports from 1960-1977 was likely to be related to iron-dextran injections given 14 yrs before (a fibrosarcoma) (6).

Repeated intramuscular and subcutaneous injections in mice, rabbits and rats produced local tumours at the injection site (1,7).

Female F344 rats injected intraperitoneally with 600 mg Fe kg^{-1} were fed 0.02% hexachlorobenzene (HCB) in diet after 1 wk for 65 wk. 8/8 rats receiving HCB after iron overload developed multiple hepatic nodules, but only 3/8 receiving HCB alone had nodules. Iron overload potentiated the neoplastic process induced by HCB with both enhancing and depressing effects on various HCB-induced enzyme activities (8).

Genotoxicity

L5178Y mouse lymphoma cell forward mutation assay with and without metabolic activation negative (9).

Other effects

Any other adverse effects

100-500 mg(Fe) kg^{-1} given to anaesthetised cats lowered blood pressure, inhibited noradrenaline and had curare-like effects but had no effect on acetylcholine, histamine or serotonin (10).

Small doses in guinea pigs protected 70% of animals from anaphylactic shock induced by horse serum (10).

Intramuscular administration to rats with dextran oedema had an anti-oedemic effect (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron guide level 50 $\mu g\ l^{-1}$, maxiumum admissible concentration 200 $\mu g\ l^{-1}$ (11).

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

Other comments

Full-term infants injected with 150 mg iron-dextran at birth had a nutritional advantage in iron status up to 15 months compared with controls (13).

References

1. *Br. J. Pharm. Chem.* 1965, **24**, 352.
2. *Toxicol. Appl. Pharmacol.* 1971, **18**, 185.
3. *Acta. Pol. Pharm.* 1961, **18**, 149.
4. *IARC Monograph* 1987, **Suppl. 7**, 226.
5. *IARC Monograph* 1973, **2**, 161-178.
6. Robertson, A. G. et al *Br. Med. J.* 1977, **i**, 946.
7. Hruby, M. et al *Sbornik Lek.* 1985, **87**, 114-120.
8. Smith, A. G. et al *Biochem. J.* 1993, **291**, 29-35.
9. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1991, **17**(3), 196-219.
10. Dilar, P. *Vet.-Med. Nauki* 1986, **23**(9), 35-44 (Bulg.) (*Chem. Abstr.* **106**, 168494v).

11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
13. Olivares, M. et al *Nutr. Rep. Int.* 1989, **40**(3), 577-583

I71 iron(III) fluoride

FeF_3

FeF_3 **Mol. Wt.** 112.84 **CAS Registry No.** 7783-50-8

Synonyms ferric fluoride; ferric trifluoride; iron trifluoride

EINECS No. 232-002-4 **RTECS No.** NI 6865000

Physical properties

M. Pt. >1000°C (sublimes) **Specific gravity** 3.87
Solubility Water: slightly soluble

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (inhalable dust fraction)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 1 mg m^{-3} (as Fe) **UK-STEL** 2 mg m^{-3} (as Fe)
US-TWA 1 mg m^{-3} (as Fe)

UN No. 3260

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 18 mg kg^{-1} (1).

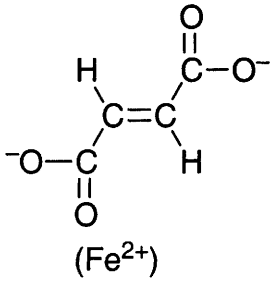
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron guide level 50 μg l^{-1}, maximum admissible concentration 200 μg l^{-1}; fluoride maximum admissible concentration 1500 μg l^{-1} at 8-12°C (700 μg l^{-1} at 25-30°C) (2).
Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *US Army Armament Research and Development Command* Report No.NX00135, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

172 iron(II) fumarate



$C_4H_4O_4Fe$ **Mol. Wt.** 171.92 **CAS Registry No.** 141-01-5

Synonyms 2-butenedioic acid (*E*)-, iron (2+) salt (1:1); fumaric acid, iron (2+) salt (1:1); Cpiron; Erzoferro; Ferrone; Ircon; Toleron

EINECS No. 205-447-7 **RTECS No.** LT 1950000

Physical properties

M. Pt. >280°C **Specific gravity** 2.435 at 25°C

Solubility Water: 1.4 g l^{-1} at 25°C. Organic solvents: ethanol

Occupational exposure

UK-LTEL 1 mg m^{-3} (as Fe) **UK-STEL** 2 mg m^{-3} (as Fe)

US-TWA 1 mg m^{-3} (as Fe)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1570, 3850 mg kg^{-1}, respectively (1,2).

LD_{50} dermal rat 500 mg kg^{-1} (2).

LD_{50} intraperitoneal rat, mouse 185, 480 mg kg^{-1}, respectively (1,2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron guide level 50 μg l^{-1}, maximum admissible concentration 200 μg l^{-1} (3).

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

1. *Am. J. Med. Sci.* 1961, **241**, 296.
2. *Drugs in Japan. Ethical Drugs* 6th ed., 1982, Japan Pharmaceutical Information Center, Tokyo, Japan.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

173 iron(III) nitrate

$$Fe(NO_3)_3$$

FeN_3O_9 **Mol. Wt.** 241.86 **CAS Registry No.** 10421-48-4

Synonyms nitric acid, iron(3+) salt; ferric nitrate; iron trinitrate

EINECS No. 233-899-5 **RTECS No.** QU 8915000

Uses As mordant in dyeing; weighting skills; tanning; corrosion inhibitor; analytical reagent.

Physical properties

M. Pt. 47°C (nonahydrate) **B. Pt.** <100°C (decomp.) **Specific gravity** 1.68 at 21°C
Solubility Water: freely soluble. Organic solvents: acetone, ethanol

Occupational exposure

UK-LTEL 1 mg m^{-3} (as Fe) **UK-STEL** 2 mg m^{-3} (as Fe)
US-TWA 1 mg m^{-3} (as Fe)

UN No. 1466; 3218 (aqueous solution) **HAZCHEM Code** 1Z; 2Z (aqueous solution)
Conveyance classification oxidising substance

Genotoxicity

Eschericha coli PQ37 SOS chromotest without metabolic activation negative (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron: guide level 50 μg l^{-1}, maximum admissible concentration 200 μg l^{-1}; nitrate: guide level 25 mg l^{-1}, maximum admissible concentration 50 mg l^{-1} (2).

References

1. Olivier et al *Mutat. Res.* 1987, **189**(3), 263-269.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

174 iron(III) oxide

$$Fe_2O_3$$

Fe_2O_3 **Mol. Wt.** 159.69 **CAS Registry No.** 1309-37-1

Synonyms C.I. Pigment Red 101; ferric oxide; γ-iron oxide; Prussian red; Venetian red; ferric sesquioxide; α-iron oxide; α-ferric oxide; C.I. 77491

EINECS No. 215-168-2 **RTECS No.** NO 7400000

Uses As pigment. Polishing agent for glass, diamonds. In electrical resistors, semiconductors, magnets, magnetic tapes. Catalyst. In colloidal solutions as stain for polysaccharides.
Occurrence α form occurs as haematite; γ form occurs as maghaemite

Physical properties

M. Pt. 1565°C **Specific gravity** 5.24

Occupational exposure

DE-MAK 1.5 mg m^{-3} (respirable fraction of aerosol)
FR-VME 5 mg m^{-3} (fume) (as Fe)
SE-LEVL 3.5 mg m^{-3} (as Fe) (respirable dust)
UK-LTEL 10 mg m^{-3} (total inhalable dust); 4 mg m^{-3} (respirable dust)
US-TWA 5 mg m^{-3} (as Fe) (dust and fume)

Ecotoxicity

Fish toxicity

There was a reduction in the percentage of carp eggs hatching, from 54 to 20 %, when exposed to 1-500 ppm (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse, rat 5400-5500 mg kg^{-1} (2).
LD_{Lo} subcutaneous dog 30 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Syrian golden hamster 3 mg iron oxide in 0.2 ml saline instilled intralaryngeally 1 × wk for 5, 10, 15 wk had increased epithelial mitotic rates of the bronchioles after 5 instillations. Bronchioalveolar hyperplasia was also seen after 5 instillations, but was less prominent after 10 or 15 treatments (4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).
18.9% of rats dosed intraperitoneally with 21.6 g (5 injections) of α-ferric oxide hydrate had sarcomas, mesothelioma or carcinomas in the abdominal cavity (6).
Ferric oxide particles instilled intratracheally to hamsters induced interstitial fibrosis, but benzo[*a*]pyrene administered bound to ferric oxide particles induced squamous-cell and anaplastic carcinomas. The ferric oxide particles act as cofactors, mainly carriers, in the system (7-9).

Genotoxicity

Induced chromosomal aberrations in rat bone marrow cells (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron guide level 50 μg, maximum admissible concentration 200 μg l^{-1} (11).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

Other comments

Reviews on human health effects, experimental toxicity, epidemiology and workplace experience listed (13).

References

1. Rao, K. S. et al *Geobios (Jodphur, India)* 1988, **15**(2-3), 111-113.
2. *Gig. Tr. Prof. Zabol.* 1982, **26**(4), 23.
3. *Abdernalden's Handbuch der Biologischen Arbeitsmethoden* 1935, **4**, 1289.
4. Marshall, H. E. et al *Fundam. Appl. Toxicol.* 1987, **9**(4), 705-714.
5. *IARC Monograph* 1987, **Suppl. 7**, 216-218.
6. Pott, F. et al *Exp. Pathol.* 1987, **32**, 129-152.

7. Saffiotti, U. *Prog. Exp. Tumor. Res.* 1969, **11**, 302-333.
8. Stenbaeck, F. et al *Oncology* 1976, **33**, 29-34.
9. Sellakumar, A. R. et al *J. Natl. Cancer Inst.* 1973, **50**, 507-510.
10. He, W. et al *Dongwuxue Yanjuu* 1988, **9**(3), 263-268 (Ch.) (*Chem. Abstr.* **110**, 109561z).
11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
13. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

175 iron pentacarbonyl

$Fe(CO)_5$

C_5FeO_5 **Mol. Wt.** 195.90 **CAS Registry No.** 13463-40-6

Synonyms (*TB*-5-11)-iron carbonyl ($Fe(CO)_5$); iron carbonyl ($Fe(CO)_5$); pentacarbonyliron

EINECS No. 236-670-8 **RTECS No.** NO 4900000

Uses To make finely divided iron ("carbonyl iron"). Anti-knock agent in motor fuels. Catalyst in organic reactions.

Physical properties

M. Pt. -20°C **B. Pt.** 103°C **Flash point** -15°C **Specific gravity** 1.453 at 25°C with respect to water at 4°C
Volatility v.p. 40 mmHg at 30.3°C

Occupational exposure

DE-MAK 0.1 ppm (0.81 mg m^{-3})
FR-VME 0.1 ppm (0.8 mg m^{-3})
UK-LTEL 0.01 ppm (0.08 mg m^{-3}) (as Fe)
US-TWA 0.1 ppm (0.23 mg m^{-3}) (as Fe) **US-STEL** 0.2 ppm (0.45 mg m^{-3}) (as Fe)

UN No. 1994 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance, danger of fire (flammable liquid)

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, guinea pig 12, 22 mg kg^{-1}, respectively (1).
LC_{50} (10 min) inhalation mouse 7 g m^{-3} (2).
Inhalation ♂ rat (1, 3, 5 hr) 10-20 mg m^{-3} (dust aerosol). Following 3-hr exposure the majority of carbonyl iron particles were located on alveolar duct bifurcations. Within 24 hr pulmonary macrophage had accumulated at site of deposition in the lung (3).
Rats were administered 50 μg g^{-1} iron pentacarbonyl intratracheally. The dust particles averaged <5μm in diameter. Bronchoalveolar lavage was performed 24 hr later. Alveolar neutrophil numbers increased, which indicated an inflammatory response, and alveolar macrophase numbers decreased. Levels of acellular lavageable lung protein were increased (4).

Other comments

Reviews on human health effects, epidemiology, work place experience and experimental toxicology listed (5).

References

1. *J. Ind. Hyg. Toxicol.* 1943, **25**, 415.
2. *NTIS Report* 158/508, Natl. Tech. Inf. Ser., Springfield, VA, USA.
3. Warheit, D. B. et al *Scanning Microsc.* 1988, **2**(2), 1069-1078.
4. Blackford, J. A., Jr. et al *J. Toxicol. Environ. Health* 1997, **51**(3), 203-218.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

176 iron(II) sulfate

$FeSO_4$

FeO_4S **Mol. Wt.** 151.91 **CAS Registry No.** 7720-78-7

Synonyms sulfuric acid, iron (2+) salt (1:1); Feosol; ferrous sulfate; green vitriol; iron monosulfate; sulferrous

EINECS No. 231-753-5 **RTECS No.** NO 8500000

Uses In the manufacture of iron and iron compounds. In fertiliser. Reducing agent. Weed killer. Wood preservative. In pesticides. In quantitative analysis.

Occurrence Hydrates occur in nature as minerals melanterite, siderotil, szomolnikite, tauriscite.

Physical properties

Solubility Water: soluble

Occupational exposure

UK-LTEL 1 mg m^{-3} (as Fe) **UK-STEL** 2 mg m^{-3} (as Fe)

US-TWA 1 mg m^{-3} (as Fe)

Ecotoxicity

Invertebrate toxicity

EC_{50} (2 day) *Crangonyx pseudogracilis* 143 mg l^{-1} (1).

LC_{50} (50 hr) *Asellus aquaticus* (calculated) 256-467 mg l^{-1} at pH 4.5 (2).

200 μg cm^{-2} on glass surface toxic to *Deroceras reticulatum* (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 319, 680 mg kg^{-1}, respectively (4,5).

TD_{Lo} oral woman 600 mg kg^{-1} (6).

LD_{50} subcutaneous mouse, rat 60, 155 mg kg^{-1}, respectively (7).

LD_{50} intraperitoneal mouse 289 mg kg^{-1} (8).

LD_{50} intravenous dog, mouse 79, 112 mg kg^{-1}, respectively (9).

Genotoxicity

Saccharomyces cerevisiae failed to induce diploid or disomic spores during meiosis (10).

Escherichia coli PQ37 without metabolic activation negative (11).

In vivo mouse gastro-intestinal cells showed no increase in chromosomal aberrations in the stomach or duodenum of fasting or feeding mice, but a dose-related increase in nuclear aberrations in the colon for feeding and fasting mice (12).
In vitro mouse lymphoma L5178Y tk^+/tk^- no significant result (13).

Other effects

Other adverse effects (human)
Gastro-intestinal disturbances, including colic, constipation and diarrhoea may occur in humans. In children, ingestion of large quantities can cause vomiting, haematemesis, hepatic damage, tachycardia and peripheral vascular collapse (14).

Any other adverse effects
Increased rat liver peroxides and lipofuscins and reduced membrane fluidity and swelling of liver mitochondria (15).
15-106 mg l^{-1} iron(II) sulfate shortened action potential duration, and decreased the contractile force of the guinea pig myocardium and decreased the action potential amplitude and maximum upstroke velocity of the myocardium, papillary muscles and K^+ depolarised papillary muscles (16).
Inhibition of transmembrane movement of Ca^{2+} and Na^+ in myocardial cells by Fe^{2+} may be one of the mechanisms of heart failure and circulatory collapse in acute iron poisoning (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron guide level 50 μg l^{-1}, maximum admissible concentration 200 μg l^{-1}; sulfates guide level 25 mg l^{-1}, maximum admissible concentration 250 mg l^{-1} (17).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Potentially explosive.

References

1. Martin, T. R. et al *Water Res.* 1986, **20**(9), 1137-1147.
2. Maltby, L. et al *Environ. Pollut.* 1987, **43**, 271-279.
3. Henderson, I. F. et al *Monogr. – Br. Crop. Prot. Counc.* 1989, (Slugs, Snails World Agric.), 289-294.
4. *J. Paediatrics* 1966, **69**, 663.
5. *Br. J. Pharmacol. Chemother.* 1965, **24**, 352.
6. *JAMA, J. Am. Med. Assoc.* 1974, **229**, 1333.
7. *Drugs in Japan. Ethical Drugs* 6th ed., 1982, 888, Japan Pharmaceutical Information Center, Tokyo, Japan.
8. *C. R. Hebd. Seances Acad. Sci. (Paris)* 1963, **256**, 1043.
9. *Am. J. Med. Sci.* 1961, **241**, 296.
10. Sora, S. et al *Mutat. Res.* 1988, **201**(2), 375-384.
11. Olivier, P. et al *Mutat. Res.* 1987, **189**, 263-269.
12. Bianchini, F. et al *J. Appl. Toxicol.* 1988, **8**(3), 179-183.
13. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1991, **17**(3), 196-219.
14. Gosselin, K. E. et al (Eds.) *Clinical Toxicology of Chemical Products*, 4th ed., 1976, Williams & Wilkins, Baltimore, MD, USA.
15. Lu, X. *Shengwu Huaxue Yu Shengwu Wuli Jinzhan* 1989, **16**(5), 372-374, (Ch.) (*Chem. Abstr.* **112**, 153221d).
16. Luo, G. et al *Zhongguo Yaoli Xuebao* 1989, **10**(6), 523-525 (Ch.) (*Chem. Abstr.* **112**, 111802p).
17. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
18. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

177 iron(III) sulfate

$$Fe_2(SO_4)_3$$

$Fe_2O_{12}S_3$ **Mol. Wt.** 399.88 **CAS Registry No.** 10028-22-5

Synonyms diiron trisulfate; ferric sulfate; iron persulfate; iron sulfate (2:3); iron tersulfate

EINECS No. 233-072-9 **RTECS No.** NO 8505000

Uses Agent for removing red tide plankton. Coagulant in water purification and sewage treatment. Iron alums, iron salts and pigment preparation. Soil conditioner. Catalyst in polymerisation. In textile dyeing and calico printing as a mordant.

Physical properties

M. Pt. 480°C (decomp.) **Specific gravity** 3.097
Solubility Water: 440 g l^{-1}

Occupational exposure

UK-LTEL 1 mg m^{-3} (as Fe) **UK-STEL** 2 mg m^{-3} (as Fe)
US-TWA 1 mg m^{-3} (as Fe)

UN No. 3215; 3216 (aqueous solution) **HAZCHEM Code** 2W; 2X (aqueous solution)
Conveyance classification oxidising substance

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) rabbit fish, striped goby 65 and 236 mg l^{-1}, respectively (1).

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Inhalation rat (7 or 21 day) 7-component mixture including iron sulfate (concentration unspecified) for 4 hr day^{-1}. Significant effects observed on pulmonary macrophage function, more pronounced after 21 days. Effects persisted to 96 hr post-exposure (2).

Other effects

Any other adverse effects
Adverse effects to the respiratory system of acidic air pollutants including iron sulfate were studied in rats, exposure time ≤4 hr. Reflex breathing patterns, lung/nasal histopathological changes and particle clearance rate were examined. Acid components had no effect on the parameters examined (3).

Legislation

Generally recommended as safe for direct use in food, including infant formula under US Federal Food, Drug and Cosmetic Act (4).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Iron: guide level 50 μg l^{-1}, maximum admissible level 200 μg l^{-1}; sulfate: guide level 25 mg l^{-1}, maximum admissible level 250 mg l^{-1} (5).

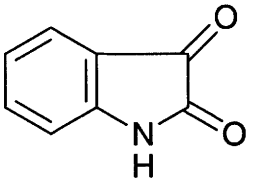
Other comments

Mutagenicity, toxicity and bioavailability of food additives reviewed (6,7).

References

1. Kanda et al *Suisan Zoshoku* 1989, **37**(3), 221-224 (Japan.) (*Chem. Abstr.* **112**, 113796p).
2. Phalen et al *Report* 1987, ARB-R-88/354, Order No. PB88-240437, NTIS.
3. Mauts et al *Report* 1988, ARB-R-88/353, Order No. PB88-235718, NTIS.
4. *Fed. Regist.* 12 May 1988, **53**(92), 16862-16867.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *Fed. Regist.* 12 April 1987, **52**(76), 13086-13107.
7. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(2), 75-79

178 isatin



$C_8H_5NO_2$ **Mol. Wt.** 147.13 **CAS Registry No.** 91-56-5

Synonyms 1*H*-indole-2,3-dione; *o*-aminobenzoylformic anhydride; 2,3-dioxoindoline; isatic acid lactam; isatinic acid anhydride

EINECS No. 202-077-8 **RTECS No.** NL 7873000

Uses In the manufacture of dyes. Analytical chemical reagent.

Physical properties

M. Pt. 203.5°C (partial sublimation)
Solubility Organic solvents: diethyl ether, boiling ethanol

Mammalian & avian toxicity

Acute data

LD_{50} (estimated) oral redwing blackbird >101 mg kg^{-1} (1).
LD_{Lo} oral rat 5 g kg^{-1} (2).
LD_{50} intraperitoneal mouse 330 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 563 mg kg^{-1} (4).

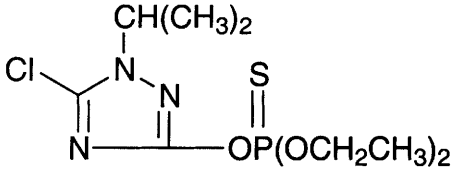
Metabolism and toxicokinetics

Showed a rapid rate of absorption and metabolism in rabbit study. Metabolites in urine were anthranilic acid, tryptophan and nicotinic acid (5).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *Indian J. Physiol. Pharmacol.* 1962, **6**, 145.
3. *Nippon Yakurigaku Zasshi* 1959, **55**, 1514.
4. *Pharm. Chem. J. (Engl. Transl.)* 1981, **15**, 858.
5. Ahmad, M. et al *Proc. Pak. Acad. Sci.* 1990, **27**(1), 1-10

179 isazofos



$C_9H_{17}ClN_3O_3PS$ **Mol. Wt.** 313.74 **CAS Registry No.** 42509-80-8

Synonyms *O*-[5-chloro-1(1-methylethyl)-1*H*-1,2,4-triazol-3-yl] *O,O*-diethyl phosphorothioic acid ester; Ciba-Geigy A 12223; Isazophos; Miral; Triumph

EINECS No. 255-863-8 **RTECS No.** TE 7760000

Uses Nematicide.

Physical properties

B. Pt. 100°C at 0.001 mmHg **Specific gravity** 1.23 at 20°C **Partition coefficient** log P_{ow} 2.99
Volatility v.p. 3.225×10^{-5} mmHg at 20°C
Solubility Water: 168 mg l^{-1} at 20°C. Organic solvents: miscible with benzene, chloroform, methanol

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Toxic in contact with skin and if swallowed – Very toxic by inhalation – May cause sensitisation by skin contact – Harmful: danger of serious damage to health by prolonged exposure through inhalation – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R26, R43, R48/20, R50/53)
Safety phrases Keep locked up and out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of insufficient ventilation, wear suitable respiratory equipment– In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Refer to manufacturer/supplier for information on recovery/recycling – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S38, S45, S59, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, carp, trout 0.01, 0.22 and 0.008 mg l^{-1}, respectively (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 0.0014 mg l^{-1} (2).

Environmental fate

Adsorption and retention
No leaching observed throughout a 21-wk rainfall study. Evaporation accounted for 44-67% (emulsifiable concentration) and 72-100% (granular formulation) (3).
Mobility and persistence in silt loam soils was studied at 1, 2, 4, 8, 12 and 21 wk, $t_{1/2}$ 3-4 wk. No mobility observed after 1 wk (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 40-60 mg kg^{-1} (5).
LC_{50} (4 hr) inhalation rat 0.24 mg l^{-1} in air (1).
LD_{50} dermal ♂, ♀ rat 118 mg, 290 mg kg^{-1}, respectively (1).

Sub-acute and sub-chronic data
No-effect level (90 day) oral rat, dog 0.2 and 0.05 mg kg^{-1} day^{-1}, respectively (1).

Irritancy
Mild irritant to skin and minimal to eyes of rabbits (no other details) (1).

Legislation

WHO Toxicity Class Ib (6).
EPA Toxicity Class I (2).

Other comments

Toxic to honey bees (details not specified) (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Bowman *Environ. Toxicol. Chem.* 1991, **10**(7), 873-879.
4. Bowman *Environ. Toxicol. Chem.* 1990, **9**(4), 453-461.
5. Thompson *Agricultural Chemicals* Volume 1, 1977, 131.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

I80 isoamyl acetate

$$(CH_3)_2CHCH_2CH_2OC(O)CH_3$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 123-92-2

Synonyms isopentyl acetate; isoamyl ethanoate; isopentyl alcohol acetate; 3-methylbutyl acetate; pear oil; banana oil

EINECS No. 204-662-3 **RTECS No.** NS 9800000

Uses Solvent. Flavouring. In textile manufacture and manufacture of photographic film, artificial pearls and leather, celluloid cements, waterproof varnishes, bronzing liquids and metallic paints.

Physical properties

M. Pt. –78°C **B. Pt.** 142°C at 756 mmHg **Flash point** 25°C **Specific gravity** 0.876 at 15°C with respect to water at 4°C
Solubility Water: 1600 mg l^{-1} at 20°C. Organic solvents: amyl alcohol, diethyl ether; miscible with ethanol, ethyl acetate

Occupational exposure

DE-MAK 50 ppm (270 mg m^{-3})
FR-VME 100 ppm (525 mg m^{-3})
JP-OEL 100 ppm (530 mg m^{-3})
UK-LTEL 100 ppm (541 mg m^{-3}) **UK-STEL** 125 ppm (676 mg m^{-3})
US-TWA 100 ppm (532 mg m^{-3})

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, rat 7420, 16,600 mg kg^{-1}, respectively (1,2).

LC_{Lo} (duration unspecified) inhalation cat 35,000 mg m^{-3} (3).
LD_{Lo} subcutaneous guinea pig 5000 mg kg^{-1} (3).

Other comments

Reviews on human health effects, experimental toxicity, ecotoxicology and workplace experience listed (4).

References

1. *Ind. Med. Surg.* 1972, **41**, 31.
2. *Yakkyoku* 1981, **32**, 1241.
3. *Arch. Gewerbepathol. Gewerbehyg.* 1933, **5**, 1.
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I81 isoamyl nitrite

$$(CH_3)_2CHCH_2CH_2NO_2$$

$C_5H_{11}NO_2$ **Mol. Wt.** 117.15 **CAS Registry No.** 110-46-3

Synonyms isopentyl nitrite

EINECS No. 203-770-8 **RTECS No.** NT 0187500

Uses Used by inhalation in treatment of angina and for cyanide and carbon monoxide poisoning (1).
Occurrence Principal component of amyl nitrite.

Physical properties

B. Pt. 97-99°C **Flash point** 10°C **Specific gravity** 0.875 at 25°C with respect to water at 25°C
Volatility v.den. 4
Solubility Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful by inhalation and if swallowed (R11, R20/22)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Avoid contact with the skin – If swallowed seek medical advice immediately and show this container or label (S2, S16, S24, S46)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 505 mg kg^{-1} (2).
LC_{50} (1 hr) inhalation rat 1274 ppm (2).
LC_{50} (4 hr) inhalation rat 716 ppm (3).
LD_{50} intravenous dog 167 mg kg^{-1} (4).

Metabolism and toxicokinetics
In humans absorbed by most mucous membranes, particularly the lungs. Inactive orally due to rapid hydrolysis. After inhalation, the onset of action is ~10 sec and the duration 5 min. It can combine with haemoglobin to form methaemoglobin which then combines with cyanide to form non-toxic cyanohaemoglobin, in cases of cyanide poisoning (5).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (6).
In vitro Chinese hamster ovary cells without metabolic activation chromosomal aberrations negative, sister chromatid exchanges positive (7).

Other effects

Other adverse effects (human)
Human volunteers exposed repeatedly showed abnormalities in lymphocyte levels within 7 days. After 4 days total number of lymphocytes had dropped, but by 7 days an overshoot in the number of lymphocytes compared with controls was seen (8).

Any other adverse effects
In rats, poisoning is accompanied by cyanosis, prostration and convulsions (4).
The compound has pronounced vasodilator effects (5).

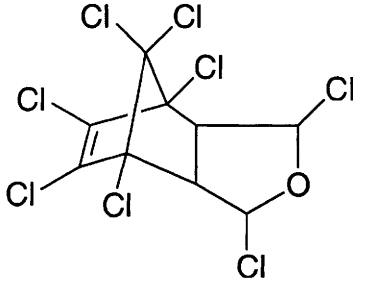
Other comments

The use, fate and toxicity of the compound have been reviewed (9).
The compound is prone to abuse for its vasodilator effects (9).
The use in treatment of cyanide and carbon monoxide poisoning described (1).
Decomposes on exposure to air.

References

1. Moore, S. J. et al *J. Pharmacol. Exp. Ther.* 1987, **24**(1), 70-73.
2. *Fed. Proc.* 1982, **41**, 1583.
3. Klonne, D. R. et al *Fundam. Appl. Toxicol.* 1987, **8**(1), 101-106.
4. *Res. Commun. Chem. Pathol. Pharmacol.* 1973, **5**, 889.
5. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
6. Galloway, S. M. *Environ. Mol. Mutagen.* 1987, **10**(Suppl. 10), 1-175.
7. Mortelmans, K. et al *Environ. Mol. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
8. Dax, E. M. et al *NIDA Res. Monogr.* 1988, **83**, 75-80.
9. Haverkos, H.et al *Gov. Rep. Announce. Index (U. S.)* 1989, **89**(5), Abstr. No. 911,952

I82 isobenzan



$C_9H_4Cl_8O$ **Mol. Wt.** 411.75 **CAS Registry No.** 297-78-9

Synonyms 1,3,4,5,6,7,8,8-octachloro-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran; Telodrin

EINECS No. 206-045-4 **RTECS No.** PC 1225000

Uses Superseded insecticide.

Physical properties

M. Pt. 120-122°C **Specific gravity** 1.87 **Volatility** v.p. 3.0×10^{-6} mmHg at 20°C
Solubility Organic solvents: acetone, benzene, diethyl ether, heavy aromatic naptha, toluene, xylene

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Very toxic in contact with skin and if swallowed – Very toxic to aquatic organisms (R27/28, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Environmental fate

Degradation studies
95% disappearance from soils in 2-4 yr (1).

Abiotic removal
Persistence in riverwater in sealed vessel kept in sunlight and artificial fluorescent light; initial concentraion 10 μg l^{-1}: after 1 hr, 1 wk, 2 wk, 4 wk the levels were, respectively, 100, 25, 10, 0% of original compound (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral housesparrow, common grackle, pigeon, 1.0, 1.33, 10.0 mg kg^{-1}, respectively (3).
LD_{50} oral dog, rabbit, rat, mouse 1, 4, 4.8, 8.4 mg kg^{-1}, respectively (4,5).
LD_{50} dermal guinea pig, rat 2-5 mg kg^{-1} (4,6).
LD_{50} dermal rabbit 12 mg kg^{-1} (7).
LD_{50} intravenous rat 1.8 mg kg^{-1} (8).
LD_{50} intraperitoneal rat, mouse 3.56, 8.17 mg kg^{-1}, respectively (4).

Sub-acute and sub-chronic data
Oral deer mouse (feeding study, 3 day) 87.5 mg kg^{-1}, killed 50% of the study population (9).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

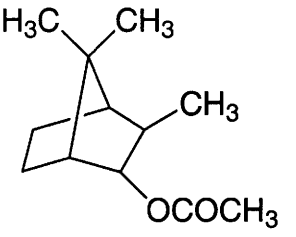
Included as one of a number of pesticides evaluated in epidemiological studies for haemotoxic effects. No leukaemogenic influence demonstrated (11).
Reviews on human health effects, environmental exposure, toxicity comprehensively listed (12).

References

1. Edwards, C. A. *Residue Rev.* 1966, **13**, 83.
2. Eichelberger, J. W. et al *Environ. Sci. Technol.* 1971, **5**, 430-435.
3. Schafer, E. W. et al *Vertebrate Pest Control and Management Materials* 1979, J. R. Beck (Ed.), ASTM STP 680, American Society for Testing and Materials, Philadelphia, PA, USA.
4. Jager *Aldrin Dieldrin Endrin and Telodrin: An Epidemiological and Toxicological Study of Long-Term Occupational Exposure* 1970, Elsevier, New York, NY, USA.
5. *Agricultural Research Service, USDA Information Memorandum* 1966, **20**, 13, Beltsville, MD, USA.
6. *World Rev. Pest Control* 1970, **9**, 119.
7. *Pesticide Chemicals Official Compendium* 1966, 1099, Association of the American Pesticide Control Officials, Inc., Topeka, KS, USA.

8. Traberger *Arch. Exp. Pathol. Pharmakol.* 1957, **232**, 227.
9. *Environmental Properties of Chemicals* 1990, 664, Research Report 91, Ministry of the Environment, VAPK-Publishing, Helsinki, Finland.
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. David, A. *Pract. Lek.* 1987, **39**(9), 421-426 (Czech.) (*Chem. Abstr.* **108**, 61698d).
12. *Environmental Health Criteria 129: Isobenzan* 1991, International Program on Chemical Safety, WHO, Geneva, Switzerland

183 isobornyl acetate



$C_{12}H_{20}O_2$ **Mol. Wt.** 196.29 **CAS Registry No.** 125-12-2

Synonyms acetic acid, *exo*-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl, ester; Pichtosin; Pichtosine; isoborneol acetate

EINECS No. 204-727-6 **RTECS No.** NP 7350000

Physical properties

M. Pt. >–50°C **B. Pt.** 220-224°C **Flash point** 88-90°C
Solubility Organic solvents: acetone, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (calc.) bluegill sunfish, rainbow trout, fathead minnow 3.97-5.18 mg l^{-1} (duration unspecified) (1).

References

1. Fiedler, H. *Toxicol. Environ. Chem.* 1990, **28**(2-3), 167-188

184 isobutane

$$(CH_3)_2CHCH_3$$

C_4H_{10} **Mol. Wt.** 58.12 **CAS Registry No.** 75-28-5

Synonyms 2-methylpropane; *iso*-butane; 1,1-dimethylethane; trimethylmethane

EINECS No. 200-857-2 **RTECS No.** TZ 4300000

Uses Aerosol propellant in consumer products. Synthesis of polyurethane foams and resins. Component of gasoline.

Physical properties

M. Pt. −160°C **B. Pt.** −12°C **Flash point** −81°C **Specific gravity** 0.5572 at 20°C **Volatility** v.den. 2.0
Solubility Water: 49 mg l^{-1} at 20°C

Occupational exposure

DE-MAK 1000 ppm (2400 mg m^{-3})

UN No. 1969 **HAZCHEM Code** 2WE **Conveyance classification** flammable gas
Supply classification extremely flammable
Risk phrases Extremely flammable (R12)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking (S2, S9, S16)

Environmental fate

Degradation studies
Scedosporium sp. oxidised isobutane to *tert*-butanol but neither substrate was used for growth (1).
Incubation with natural flora in ground water (in the presence of other components of high-octane gasoline 100 μg l^{-1}) 0% remained after 192 hr at 13°C (2).

Abiotic removal
Estimated $t_{1/2}$ 17 hr under photochemical smog conditions in S.E. England (3,4).

Mammalian & avian toxicity

Acute data
Inhalation human 250-1000 ppm (1 min to 8 hr) and 500 ppm (10 day) 1 to 8 hr day^{-1} no deleterious effects (5).
LC_{50} (1 hr) inhalation mouse 52 mg kg^{-1} (6).

Sub-acute and sub-chronic data
Inhalation (13 wk) F344 rats 50:50 wt% mixture of isobutane and isopentane target concentration 4500 and 1000 ppm 6 hr day^{-1} 5 day wk^{-1}. No evidence of hydrocarbon-induced nephropathy in either sex (7).
Inhalation (90 day) of aerosol (22%) rabbit 30 sec bursts twice daily 5 days wk^{-1}. No adverse effects (8).

Metabolism and toxicokinetics
In vitro rat liver microsomes oxidatively metabolised to its parent alcohol (9).
Blood levels of 20-90 ng ml^{-1}, humans exposed to 500 ppm, indicating isobutane can be absorbed through the lungs (10).
Inhalation rats detected in adipose, brain, liver and lungs (11).

Genotoxicity

Salmonella typhimurium (strain unspecified) with and without metabolic activation negative (12).

Other effects

Any other adverse effects
Mice at near LD_{50} concentrations showed depression, rapid and shallow breathing and apnoea (6,13).

Other comments

Emitted in waste gases from printing presses, paint booths, incinerators and car exhausts (14).
Reviews on human effects, epidemiology, workplace experience, experimental toxicology, safety test data and exposure conditions listed (15).
The gas will support growth of *Mycobacterium phlei* (16).

References

1. Onodera *Agric. Biol. Chem.* 1990, **54**(9), 2413-16.
2. Jamison, V. W. et al *Proceedings of the Third International Biodegradation Symposium* 1976, Applied Science Publishers.
3. Brice, K. A. et al *Atmos. Environ.* 1978, **12**, 2045-2054.
4. Greiner, N. R. *J. Chem. Phys.* 1967, **46**, 3389-3392.
5. Sperling, F. et al *Environ. Res.* 1972, **5**(2), 164.
6. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
7. Aranyi et al *Toxicol. Ind. Health* 1986, **2**(1), 85-89.
8. Moore, A. F. *J. Am. Coll. Toxicol.* 1982, **1**, 127-142.
9. Brown, V. K. H. et al *Br. J. Ind. Med.* 1968, **25**, 75.
10. Snyder, R. (Ed.) *Ethel Browning's Toxicity and Metabolism of Industrial Solvents* 2nd ed., 1987, Elsevier, Amsterdam, Netherlands.
11. Shuyaev, B. B. *Arch. Environ. Health* 1969, **18**, 878-882.
12. Kirwin, C. J. et al *J. Soc. Cosmet. Chem.* 1980, **31**, 367-370.
13. Brown, V. K. H. et al *Ann. Occup. Hyg.* 1967, **10**, 123.
14. Kzumikawa et al *Tokyo-to Kunkyo Kagaku Kenkyusho Nenpo* 1989, 36-43 (Japan.) (*Chem. Abstr.* **112**, 24938u).
15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
16. Tsuji M. et al *Oyo Yakuri* 1974, **8**(10), 1439

I85 isobutanol

$$CH_3CH(CH_3)CH_2OH$$

$C_4H_{10}O$ **Mol. Wt.** 74.12 **CAS Registry No.** 78-83-1

Synonyms 2-methyl-1-propanol; isobutyl alcohol; isopropylcarbinol; 2-methylpropyl alcohol

EINECS No. 201-148-0 **RTECS No.** NP 9625000

Uses Solvent in varnish remover and paint. Manufacturing esters for fruit flavouring essences.

Physical properties

M. Pt. –108°C **B. Pt.** 108°C **Flash point** 28°C (closed cup) **Specific gravity** 0.806 at 15°C
Partition coefficient log P_{ow} 0.76 **Volatility** v.p. 10 mmHg at 21.7°C ; v.den. 2.6
Solubility Water: 1 in 20. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

DE-MAK 100 ppm (310 mg m^{-3})
FR-VME 50 ppm (150 mg m^{-3})
JP-OEL 50 ppm (150 mg m^{-3})
SE-LEVL 50 ppm (150 mg m^{-3}) **SE-STEL** 75 ppm (250 mg m^{-3})
UK-LTEL 50 ppm (154 mg m^{-3}) **UK-STEL** 75 ppm (231 mg m^{-3})
US-TWA 50 ppm (152 mg m^{-3})

UN No. 1212 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation (R10, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking (S2, S16)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) ide 1520 mg l^{-1} (1).
LC_{50} (24 hr) goldfish 2600 mg l^{-1} (2).
LC_{50} (96 hr) bleak 1000-3000 mg l^{-1} (3).

Invertebrate toxicity

EC_{50} (24, 48 hr) *Daphnia magna* 1463 and 1439 mg l^{-1}, respectively, EC_{100} (24, 48 hr) *Daphnia magna* both 2143 mg l^{-1}, as determined by acute *Daphnia* test (4).
Daphnia sp. reproduction test to measure mortality of parent animals, the reproduction rate and the appearance of the 1st offspring, 21-day NOEC 3.4 mg l^{-1}, with the reproduction rate being the most affected (5).
EC_{50} (0-48 hr) *Scenedesmus subspicatus* 2300 mg l^{-1} cell multiplication test (6).
NOEC on biomass *Uronema paraduczi* (20 hr), *Pseudomonas putida* (16 hr) and *Entosiphon sulatum* (72 hr) 169-296 mg l^{-1} (7).
NOEC of growth *Microcystis aeruginosa, Scenedesmus quadricauda* (8 day) 290-350 mg l^{-1} (8).
EC_{50} (5 min) *Photobacterium phosphoreum* 1659 ppm Microtox test (9).

Toxicity to other species

Threshold for narcosis, tadpole 4000 mg l^{-1} (10).

Bioaccumulation

Does not bioaccumulate (11).

Environmental fate

Degradation studies

Oxidised to corresponding acid by *Desulfovibrio vulgaris* (12).
5-day BOD determined using acclimated mixed microbial cultures was 3.92 mg l^{-1} O_2 (13).
An oxygen requirement of 1.4 mg needed to oxidise 1 mg (14).
ThOD 37.4% (15).
Readily biodegradable. Degraded significantly within hours and does not persist beyond a few days (16).

Adsorption and retention

Low adsorption in soils and sediments. Liable to leaching (16).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2.46 g kg^{-1} (17).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (17).
LD_{50} dermal rabbit 3.4 g kg^{-1} (18).
LD_{50} intravenous rat 340 mg kg^{-1} (19).
LD_{50} intraperitoneal rabbit, rat 323, 720 mg kg^{-1}, respectively (19).

Sub-acute and sub-chronic data

Oral (4 month) Wistar rat 74 g l^{-1} as sole drinking liquid showed no adverse effect to liver. Oral (2 month) 148 g l^{-1} as sole drinking liquid showed reduction in liver size and also a reduction in fat, glycogen and RNA content of the liver (20).
Inhalation (4 month) rat, continuous exposure 3 mg m^{-3}. Depression of leg withdrawal response to electrical stimulation, minor changes to formed elements of blood and serum enzymes. Estimated NOEC level 0.1 mg m^{-3} (20).

Carcinogenicity and chronic effects

In a lifetime study, two groups of rats were given subcutaneous 0.05 ml kg^{-1} body weight twice a wk or oral 0.2 mg kg^{-1} body weight twice a wk. Both groups exhibited liver damage ranging from steatosis to cirrhosis. Subcutaneous group showed 8 animals with malignant tumours, 3 in the oral group and none in the control group. The majority of treated animals also showed hyperplasia in blood-forming tissues (20).

Teratogenicity and reproductive effects
No adequate data are available to assess teratogenicity or effects on reproduction (20).

Metabolism and toxicokinetics
Adsorbed through skin, lungs and gastro-intestinal tract. Metabolised by alcohol dehydrogenase to isobutyric acid, It may enter the tricarboxylic acid cycle. Small amounts are excreted unchanged or as glucuronide in urine. In rabbits metabolites in urine included acetaldehyde (21).

Irritancy
Eye rabbit (24 hr) 100 vol% severe irritation, 30 vol % moderate irritation 10-20 vol % mild irritation, Draize test (22).
Dermal rabbit (24 hr) 500 mg caused severe irritation (23).
Mildly irritating to eyes (details unspecified) (20).

Genotoxicity

Single intragastric administration at equitoxic dose. 0.2 LD_{50} induced chromosomal aberrations and polyploidy in rat bone marrow (24).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (25).
Included in Council of Europe, 1981, list of flavouring substances that can be included in food and beverages at 25 mg kg^{-1} without hazard to health (20).

Other comments

Occurs in emissions from wastewater treatment plants (26).
Found in fusel oil.
Produced by fermentation of carbohydrates.
Reviews on human health effects, experimental toxicology, physico-chemical properties, environmental effects, ecotoxicology, exposure levels and workplace experience listed (27).
Chemical properties, industrial uses and toxicity reviewed (28).

References

1. Junkhe, J. et al *Z. Wasser-Abwasser Forsch.* 1978, **11**, 161-164.
2. Bridie, A. L. et al *Water Res.* 1979, **13**, 623.
3. Linden et al *Chemosphere* 1979, **11/12**, 843-851.
4. Kuoehn, R. et al *Water Res.* 1989, **23**(4), 495-499.
5. Kuoehn, R. et al *Water Res.* 1989, **23**(4), 501-510.
6. Kuoehn, R. et al *Water Res.* 1990, **24**(1), 31-38.
7. Bringmann, G. et al *GWF, Gas- Wasserfach: Wasser/Abwasser* 1981, **122**(7), 308-312.
8. Bringmann, G. et al *Vom Wasser* 1978, **50**, 45-60.
9. Curtis, C. A. et al *Aquatic Toxicology and Hazard Assessment: 5th Conference* 1982, 170-178, Pearson, J. G. et al (Eds), ASTM STP766, American Society for Testing of Materials, Philadelphia, PA, USA.
10. Muoench, J. C. *Ind. Med.* 1972, **41**(4), 31-33.
11. Chiou, C. T. et al *Environ. Sci. Technol.* 1977, **11**(5), 475-478.
12. Tanaka *Arch. Microbiol.* 1990, **155**(1), 18-21.
13. Babeu, L. et al *J. Ind. Microbiol.* 1987, **2**(2), 107-115.
14. Nazarenko, I. O. *Sanit. Ochrana. Vodojemov at Zagrazen. Strochn. Vodami. M, Medgiz* 1969, **4**, 65-75.
15. Vaisnav, D. D. et al *Chemosphere* 1986, **16**(4), 695-703.
16. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1990, Lewis Publishers, Chelsea, MI, USA.
17. Smyth et al *Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
18. *Raw Material Data Handbook: Organic Solvents* 1974, Volume 1, National Association of Printing Ink Research Institute, Francis McDonald Sinclair Memorial Laboratory, Lehigh University, Bethlehem, PA, USA.
19. *Environ. Health Perspect.* 1985, *61*, 321.

20. WHO *Environmental Health Criteria 65* 1987, WHO, Geneva, Switzerland.
21. *Environmental Properties of Chemicals*, 1990, Research Report 91, 658-662 Ministry of the Environment, VAPK-Publishing, Helsinki, Finland.
22. Kennah, H. E. et al *Appl. Toxicol.* 1989, **12**(2), 258-268.
23. Lewis, R. J. *Sax's Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
24. Burilyak *Tsitol. Genet.* 1988, **22**(2), 49-52, (Russ.) (*Chem. Abstr.* **109** 68639b).
25. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
26. Hangartner, M. *Int. J. Environ. Anal. Chem.* 1979, **6**, 161-169.
27. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
28. Sejbl *Rudy* 1986, **34**(12), 364-367, (Czech.) (*Chem. Abstr.* **106**, 181925f)

I86 isobutene

$$CH_3C(CH_3)=CH_2$$

C_4H_8 **Mol. Wt.** 56.11 **CAS Registry No.** 115-11-7

Synonyms γ-butylene; isobutylene; 2-methylpropene; 1-propene-2-methyl

EINECS No. 204-066-3 **RTECS No.** UD 0890000

Uses Producing polymers and antioxidants for foods, packaging, food supplements and plastics. Production of high octane aviation gasoline.

Occurrence As minor environmental contaminant in urban air.

Physical properties

M. Pt. –140.3°C **B. Pt.** –6.9°C **Flash point** –76.1°C **Specific gravity** 0.5942 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.35 **Volatility** v.p. 400 mmHg at 21.6°C ; v.den. 2.01

Solubility Water: 263 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1055 **HAZCHEM Code** 2WE **Conveyance classification** flammable gas

Supply classification extremely flammable

Risk phrases Extremely flammable (R12)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Mammalian & avian toxicity

Acute data

LC_{50} (4 hr) inhalation rat 620 g m^{-3} (1).

LC_{50} (2 hr) inhalation mouse 415 g m^{-3} (1).

Mice (1-2 min) 50-70% isobutene resulted in immediate narcosis (2).

Inhalation mouse 30% no effect, 40% (7-8 min) excitement and narcosis (3).

Carcinogenicity and chronic effects

A study of 62 ♂ and 29 ♀ workers; 50% with ≥ 11 yr service in a plant producing isobutylene and other hydrocarbons had symptomatic effects including anaemia, reduction of peroxidase activity in granulocytes and granulocytopenia (4).

Exposure of rubber workers to isobutylene, combined with isoprene and chloromethane depressed succinate dehydrogenase activity in the immunocompetent blood cells (5).
Inhalation rat (Fisher 344), mouse ($B6C3F_1$) prechronic study in progress (6).

Metabolism and toxicokinetics
In vitro mice liver homogenates supplemented with NADH metabolised to 2-methyl-1,2-epoxypropene. The epoxidation is cytochrome P_{450}-dependent, concentrations reaching maximum after 20 min, and is followed by conversion into 2-methyl-1,2-propanediol and the glutathione conjugate by epoxide hydratase and glutathione *S*-transferase activity (7).
Inhalation rats, mice steady-state concentration was reached at 1200 ppm in rats and 1800 ppm in mice. At exposure concentrations of 500 ppm, rate of metabolism was directly proportional to its concentration. Metabolite detected 1,1-dimethyloxirane (8).

Genotoxicity

Butenes (isomer unspecified) in vapour phase, *Salmonella typhimurium* TA97, TA98, TA100 with and without metabolic activation negative (9).

Other effects

Other adverse effects (human)
Acute exposure to organic chemicals in humans and chronic poisoning resulting from occupational exposure caused narcotic effects. Isobutylene caused disorders of the hypothalamo-hypophyseal system which were manifested in abnormally increased basal levels of immunoreactive insulin and somatotropin in blood serum (10).

Any other adverse effects
Rubber which contains isobutylene may release anaesthetic and asphyxiant gases if isobutylene concentration is high (11).
Exposure of rats and mice to vapours of isobutylene showed concentrations found in brain, liver, kidney, spleen, perinephric fat, and hypodermic fat (12).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties and work place experience listed (13).
Explosion and fire risk. Butenes are weak anaesthetics and asphyxiant, and narcotic at high concentrations when heated to decomposition emits acrid smoke and irritating fumes.

References

1. Clayton, G. et al *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1982, **2B**, 3175-3220, John Wiley, New York, NY, USA.
2. von Oettingen, W. R. *Toxicity and Potential Dangers of Aliphatic and Aromatic Hydrocarbons* 1940, Public Health Bulletin No. 255.
3. Foss, P. *Ann. N. Y. Acad. Sci.* 1971, **180**, 126.
4. Khristeva, V. et al *Khig. Zdraveopaz.* 1985, **28**(6), 28-33 (Bulg.) (*Chem. Abstr.* **104**, 173617a).
5. Mamedov, A. M. et al *Azerb. Med. Zh.* 1985, **62**(1), 25-29 (Russ.) (*Chem. Abstr.* **102**, 225331h).
6. *Directory of Agents Being Tested for Carcinogenicity* 1992, IARC, Lyon, France.
7. Cornet, M. et al *Arch. Toxicol.* 1991, **65**(4), 263-267.
8. Csanady, G. A. *Arch. Toxicol.* 1991, **65**(2), 100-105.
9. Hughes, T. J. et al *Gov. Rep. Announce. Index (U.S.)* 1984, **84**(10), 65 (*Chem. Abstr.* **101**, 85417t).
10. Danilin, V. A. *Gig. Tr. Prof. Zabol.* 1983, **12**, 29-32 (Russ.) (*Chem. Abstr.* **100**, 197080p).
11. Hamilton, A. *Industrial Toxicology* 3rd ed., 1974, 345-348, Publ. Sci. Group, MA, USA.
12. Shugaev, B. B. *Arch. Environ. Health* 1969, **18**(6), 878-882.
13. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

187 isobutyl acetate

$$CH_3CO_2CH_2CH(CH_3)CH_3$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 110-19-0

Synonyms 2-methylpropyl acetic acid ester; acetic acid, isobutyl ester; 2-methylpropyl acetate; β-methylpropyl ethanoate

EINECS No. 203-745-1 **RTECS No.** AI 4025000

Uses Solvent, flavouring.

Occurrence Wood rotting fungus. Animal (cattle) waste.

Physical properties

M. Pt. -99°C **B. Pt.** 115-117°C **Flash point** 21°C (closed cup) **Specific gravity** 0.871 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.60 (1) **Volatility** v.p. 10 mmHg at 12.8°C ; v.den. 4.0

Solubility Water: 7.5 g l^{-1}. Organic solvents: ethanol

Occupational exposure

DE-MAK 100 ppm (480 mg m^{-3})

FR-VME 150 ppm (710 mg m^{-3}) **FR-VLE** 200 ppm (940 mg m^{-3})

SE-LEVL 100 ppm (500 mg m^{-3}) **SE-STEL** 150 ppm (700 mg m^{-3})

UK-LTEL 150 ppm (724 mg m^{-3}) **UK-STEL** 187 ppm (903 mg m^{-3})

US-TWA 150 ppm (713 mg m^{-3})

UN No. 1213 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Supply classification highly flammable

Risk phrases Highly flammable (R11)

Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Do not breathe vapour – Do not empty into drains – Take precautionary measures against static discharges (S2, S16, S23, S29, S33)

Ecotoxicity

Invertebrate toxicity

LOEC on reproduction (semichronic exposure) *Scenedemus quadricauda* 80 mg l^{-1} (2).

Toxicity threshold (cell multiplication inhibition test) *Pseudomonas putida, Microcystis aeruginosa* 200-205 mg l^{-1} (2,3).

Toxicity threshold (cell multiplication inhibition test) *Entosiphon sulcatum, Uronema parduczi* 411-727 mg l^{-1} (2,4).

Environmental fate

Degradation studies

Filtered sewage seed (5 and 20 day) theoretical BOD 60 and 81%, respectively, in fresh water and 23 and 37%, respectively, in salt water (5).

Significantly biodegradable suggesting soil microbial action (6).

Abiotic removal

$t_{1/2}$ for vapour phase reaction with photochemically produced hydroxyl radicals (average concentration 5×10^5 molecules cm^{-3}) in the atmosphere is about 6 hr (7).

Chemical hydrolysis may be important at ≥pH 9 (6).

Volatilisation $t_{1/2}$ from a 1 m deep river, flowing at 1 m sec^{-1} with a wind velocity of 3 m sec^{-1} estimated to be 5.3 hr (6).

Adsorption and retention
Moderate to high soil leaching based on K_{oc} values of 36 and 177 (8,9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 13,400 mg kg^{-1} (10).
LD_{50} oral rabbit 4763 mg kg^{-1} (11).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (12).

Irritancy
Dermal (24 hr) rabbit 500 mg caused moderate to severe erythema and moderate oedema and 500 mg instilled into rabbit eye (24 hr) caused moderate irritation (13).

Other comments

Reviews on human health effects, epidemiology, workplace experience, experimental toxicology, safety test data and exposure conditions listed (14).

References

1. *GEMS: Graphic Exposure Modeling System* CLOGP3 Program, Office of Toxic Substances, US EPA, 1989.
2. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
3. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9) (Ger.).
4. Bringmann, G. et al *Z. Wasser/Abwasser Forsch.* 1980, **1**, 26-31.
5. Price, K. S. *J. Water Pollut. Control Fed.* 1974, **46**, 63.
6. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1990, **II**, 290-295, Lewis Publications, Chelsea, MI, USA.
7. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
8. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods. Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
9. Swann, R. L. et al *Res. Rev.* 1983, **85**, 17.
10. *Raw Material Data Handbook: Organic Solvents* 1974, **1**, 8, National Association of Printing Ink Research Institute, Francis McDonald Sinclair Memorial Laboratory, Lehigh University, Bethlehem, PA, USA.
11. *Ind. Med. Surg.* 1972, **41**, 31.
12. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
13. *Food Cosmet. Toxicol.* 1978, **16**, 637.
14. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

188 isobutyl acrylate

$$CH_2{=}CHCO_2CH_2CH(CH_3)CH_3$$

$C_7H_{12}O_2$ **Mol. Wt.** 128.17 **CAS Registry No.** 106-63-8
Synonyms 2-methylpropyl 2-propenoic acid ester; acrylic acid, isobutyl ester; isobutyl 2-propenoate
EINECS No. 203-417-8 **RTECS No.** AT 2100000

Physical properties

B. Pt. 61-63°C at 15 mmHg **Flash point** 30°C (open cup) **Specific gravity** 0.9 (liquid) **Volatility** v.den. 0.9

Occupational exposure

UN No. 2527 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation and in contact with skin – Irritating to the skin – May cause sensitisation by skin contact (R10, R20/21, R38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Avoid contact with the skin – Wear suitable gloves (S2, S9, S24, S37)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 2.09 mg l^{-1} (1).
5 ppm caused death in 1, 7 or 23 hr in trout, bluegill sunfish and goldfish, respectively. Test conditions: pH 7; dissolved oxygen content 7.5 ppm; total hardness (soap method) 300 ppm; methyl orange alkalinity 310 ppm; free carbon dioxide 5 ppm; temperature 12.8°C (2).
2-5 mg l^{-1} steelhead trout, bridgelip sucker, stickleback caused death within 5 hr of exposure. Test conditions: artesian well water; total hardness 67-120 mg l^{-1}; methyl orange alkalinity 151-183 mg l^{-1}; total dissolved solids 160-175 mg l^{-1}; pH 7.1 (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 6106, 7070 mg kg^{-1}, respectively (4,5).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (6).
LD_{50} dermal rabbit 890 mg kg^{-1} (6).
LD_{50} intraperitoneal rat, mouse 654, 760 mg kg^{-1}, respectively (7,8).

Irritancy
Dermal rabbit (duration unspecified) 500 mg open to atmosphere caused mild irritation (6).

Genotoxicity

Salmonella typhimurium TA 98, TA100, TA1535, TA1537 with and without metabolic activation negative (9).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (10).
Toxicity and hazards reviewed (11).

References

1. Russom, C. L. *Bull. Environ. Contam. Toxicol.* 1988, **4**, 589-596.
2. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, PB 87-200-275, Washington, DC, USA.
3. *Fish Toxicity Screening Data* 1989, EPA 560/6-89-001, PB 89-156715, Washington, DC, USA.
4. *Toxicol. Lett.* 1982, **11**, 125.
5. *Toxicol. Appl. Pharmacol.* 1974, **28**, 313.
6. *Union Carbide Data Sheet* 28-3-68, Industrial Medicine and Toxicology Department, Union Carbide Corp., New York, NY, USA.
7. *Arch. Mal. Prof. Med. Trav. Secur. Soc.* 1975, **36**, 58.
8. *J. Dent. Res.* 1975, **51**, 526.
9. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(9), 1-109.
10. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
11. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(6), 65-67

189 isobutylamine

$$CH_3CH(CH_3)CH_2NH_2$$

$C_4H_{11}N$ **Mol. Wt.** 73.14 **CAS Registry No.** 78-81-9

Synonyms 2-methyl-1-propanamine; 2-methylpropylamine; monoisobutylamine; Valamine

EINECS No. 201-145-4 **RTECS No.** NP 9900000

Uses Organic synthesis. In the manufacture of insecticides.

Occurrence In various species of marine algae and Latakia tobacco leaves.

Physical properties

M. Pt. –85°C **B. Pt.** 64-71°C **Flash point** –20°C **Specific gravity** 0.724 at 25°C with respect to water at 4°C

Partition coefficient log P_{ow} 0.73 **Volatility** v.p. 100 mmHg at 20°C ; v.den. 2.5

Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (15 mg m^{-3})

UN No. 1214 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive

Ecotoxicity

Fish toxicity

LC_0 creek chub (24 hr) 20 mg l^{-1}, LC_{100} creek chub (24 hr) 60 mg l^{-1} (1).

Environmental fate

Degradation studies

Utilised by *Aspergillus versicolor* as a nitrogen source, but only amines with alkyl chains ≥5 carbon atoms long supported significant growth in absence of a separate carbon substrate (2).

Confirmed to be biodegradable (3).

Adsorption and retention

Not expected to be significantly adsorbed onto sediments or soils, therefore leaching is possible (4).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

LD_{50} (14 day) oral ♂, ♀ rat 224 and 232 mg kg^{-1}, respectively (5).

Irritancy

In humans skin contact can result in erythema and blistering (6).

Other effects

Other adverse effects (human)

Inhalation causes headache, dryness of nose and throat (6).

Any other adverse effects

Upper airway irritation, RD_{50} inhalation mouse 91 ppm. Pulmonary toxicity, RD_{50} tracheally cannulated inhalation mouse 406 ppm (7).

Other comments

Reviews on human health effects, epidemiology, workplace experience and experimental toxicology listed (8).

Has been detected in air samples from "sick-building syndrome" workplaces. Pollution from isobutylamine has been attributed to biodegradation of casein by alkali-resistant *Clostridium* (9).

References

1. Gillette, L. A. et al *Sewage Ind. Wastes* 1952, **24**(11), 1397-1401.
2. Lindley, N. D. *Appl. Environ. Microbiol.* 1987, **53**(2), 246-248.
3. *The list of the existing chemical substances tested on biodegradability by microorganisms of bioaccumulation in fish bodies* 1987, Chemicals Inspection and Testing Institute, Japan.
4. Howard, P. H. *Handbook of Environmental Fate and Exposure Data for Organic Chemicals* 1990, Lewis Publishers, Chelsea, MI, USA.
5. Cheever, K. L. et al *Toxicol. Appl. Pharmacol.* 1982, **62** 150.
6. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
7. Gagnair, F. et al *J. Appl. Toxicol.* 1989, **9**(5), 301-4.
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
9. Karlsson et al *Mater. Struct.* 1989, **22**(129), 163-169

190 isobutyl formate

$$HCO_2CH_2CH(CH_3)CH_3$$

$C_5H_{10}O_2$ **Mol. Wt.** 102.13 **CAS Registry No.** 542-55-2

Synonyms formic acid, 2-methylpropyl ester; formic acid, isobutyl ester; 2-methylpropyl formate

EINECS No. 208-818-1 **RTECS No.** LQ 8650000

Physical properties

M. Pt. –95°C **B. Pt.** 98°C **Flash point** 5°C **Specific gravity** 0.885 at 20°C with respect to water at 4°C

Volatility v.den. 3.5

Solubility Water: 1 in 100. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 2393 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3.06 g kg^{-1} (1).

References

1. *Ind. Med. Surg.* 1972, **41**, 31

191 isobutyl isobutyrate

$$CH_3CH(CH_3)CO_2CH_2CH(CH_3)CH_3$$

$C_8H_{16}O_2$ **Mol. Wt.** 144.21 **CAS Registry No.** 97-85-8

Synonyms 2-methylpropanoic acid, 2-methylpropyl ester; isobutyric acid, isobutyl ester; isobutyl isobutanoate; 2-methylpropyl isobutyrate

EINECS No. 202-612-5 **RTECS No.** NQ 5250000

Physical properties

M. Pt. –81°C **B. Pt.** 147°C **Flash point** 38°C **Specific gravity** 0.850-0.860 at 20°C with respect to water at 20°C **Volatility** v.p. 10 mmHg at 39.9°C ; v.den. 5.0
Solubility Organic solvents: miscible with ethanol

Occupational exposure

UN No. 2528 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 128 g kg^{-1} (1).
LD_{50} (6 hr) inhalation rat 5000 ppm (1).

References

1. *Raw Material Data Handbook: Organic Solvents* 1974, Volume 1, National Association of Printing Ink Research Institute, Francis McDonald Memorial Laboratory, Lehigh University, Bethlehem, PA, USA

192 isobutyl methacrylate

$$CH_2=C(CH_3)CO_2CH_2CH(CH_3)CH_3$$

$C_8H_{14}O_2$ **Mol. Wt.** 142.20 **CAS Registry No.** 97-86-9

Synonyms 2-methyl-2-propenoic acid, 2-methylpropyl ester; methacrylic acid, isobutyl ester; isobutyl α-methylacrylate; 2-methylpropyl methacrylate

EINECS No. 202-613-0 **RTECS No.** OZ 4900000

Uses Monomer for acrylic resins. To make concrete water repellant. Manufacture of contact lenses.

Physical properties

B. Pt. 155°C **Flash point** 41°C (closed cup) **Specific gravity** 0.886 at 20°C **Partition coefficient** log P_{ow} 2.66
Volatility v.p. 1.8 mmHg at 20°C ; v.den. 4.9
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

SE-LEVL 50 ppm (300 mg m^{-3}) **SE-STEL** 75 ppm (450 mg m^{-3})

UN No. 2283 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification irritant
Risk phrases Flammable – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact (R10, R36/37/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – Wear suitable gloves (S2, S24, S37)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 38 mg l^{-1} (1).

Bioaccumulation
A calculated bioconcentration factor of 62 indicates that bioaccumulation in aquatic organisms is unlikely (2).

Environmental fate

Degradation studies
Will undergo significant biodegradation according to the MITI test (biodegradation test of the Japanese Ministry of International Trade and Industry) (3).

Abiotic removal
Based on the hydrolysis of methylmethacrylate it may be susceptible to hydrolysis especially in alkaline soils (4).
It will significantly volatilise from water $t_{1/2}$ 5.62 hr (estimate model river) (2).
Volatilisation $t_{1/2}$ 4.2 day model pond (5).

Adsorption and retention
Has low mobility in soil, it is therefore possible that it may slowly leach into ground water (2,6,7).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 12 g kg^{-1} (8).
LD_{50} intraperitoneal mouse 1.34 g kg^{-1} (9).

Teratogenicity and reproductive effects
Has some developmental toxicity in rats (details not stated), calculated to have no human risk (10).
Pregnant rats on days 5, 10 and 15 of gestation, doses of 1/10, 1/5 or 1/3 of their individual acute LD_{50} values generally produced a dose-related increase in resorptions and gross and skeletal abnormalities, foetal birth weight also decreased (11).

Irritancy
Vapour mist is lachrymatory and irritating to the eyes and also irritating to the skin; it may be harmful if absorbed through the skin (species not specified) (12).

Genotoxicity

Salmonella typhimurium TA 98, TA100, TA1535, TA1537 with and without metabolic activation negative (13).

Other effects

Other adverse effects (human)
Harmful if swallowed, inhaled or absorbed through the skin (12).

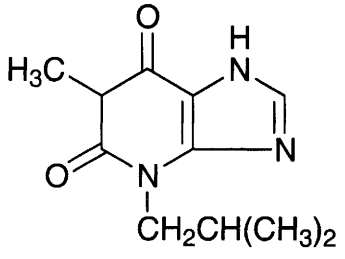
Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (14).
Occupational exposure occurs during production of synthetic fingernails (15).

References

1. Russom, C. L. et al *Bull. Environ. Contam. Toxicol.* 1988, **41**, 589-596.
2. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods: Environmental Behaviour of Organic Compounds* 1982, 5-29, McGraw-Hill, NY, USA.
3. Susaki, S. *Aquatic Pollutants Transformation and Biological Effects* 1978, 283-298, Pergamon Press, Oxford, UK.
4. Ellington, J. J. et al *Measurement of Hydrolysis Rate Constants for Evaluation of Hazardous Wastes* US EPA-600/3-88/028, 1988, 18.
5. *US EPA; EXAMS II Computer Simulations* 1987.
6. Hansch, C. et al *Medchem Project Issue No. 26* 1985, Pomona College, Claremont, CA, USA.
7. Swann, R. L. et al *Res. Rev.* 1983, **85**, 17-28.
8. *Toxicol. Lett.* 1982, **11**, 125.
9. *J. Pharm. Sci.* 1973, **62**, 778.
10. Jelovsek, F. R. et al *Obstet. Gynecol.* 1989, **74**(4), 624-636.
11. Singh, A. R. et al *J. Dent. Res.* 1972, **51**(6), 1632-1638.
12. *Chemical Safety Data Sheets* 1990, **3**, 39, The Royal Society of Chemistry, London, UK.
13. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(9), 1-109.
14. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
15. Crable, J. V. et al *Appl. Ind. Hyg.* 1986, **1**(4), 200

193 isobutylmethylxanthine



$C_{10}H_{14}N_4O_2$ **Mol. Wt.** 222.25 **CAS Registry No.** 28822-58-4

Synonyms 3,7-dihydro-1-methyl-3-(2-methylpropyl)-1*H*-purine-2,6-dione; 3-isobutyl-1-methylxanthine; methylisobutylxanthine

EINECS No. 249-259-3 **RTECS No.** ZD 8500000

Physical properties

M. Pt. 200-201°C

Other effects

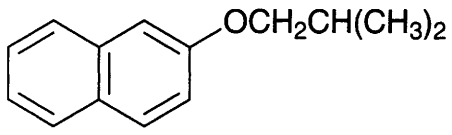
Any other adverse effects

Rat pups 7-10 days old, transient exposure (dose, route not specified) can cause learning impairments and other undesirable behavioural consequences (1).

References

1. Neal, B. S. *Psychopharmacology (Berlin)* 1991, **103**(3), 388-397

194 isobutyl 2-naphthyl ether



$C_{14}H_{16}O$ **Mol. Wt.** 200.28 **CAS Registry No.** 2173-57-1

Synonyms 2-(2-methylpropoxy)naphthalene; 2-isobutoxynaphthalene

EINECS No. 218-529-2 **RTECS No.** KO 1255000

Physical properties

M. Pt. 30-33.5°C **B. Pt.** 304.5-307°C

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 4.75 g kg^{-1} (1).

References

1. *Food Cosmet. Toxicol.* 1964, **2**, 327

195 isobutyl propionate

$$CH_3CH_2CO_2CH_2CH(CH_3)CH_3$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 540-42-1

Synonyms 2-methylpropyl propanoic acid ester; propionic acid, isobutyl ester; isobutyl propanoate; 2-methylpropyl propanoate; 2-methylpropyl propionate

EINECS No. 208-746-0 **RTECS No.** UF 4930000

Uses Manufacture of fruit essences.

Physical properties

M. Pt. –71°C **B. Pt.** 137°C **Flash point** 26°C **Specific gravity** 0.888 at 20°C with respect to water at 4°C

Solubility Organic solvents: miscible with ethanol

Occupational exposure

UN No. 2394 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Risk phrases Flammable (R10)

Safety phrases Keep out of reach of children (if sold to general public) (S2)

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit 5.60 g kg^{-1} (1).

References

1. *Ind. Med. Surg.* 1972, **41**, 31

196 isobutyl vinyl ether

$$CH_2=CHOCH_2CH(CH_3)CH_3$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 109-53-5

Synonyms vinyl isobutyl ether; 1-(ethenyloxy)-2-methylpropane

EINECS No. 203-678-8 **RTECS No.** KO 1300000

Uses Organic synthesis. Manufacture of polymers.

Physical properties

M. Pt. –112°C **B. Pt.** 82.9-83.2°C **Flash point** –9°C **Specific gravity** 0.76 at 25°C with respect to water at 4°C **Volatility** v.den. 3.45

Occupational exposure

UN No. 1304 (inhibited) **HAZCHEM Code** 3YE (inhibited) **Conveyance classification** flammable liquid (inhibited)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 17,000 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 16,000 ppm (1).
LD_{50} dermal rabbit 20,000 mg kg^{-1} (1,2).

Metabolism and toxicokinetics

May be adsorbed by inhalation, injection or through the skin (species unspecified) (2).

Irritancy

Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (2).

References

1. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
2. Lenga, R. E. *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 2020, Sigma-Aldrich, Milwaukee, WI, USA

197 isobutyraldehyde

$CH_3CH(CH_3)CHO$

C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 78-84-2

Synonyms 2-methylpropanal; isobutanal; methylpropanal; isopropyl aldehyde; isopropylformaldehyde; 2-methylpropionaldehyde

EINECS No. 201-149-6 **RTECS No.** NQ 4025000

Uses Synthesis of pantothenic acid, plasticisers, resins, cellulose esters.

Physical properties

M. Pt. –65.9°C **B. Pt.** 64°C **Flash point** <–18°C (open cup) **Specific gravity** 0.7938 at 20°C with respect to water at 4°C **Volatility** v.p. 98.3 mmHg at 12.9°C ; v.den. 2.5
Solubility Water: 110 g l^{-1}. Organic solvents: miscible with acetone, benzene, carbon disulfide, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2045 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity
5 ppm (24 hr) no toxic effects on trout, bluegill sunfish, yellow perch or goldfish. Test conditions: pH 7; dissolved oxygen content 7.5 ppm; total hardness (soap method) 300 ppm; methyl orange alkalinity 310 ppm; free carbon dioxide 5 ppm; and temperature 12.8°C (1).

Environmental fate

Degradation studies
Confirmed to be biodegradable (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3.7 g kg^{-1} (3).
LC_{50} (2 hr) inhalation mouse 39500 mg m^{-3} (4).
LD_{50} dermal rabbit 7.13 g kg^{-1} (3).

Carcinogenicity and chronic effects
National Toxicology Program studied inhalation Fisher 344 rat, B6C3F_1 mouse 500, 1000 or 2000 ppm in air. No evidence of carcinogenic activity (5).

Teratogenicity and reproductive effects
Rat (13 wk) inhalation 500, 1000, 2000, 4000 ppm reduced body weight, epididymis and cauda epididymis weight. No effect on testis weight. Mice (13 wk) inhalation 500, 1000, 2000 ppm no effect on any of the above (6).

Irritancy
Dermal rabbit (duration not stated) 397 mg open to atmosphere mild irritation (7).
Dermal rabbit (24 hr) 500 mg severe irritation (8).
Eye rabbit (24 hr) 100 mg moderate irritation (8).

Sensitisation
May cause sensitisation (species not specified) (9).

Genotoxicity

Mouse (13 wk) inhalation 500, 1000, 2000 ppm, rat (13 wk) inhalation 500, 1000, 2000, 4000 ppm no effects on sperm motility, density or morphology (6).
Salmonella typhimurium TA 98, TA100, TA1535, TA1537 with and without metabolic activation negative (10).
Salmonella typhimurium G46, TA100, *Escherichia coli* WP2, WP2 *uvrA*$^-$ without metabolic activation, base pair substitution mutation (11).

Other effects

Any other adverse effects
Based on inhalation studies will cause central nervous system depression (as in alcohol intoxication) if swallowed (species not specified) (12).

Other comments

Recommended for sub-chronic toxicity testing under the US Federal Toxic Substances Control Act (13).
Autoignition temperature 223.33°C.

References

1. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, PB 87-200-275, Washington, DC, USA.
2. *The list of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body.* 1987, Chemicals Inspection and Testing Institute, Japan.
3. Smyth et al *Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
4. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
5. *National Toxicology Program Research and Testing Division* 1999, Report No. TR 472, NIEHS, Research Triangle Park, NC, USA.
6. Morrisey, R. E. et al *Fundam. Appl. Toxicol.* 1988, **11**(2), 343-358.
7. *Union Carbide Data Sheet* 3/11/71, Industrial Medicine and Toxicology Dept., Union Carbide Corp., New York, NY, USA.
8. Sax, N. I. et al *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
9. *Chemical Safety Data Sheets* 1992, **5**, 159-161, The Royal Society of Chemistry, London, UK.
10. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
11. McMahon, R. E. et al *Cancer Res.* 1979, **39**, 682-693.
12. Gosselin, R. E. et al *Chemical Toxicology of Commercial Products* 5th ed., 1984, Williams and Wilkins, Baltimore, MD, USA.
13. *Fed. Regist.* 1991, **56**(44), 9534-9572

198 isobutyric acid

$$CH_3CH(CH_3)CO_2H$$

$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 79-31-2

Synonyms 2-methylpropanoic acid; dimethylacetic acid; isobutanoic acid; isopropylformic acid; 2-methylpropionic acid

EINECS No. 201-195-7 **RTECS No.** NQ 4375000

Physical properties

M. Pt. –47°C **B. Pt.** 152-155°C **Flash point** 55°C (open cup) **Specific gravity** 0.950 at 20°C with respect to water at 4°C **Volatility** v.p. 1 mmHg at 14.7°C ; v.den. 3.0
Solubility Water: 1 in 6. Organic solvents: miscible with chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2529 **HAZCHEM Code** 2X **Conveyance classification** flammable liquid, corrosive
Supply classification harmful
Risk phrases Harmful in contact with skin and if swallowed (R21/22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Invertebrate toxicity
EC_{50} *Chlorella pyrenoidosa* 345 mg l^{-1} toxic (1).

Environmental fate

Degradation studies
Desulfococcus multivorum utilised isobutyrate as sole carbon source. In the presence of fresh water and marine sediments and sludge degraded to acetate and methane (2).

Mammalian & avian toxicity

Acute data
LD_{50} (estimated) oral redwing blackbird >100 mg kg^{-1} (3).
LD_{50} oral rat 280 mg kg^{-1} (4).
LD_{50} dermal rabbit 500 mg kg^{-1} (4).
LC_{50} (duration unspecified) inhalation rat 400->800 mg kg^{-1} (5).

Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (6). Toxicology in relation to water pollution and waste water treatment reviewed (7).

References

1. Jones, H. R. *Environmental Control in the Organic and Petrochemical Industries* 1971, Noyes Data Corporation.
2. Stieb, M. et al *Arch. Microbiol.* 1989, **51**(2), 126-132.
3. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
4. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
5. Patty, F. A. *Industrial Hygiene and Toxicology* 1967, Vol. 2, Interscience Publishers, New York, NY, USA.
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
7. Speece, R. E. et al *Int. Conf. Innovative Biol. Treat. Toxic. Wastewaters* 1986, 37-64, Scholze R. J. (Ed.), NTIS, Springfield, VA, USA

199 isobutyronitrile

$$CH_3CH(CH_3)CN$$

C_4H_7N **Mol. Wt.** 69.11 **CAS Registry No.** 78-82-0
Synonyms 2-methylpropanitrile; 2-cyanopropane; dimethyl acetonitrile; isopropyl cyanide; isopropyl nitrile
EINECS No. 201-147-5 **RTECS No.** TZ 4900000

Physical properties

M. Pt. –72°C **B. Pt.** 107-108°C **Flash point** 3°C **Specific gravity** 0.773 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} 0.46 **Volatility** v.den. 2.4
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2284 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic

Ecotoxicity

Toxicity to other species
LD_{Lo} subcutaneous frog 4800 mg kg^{-1} (1).

Environmental fate

Degradation studies
Pseudomonas putida utilised as sole source of carbon and nitrogen (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 102 mg kg^{-1} (3).
LC_{Lo} (4 hr) inhalation rat 1000 ppm (4).
LD_{50} dermal rabbit 310 mg kg^{-1} (4).
LD_{Lo} subcutaneous rabbit 9 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral mouse, rat 6-month study (dose not specified) isobutyronitrile was moderately cumulative and affected blood indices, organ enzymes and nervous system (5).

Teratogenicity and reproductive effects
Oral mouse, rat 6-month study (dose not specified). No embryotoxicity or teratogenic action was observed (5).

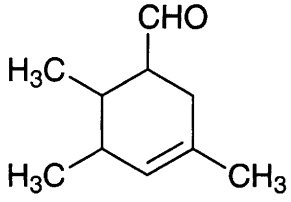
Other comments

Reviews on human health effects, experimental toxicology and exposure listed (6).
Inhaled organonitriles are substantially detoxified by microsomal metabolism in the nasal cavity (7).

References

1. *Arch. Int. Pharmacodyn. Ther.* 1899, **5**, 161.
2. Nawaz, M. S. *Appl. Environ. Microbiol.* 1989, **55**(9), 2267-2274.
3. *Union Carbide Data Sheet* 29-10-59, Industrial Medicine and Toxicology Department, Union Carbide Corp., New York, NY, USA.
4. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
5. Fomochkin, I. P. et al *Gig. Sanit.* 1988, (10), 77-78 (Russ), (*Chem. Abstr.* **110**, 34923h).
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
7. Dahl, A. R. *Xenobiotica* 1989, **19**(11), 1201-1205

I100 isocyclocitral



$C_{10}H_{16}O$ **Mol. Wt.** 152.24 **CAS Registry No.** 1335-66-6

Synonyms 1-formyl-3,5,6-trimethyl-3-cyclohexene; 1,3,4-trimethylcyclohex-1-ene-4-carboxaldehyde; 3,5,6-trimethyl-3-cyclohexene-1-carboxaldehyde

EINECS No. 215-638-7 **RTECS No.** GW 3400000

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4500 mg kg^{-1} (1).

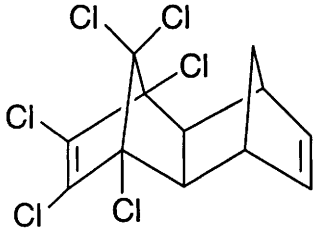
Irritancy

500 mg applied to rabbit skin for 24 hr caused mild irritation (1).

References

1. *Food Chem. Toxicol.* 1976, **14**, 313

I101 isodrin



$C_{12}H_8Cl_6$ **Mol. Wt.** 364.91 **CAS Registry No.** 465-73-6

Synonyms 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-*endo,endo*-dimethanonaphthalene; ENT 19244; Compound 711; RCRA waste number P060

EINECS No. 207-366-2 **RTECS No.** IO 1925000

Uses Superseded insecticide.

Physical properties

M. Pt. 240-242°C

Occupational exposure

Supply classification very toxic
Supply classification dangerous for the environment
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R26/27/28, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – After contact with skin, wash immediately with plenty of water – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S13, S28, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} fathead minnow, bluegill sunfish 0.006-0.012 mg l^{-1} (1).

Invertebrate toxicity
Moderately toxic to grasshopper (details unspecified) (2).
LD_{50} (duration unspecified) house fly 0.054 μg fly^{-1} (isodrin), 0.113 μg fly^{-1} (photoisodrin) (3).
LD_{50} (duration unspecified) mosquito larvae 0.019 ppm (isodrin), 0.058 ppm (photoisodrin) (3).
LC_{50} (48 hr) *Spodoptera litura* (Fibricius) 0.00524 g 100 ml^{-1} (4).

Environmental fate

Abiotic removal
Converted into photoisodrin by sunlight and UV light (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 7, 8.8 mg kg^{-1}, respectively (6,7).
LD_{50} dermal rat 23 mg kg^{-1} (6).
LD_{Lo} intraperitoneal mouse 6.4 mg kg^{-1} (8).
Chicken embryos injected with 10-500 ppm, isodrin was the most toxic of 25 organochloride compounds tested. The toxicity was greater in starved chicks than in fed chicks (9).

Legislation

Land disposal prohibited under US Federal Resource Conservation and Recovery Act (10).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).
Reportable quantity regulated under the US Federal Comprehensive Environmental Response, Compensation and Liability Act (13).
Quality objective under EC Directives 86/280/EEC and 88/347/EEC 0.005 μg l^{-1} for all waters. A 'standstill' provision applies to concentrations in sediments, molluscs, shellfish and for fish (14).

Other comments

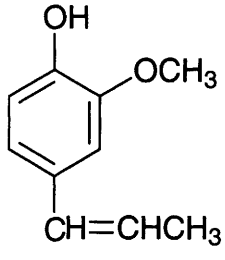
Isodrin applied as a spray was the most toxic of a selection of cyclodiene insecticides tested against larvae of tobacco budworm (15).
Pretreatment with 2.5 μg fly^{-1} sesamex synergised isodrin toxicity. This synergism appeared to be related to the inhibition of its detoxification by a system which can be stimulated by phenobarbital (16).
Isodrin is converted into photoisodrin by sunlight and UV light. Unlike photoisomers of aldrin, dieldrin and heptachlor, photoisodrin is less toxic to house flies and the mosquito *Aedes aegypti* due to its rapid detoxification.

Photoisodrin is 3-5 times slower than isodrin in its toxicity to *Daphnia pulex, Asellus* sp., *Gammarus* sp., *Cambarus* sp., *Gambia affinis, Pimephales promelas* and *Lepomis macrochirus* (5).
Hazards reviewed (17).
The photoisomer is less toxic, partly due to its more rapid metabolism (18,19).

References

1. Khan, M. A. Q. et al *Arch. Environ. Contam. Toxicol.* 1973, **1**(2), 159-169.
2. Olaifa, J. I. *Insect Sci. Its Appl.* 1986, **7**(2), 135-138.
3. Rosen, J. D. et al *J. Agric. Food Chem.* 1969, **17**(2), 404-405.
4. Mukherjee, A. B. et al *Indian J. Entomol.* 1970, **32**(3), 251-255.
5. Georgacakis, E. et al *Bull. Environ. Contam. Toxicol.* 1971, **6**(6), 535-538.
6. *World Rev. Pest Control* 1970, **9**, 119.
7. *Gig. Tr. Prof. Zabol.* 1964, **8**(4), 30.
8. *Toxicol. Appl. Pharmacol.* 1972, **23**, 288.
9. Dunachie, J. F. et al *Ann. Appl. Biol.* 1969, **64**(3), 409-423.
10. US EPA *Fed. Regist.* 1991, **56**(21), 3864-3928.
11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
13. *Fed. Regist.* 14 Aug 1989, **54**(155), 33462-33484.
14. *DoE Circular 7/89: Water and the environment. The implementation of EC directives on pollution caused by certain dangerous substances discharged into the aquatic environment* 1989, HMSO, London, UK.
15. Wolfenbarger, D. A. et al *J. Econ. Entomol.* 1970, **63**(5), 1563-1573.
16. Khan, M. A. Q. et al *J. Econ. Entomol.* 1970, **63**(2), 470-475.
17. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(6), 72-75.
18. Rosen, J. D. et al *J. Agric. Food Chem.* 1969, **17**(2), 404-405.
19. Georgacakis, E. et al *Nature (London)* 1971, **233**(5315), 120-1211

I102 isoeugenol



$C_{10}H_{12}O_2$ **Mol. Wt.** 164.20 **CAS Registry No.** 97-54-1

Synonyms 2-methoxy-4-(1-propenyl)phenol; 4-hydroxy-3-methoxy-1-propenylbenzene; 4-propenylguaiacol; NCI-C6 0979; FEMA No.2468

EINECS No. 202-590-7 **RTECS No.** SL 7875000

Uses In vanillin manufacture.
Occurrence In ylang ylang and other essential oils. In cigarette smoke condensate.

Physical properties

M. Pt. -10°C **B. Pt.** 266°C **Specific gravity** 1.08 at 25°C with respect to water at 4°C
Solubility Water: slightly soluble. Organic solvents: miscible with diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1560 mg kg^{-1} (1).

LD_{50} oral guinea pig 1410 mg kg^{-1} (2).

Sensitisation

Induces allergic contact dermatitis (species unspecified) (3).

Positive in guinea pig maximisation test (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (5).

Induced sister chromatid exchanges in human lymphocytes *in vitro* (6).

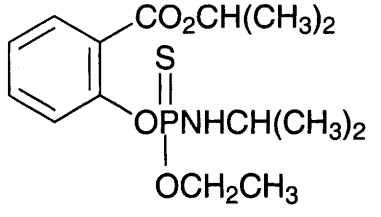
Other comments

Selected for general toxicology study by US National Toxicology Program (7).

References

1. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1964, **2**, 327.
2. *Toxicol. Appl. Pharmacol.* 1964, **6**, 378.
3. Sekine, M. et al *Nippon Hifuka Gakkai Zasshi* 1988, **98**(5), 513-519 (Japan.) (*Chem. Abstr.* **109**, 228065e).
4. Maurer, T. et al *Food Chem. Toxicol.* 1989, **27**(12), 807-811.
5. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
6. Jansson, T. et al *Mutat. Res.* 1986, **169**, 129-139.
7. *National Toxicology Program Research and Testing Division Management Status Report* 1999, NIEHS, Research Triangle Park, NC, USA

I103 isofenphos



$C_{15}H_{24}NO_4PS$ **Mol. Wt.** 345.40 **CAS Registry No.** 25311-71-1

Synonyms 2-[[ethoxy[(1-methylethyl)amino]phosphinothioyl]oxy] benzoic acid, 1-methylethyl ester; isophenphos; Amaze; Oftanol; Isofos

EINECS No. 246-814-1 **RTECS No.** VO 4395500

Uses Systemic insecticide.

Physical properties

M. Pt. <–12°C **Specific gravity** 1.13 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 4.12

Volatility v.p. 4×10^{-6} mmHg at 20°C

Solubility Water: 23.8 mg kg^{-1} at 20°C. Organic solvents: acetone, benzene, cyclohexanone, dichloromethane, diethyl ether, ethanol

Occupational exposure

Supply classification toxic
Risk phrases Toxic in contact with skin and if swallowed (R24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rudd, orfe, goldfish, carp 1-4 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (5 min) *Photobacterium phosphoreum* 97.3 ppm Microtox test (2).

Environmental fate

Degradation studies
Persistence and degradation strongly affected by interaction of pH, soil temperature and moisture; degradation is greatest at higher temperatures (35>25>15°C) (except at alkaline pH), medium moisture (25>20>15%) and in both acidic (pH 6) and alkaline (pH8) compared with neutral soils (3).
An *Arthrobacter* isolated from soil with a history of isofenphos use rapidly metabolised isofenphos in pure culture (4).
Treatment of soil with 10 ppm enhanced microbial activity within 6 wk by up to 100×; time to non-detectability of enhanced activity was >164 wk (5).
Treatment with manure increases persistence in soil due to binding effect of organic matter decreasing availability for microbial degradation (6).

Adsorption and retention
Insecticidal activity of isofenphos detectable 2 wk after initial application to clay loam in May and was still present the following spring (7).
Soil mobility in relation to organic matter, clay, cation exchange capacity, pH, water-holding capacity and log P_{ow} reviewed. Soil mobility expressed as R_f varied from 0.09 for clay loam and silty clay loam, to 0.16 for silt loam and sandy loam (8).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken, quail 3, 13 mg kg^{-1}, respectively (9,10).
LD_{50} oral rat 28 mg kg^{-1} (11).
LC_{50} (4 hr) inhalation rat 0.144-0.210 mg l^{-1} (11).
LD_{50} dermal rabbit 162 mg kg^{-1} (12).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral Japanese quail 5-12.5 mg kg^{-1} (11).

Carcinogenicity and chronic effects
No-effect level in 2-yr feeding trials in rats 1 mg kg^{-1} diet (11).

Metabolism and toxicokinetics
After single oral administration to rats it was distributed throughout the body within 6 hr, then gradually eliminated, mainly via urine. Major metabolites were *O*-ethyl-(isopropylcarboxyphenyl)phosphoric acid; amino, *O*-ethyl phosphorous acid and (isopropylamino)phosphorothioic acid, *O*-ethyl ester (13).

Other effects

Any other adverse effects
Oral toxicity in grey partridge greater in birds fed on insect-poor diet as juveniles (14).

Legislation

EEC maximum residue limit for bananas 0.1 ppm (11).
WHO Toxicity Class Ib (15).
EPA Toxicity Class I (16).
ADI 0.001 mg kg^{-1} body weight (16).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (17).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (18).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (19).

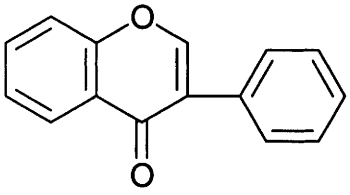
Other comments

Metabolism reviewed (20).
Toxicity of organophosphate pesticides reviewed (21).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Abou-Assaf, N. et al *J. Environ. Sci. Health, Part B* 1987, **B22**(3), 285-301.
4. Racke, K. D. et al *J. Agric. Food Chem.* 1988, **36**(1), 193-199.
5. Chapman, R. A. et al *ACS Symp. Ser.* 1990, **426**(Enhanced Biodegrad. Pestic. Environ.), 82-96.
6. Somasundaram, L. et al *Bull. Environ. Contam. Toxicol.* 1987, **39**(4), 579-586.
7. Harris, C. R. et al *J. Environ. Sci. Health, Part B* 1988, **B23**(1), 1-32.
8. Somasundaram, L. et al *Environ. Toxicol. Chem.* 1991, **10**(2), 185-194.
9. *Bull. Environ. Contam. Toxicol.* 1984, **33**, 386.
10. *Ecotoxicol. Environ. Saf.* 1984, **8**, 551.
11. *Agricultural Chemicals* 1976, Thomson Publications, Fresno, CA, USA.
12. *Farm Chemicals Handbook* 1983, Meister Publishing Co., Willoughby, OH, USA.
13. Ueji, M. et al *Nippon Noyaku Gakkaishi* 1987, **12**(2), 245-251.
14. Dahlgren, J. *Environ. Pollut.* 1988, **49**(3), 177-181.
15. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
16. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
17. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
18. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
19. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
20. Ueji, M. et al *J. Pestic. Sci.* 1987, **12**, 245-269.
21. *Environmental Health Criteria 63* 1986, IPCS/WHO, Geneva, Switzerland

I104 isoflavone



$C_{15}H_{10}O_2$ **Mol. Wt.** 222.24 **CAS Registry No.** 574-12-9

Synonyms 3-phenyl-4*H*-1-benzopyran-4-one; 3-phenylchromone

Physical properties

M. Pt. 148°C

Environmental fate

Degradation studies

Fermentation with microorganisms resulted in the formation of the metabolites 4'-hydroxyisoflavone and 3',4'-dihydroxyisoflavone (1).

References

1. Ibrahim, A. R. S. et al *Xenobiotica* 1990, **20**(4), 363-373

I105 isoflurane

$$CF_3CH(Cl)OCHF_2$$

$C_3H_2ClF_5O$ **Mol. Wt.** 184.49 **CAS Registry No.** 26675-46-7

Synonyms 2-chloro-2-(difluoromethoxy)-1,1,1-trifluoroethane; 1-chloro-2,2,2-trifluoroethyl ether difluoromethyl; Compound 469; Forane

EINECS No. 247-897-7 **RTECS No.** KN 6799000

Uses Anaesthetic. Used for maintenance when anaesthesia induced by an intravenous agent; if used for induction it is given with oxygen or oxygen and nitrous oxide. Solvent and dispersant for fluorinated compounds.

Physical properties

B. Pt. 49°C **Specific gravity** 1.45 **Volatility** v.p. 330 mmHg at 25°C

Solubility Organic solvents: miscible with organic solvents including oils and fats

Occupational exposure

SE-LEVL 10 ppm (80 mg m^{-3}) **SE-STEL** 20 ppm (150 mg m^{-3})

UK-LTEL 50 ppm (383 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 4770, 5080 mg kg^{-1}, respectively (1).
LC_{50} (3 hr) inhalation rat, mouse 15,300, 16,800 ppm, respectively (1).
LD_{50} intraperitoneal mouse, rat 3030, 4280 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects

No increased incidence of tumours in mice exposed to 0.1 or 0.4% 4 hr day^{-1}, 5 days wk^{-1} for 78 wk (2).

Teratogenicity and reproductive effects

Isofluorane at concentrations similar to those used during human oocyte recovery for *in vitro* fertilisation inhibited mouse embryo development *in vitro* (3).
No major or minor teratogenic effects reported in rats exposed to 1.05%, 6 hr day^{-1}, on days 14-16, 11-13 or 8-10 of pregnancy (4).

Metabolism and toxicokinetics

Absorbed on inhalation by humans; blood/gas coefficient <enflurane or halothane. 0.2% metabolised mainly to inorganic fluoride (5).
In patients sedated for 24 hr, plasma inorganic fluoride increased from 0.79 to 2.49 mg l^{-1}, a level too low to cause renal dysfunction (6).

Genotoxicity

Did not induce sister chromatid exchanges in Chinese hamster lung cells (7).
Sex-linked recessive lethal assay in *Drosophila melanogaster* negative for a mixture of isofluorane and nitrous oxide (8).

Other effects

Other adverse effects (human)

Hepatic function was unaffected by exposure for 64 min (9).
Levels of urinary D-glucaric acid excretion was increased in operating theatre personnel exposed to 1 ppm plus <100 ppm nitrous oxide (10).
Isofluorane was not considered the likely cause of post-operative liver impairment in 45 cases of isofluorane-associated hepatotoxicity reported to the US FDA between 1981 and 1984 (11).
A subsequent case of post-operative hepatic necrosis and death may be attributable to isofluorane (12).
Respiratory depression, hypotension, arrhythmias and malignant hyperthermia have been reported. Post-operative shivering, nausea and vomiting may occur and coughing and laryngospasm on induction (5).

Any other adverse effects

No pulmonary or renal injury, but slight liver injury, reported in organ specimens taken from enzyme-induced, hypoxic rats 24 hr after exposure to 1.2 min alveolar concentration (13).

Other comments

Metabolism in humans and laboratory animals reviewed (14).
Pharmacokinetics reviewed (15).
Metabolism and possible effects on liver, kidneys and nervous system of operating room personnel reviewed (16).

References

1. *Kiso to Rinsho* 1987, **21**, 3031.
2. Baden, J. M. et al *Anesthesiology* 1988, **69**(5), 750-753.
3. Chetkowski, R. J. et al *J. Periodontal Res.* 1987, **22**(6), 171-173.
4. Mazze, R. I. et al *Anesthesiology* 1986, **64**, 339-344.
5. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
6. Kong, K. L. et al *Br. J. Anaesth.* 1990, **64**, 159-162.

7. Trudnowski, R. J. et al *J. Med. (Westbury, N. Y.)* 1987, **18**(1), 55-60.
8. Baden, J. M. et al *Br. J. Anaesth.* 1987, **59**(6), 772-775.
9. Chulia, V. et al *Anaesthesiol. Intensivmed. (Berlin)* 1986, **182**(Isoflurane), 45-51.
10. Franco, G. et al *Appl. Occup. Environ. Hyg.* 1992, **7**(10), 677-681.
11. Stoelting, R. K. et al *Anesth. Analg. (N. Y.)* 1987, **66**, 147-153.
12. Carrigan, T. W. et al *Anaesthesiology* 1987, **67**, 581-583.
13. Eger, E. I. et al *Anesth. Analg. (N. Y.)* 1987, **66**(12), 1227-1229.
14. Hempel, V. *Anaesthesiol. Intensivmed. (Berlin)* 1986, **182**(Isoflurane), 29-31.
15. Norlander, O. *Anaesthesiol. Intensivmed. (Berlin)* 1986, **182**(Isoflurane), 18-23.
16. Efthymiou, M. L. *Arch. Mal. Prof. Med. Trav. Secur. Soc.* 1988, **49**(4), 236-247 (Fr.) (*Chem. Abstr.* **110**, 44014b)

I106 isoflurophate

$$[(CH_3)_2CHO]_2P(O)F$$

$C_6H_{14}FO_3P$ **Mol. Wt.** 184.15 **CAS Registry No.** 55-91-4

Synonyms isofluorphate; isopropyl phosphorofluoridate; diisopropoxylphosphoryl fluoride; diisopropyl fluorophosphonate; isopropyl fluophosphate; diisopropyl fluorophosphate; diisopropyl phosphofluoridate; phosphorofluoridic acid, bis(1-methylethyl) ester; phosphorofluoridic acid, diisopropyl ester; Floropryl

EINECS No. 200-247-6 **RTECS No.** TE 5075000

Uses FDA proprietary drug, meiotic agent; cholinergic. It is an irreversible cholinesterase inhibitor similar in action to ecothiopate. Used mainly in treatment of open-angle glaucoma and in diagnosis and management of accommodative convergent strabismus. It is administered locally as an ointment.

Physical properties

M. Pt. –82°C **B. Pt.** 46°C at 5 mmHg **Specific gravity** 1.055 **Volatility** v.p. 0.579 mmHg at 20°C ; v.den. 5.24
Solubility Water: 1.54% (w/w) at 25°C. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 2-5 mg kg^{-1} (1).
LC_{50} (10 min) inhalation rat, mouse 360, 440 mg m^{-3}, respectively (2,3).
LD_{50} dermal mouse 72 mg kg^{-1} (4).
LD_{50} intraperitoneal rat, mouse 1280, 2450 μg kg^{-1} respectively (5,6).
LD_{50} subcutaneous mouse 3 mg kg^{-1} (7).

Teratogenicity and reproductive effects

0.920 mg l^{-1} had no effect on human sperm motility, but inhibited penetration of zona-free hamster ova by human sperm; it is capable of inhibiting sperm function and associates with the proacrosin-acrosin system in live, motile sperm (8).

Metabolism and toxicokinetics

Readily absorbed from the human gut, skin, mucous membranes and lungs. Interacts with cholinesterases producing stable phosphonylated and phosphorylated derivatives which are then hydrolysed by phosphorylphosphatases. These hydrolysis products are excreted mainly in the urine (9).

Irritancy

Vapour is extremely irritating to eye and mucous membranes in humans (9).
Prolonged exposure to the eye can cause slowly reversible depigmentation of lid margins of dark-skinned patients (9).

Other effects

Any other adverse effects

In adult hens 1.5 mg kg^{-1} in diet caused >88% brain neurotoxic esterase inhibition. Maximal ataxia was observed and an increase in lesions to the dorsal and ventral thoracic spinal cord, lateral lumbar spinal cord, and peripheral nerves (10).

Legislation

Land disposal prohibited under US Federal Resource Conservation and Recovery Act (11).

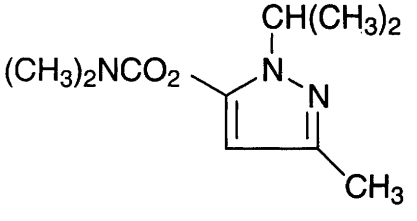
Other comments

Isoflurophate-contaminated material should be immersed in 2% aqueous sodium hydroxide for several hours (9).
Long-term effects on memory reviewed (12,13).
Pharmacokinetics and use in Alzheimer's therapy reviewed (14).

References

1. *NTIS Report PB158-508* Natl. Tech. Inf. Ser., Springfield, VA, USA.
2. *J. Chem. Soc.* 1948, 695.
3. *Nature (London)* 1946, **157**, 287.
4. *J. Pharmacol. Exp. Ther.* 1946, **87**, 414.
5. *Arzneim.-Forsch.* 1964, **14**, 85.
6. *Arch. Immunol. Ther. Exp.* 1975, **23**, 769.
7. *J. Pharm. Pharmacol.* 1982, **34**, 603.
8. Odem, R. R. et al *Biol. Reprod.* 1990, **42**(2), 329-336.
9. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
10. Randall, J. C. et al *J. Toxicol. Environ. Health* 1997, **51**(6), 571-590.
11. US EPA *Fed. Regist.* 1991, **56**(21), 3864-3928.
12. Olton, D. S. et al *NIDA Res. Monogr.* 1990, **97**(Neurobiol. Drug Abuse: Learn. Mem.), 37-47.
13. Raffaele, K. C. et al *Neurotoxicology* 1990, **11**(2), 237-256.
14. Waser, P. G. et al *Curr. Res. Alzheimer Ther.: Cholinesterase Inhib.* 1988, 31-42

I107 isolan



$C_{10}H_{17}N_3O_2$ **Mol. Wt.** 211.26 **CAS Registry No.** 119-38-0

Synonyms dimethylcarbamic acid, 3-methyl-1-(methylethyl)-1*H*-pyrazol-5-yl ester; 1-isopropyl-3-methyl-5-pyrazolyl dimethylcarbamate; isolane

EINECS No. 204-318-2 **RTECS No.** FA 2100000

Uses Superseded insecticide.

Physical properties

B. Pt. 103°C at 0.7 mmHg **Specific gravity** 1.07 **Volatility** v.p. v.p 0.001 mmHg at 20°C

Occupational exposure

Supply classification very toxic
Risk phrases Very toxic in contact with skin and if swallowed (R27/28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S36/37/39, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 9800, 10,800 μg kg^{-1}, respectively (1).
LD_{50} oral starling 7.94 mg kg^{-1} (2).
LD_{50} dermal rat 5600 μg kg^{-1} (3).
LD_{50} intraperitoneal mouse 1 mg kg^{-1} (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

References

1. *Proc. Eur. Soc. Toxicol.* 1976, **17**, 351.
2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
3. *Wirksubstanzen der Pflanzenschutz und Schaedlingsbekaempfungsmittel* 1971-76, Verlag Paul Parey, Berlin, Germany.
4. *Toxicol. Appl. Pharmacol.* 1964, **6**, 402.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

I108 D-isoleucine

$$CH_3CH_2CH(CH_3)CH(NH_2)CO_2H$$

$C_6H_{13}NO_2$ **Mol. Wt.** 131.17 **CAS Registry No.** 319-78-8
Synonyms *d*-2-amino-3-methylpentanoic acid; *d*-α-amino-β-methylvaleric acid
EINECS No. 206-269-2 **RTECS No.** NR 4700000
Occurrence Dietary amino acid.

Physical properties

M. Pt. 283°C (decomp.)
Solubility Water: 41,200 mg l^{-1} at 25°C

Environmental fate

Degradation studies

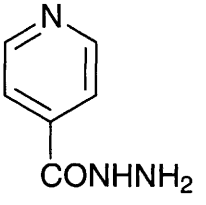
2.4, 5.3 and 15.8% of ThOD after 6, 12 and 24 hr, respectively, in bench scale activated sludge, fill and draw operations (1).

Halobacterium halobium R1mR utilised D-isoleucine after an induction period (2).

References

1. Malaney, G. W. et al *J. Water Pollut. Control Fed.* 1969, **41**(2), Part 2, R18-R33.
2. Tanaka, M. et al *Viva Origino* 1991, **18**(3), 109-117 (Japan.) (*Chem. Abstr.* **115**, 154696m)

I109 isoniazid



$C_6H_7N_3O$ **Mol. Wt.** 137.14 **CAS Registry No.** 54-85-3

Synonyms isonicotinic acid hydrazide; isonicotinoyl hydrazide; 4-pyridinecarboxylic acid hydrazide; Cotinazin; INH; Isonex; Nydrazin

EINECS No. 200-214-6 **RTECS No.** NS 1751850

Uses Antitubercular, antibacterial and antiactinomycotic agent.

Physical properties

M. Pt. 171.4°C

Solubility Water: 14% at 25°C. Organic solvents: chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 133 mg kg^{-1} (1).

LD_{50} oral rat 1250 mg kg^{-1} (2).

LD_{50} intravenous mouse, rat 150, 365 mg kg^{-1}, respectively (2,3).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity in animals, IARC classification group 3 (4).

Carcinogenic in mice, causing lung tumours, after oral, subcutaneous and intraperitoneal administration. Did not induce tumours in hamsters, and evidence in rats is inconclusive, after oral administration (5).

Teratogenicity and reproductive effects

95% of 1480 pregnancies in which isoniazid was used resulted in normal term infants; 1% of foetuses/infants had abnormalities, mainly of the central nervous system. It is recognised as suitable for use in pregnant women and neonates (6).

Embryotoxic, inducing resorption and neonatal death, in mice given 2.2 mg $mouse^{-1}$ day^{-1} intragastrically at day 1-4 or 10-13 of pregnancy (7).

Did not inhibit chondrogenesis in rat embryo limb bud cell culture teratogen screening (8).
Isoniazid had been used to evaluate the embryo malformation endpoint of the aquatic FETAX (frog embryo teratogenesis assay: *Xenopus*) test system (9).

Metabolism and toxicokinetics

Readily absorbed from the gut after intramuscular injection. Plasma $t_{1/2}$ 1-4 hr; rate of acetylation and hence $t_{1/2}$ is genetically determined. Acetylation to acetylisoniazid by *N*-acetyltransferase in liver and small intestine is the major metabolic route. This is then hydrolysed to isonicotinic acid, which is further conjugated with glycine to isonicotinyl glycine, and monoacetylhydrazine, which is further acetylated to diacetylhydrazine. Some unmetabolised isoniazid is conjugated to hydrazones. Metabolites are less toxic and not tuberculostatic (6,10).
Major urinary metabolites in humans are 1-acetyl-2-isonicotinoylhydrazine, *N*-acetyl-*N'*-isonicotinic acid, isonicotinylglycine, pyruvic acid isonicotinylhydrazone, and α-oxoglutaric acid isonicotinylhydrazone (5).
Liver injury may be caused by the metabolite acetylhydrazine formed by metabolic hydrolysis of acetylisoniazid by cytochrome P_{450} (11).
Distributed in breast milk and althoughadverse effects in breast feeding infants have not been reported, they should be monitored (11).

Genotoxicity

Salmonella typhimurium TA100 (12), TA1530 and TA1535 (13) with and without metabolic activation positive. Negative results have also been reported in TA100 (14).
Salmonella typhimurium TA98 (15) and TA1538 (16) with and without metabolic activation negative; TA1537 without metabolic activation negative (17).
Salmonella typhimurium TA1530, TA1535 without metabolic activation positive in plate test; TA1530, TA1535, *his*G46, and *Escherichia coli* TA85, TA86 and WP2 *uvr*A with or without metabolic activation positive in fluctuation assays (13).
Escherichia coli with and without metabolic activation negative (13).
Did not induce unscheduled DNA synthesis in rat primary hepatocytes *in vitro* (11,18,19).
Induced sister chromatid exchanges (20,21) and chromosome aberrations in Chinese hamster cells *in vitro* (22).
Did not induce unscheduled DNA synthesis in human fibroblasts *in vitro* (22).
Inhibited recovery of DNA synthesis in human fibroblasts but did not inhibit protein synthesis (23).
Did not induce sister chromatid exchanges or chromosome aberrations in human lymphocytes *in vitro* (24).
Negative (25) and equivocal results reported for induction of chromosome aberrations in animal bone marrow cells *in vivo* (26).
Dominant lethal test in mice negative (7).

Other effects

Other adverse effects (human)

Side-effects include peripheral neuritis (especially in poorly nourished patients), psychotic reactions, convulsions, optic neuritis, nausea and vomiting. Incidence of hepatic damage is higher in patients over 35-yr-old who are slow inactivators and those who consume alcohol (6,27).
Haematological effects include anaemias, agranulocytosis, thrombocytopenia, and eosinophilia. Hypersensitivity reactions occur infrequently including skin eruptions, fever, lymphadenopathy and vasculitis. Other effects include hyperglycaemia, metabolic acidosis, lupus-like syndrome, rheumatoid syndrome, urinary retention and gynaecomastia (6).
Symptoms of overdose include slurred speech, metabolic acidosis, hypoglycaemia, respiratory and central nervous system depression, convulsions, coma and can be fatal (6,28,29).
Non-acetylator populations are more susceptible to isoniazid toxicity (6).

Other comments

Young rats administered a combination of isoniazid and rifampicin (50 mg kg^{-1} day^{-1} for 2 wk) suffered hepatoxicity which appeared to be mediated through oxidative stress (30).

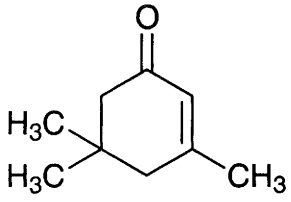
Isoniazid-induced liver injury reviewed (31).

The human embryonic palatal mesenchymal cell growth inhibition and the mouse ovarian tumour cell attachment inhibition assay has also been evaluated (32).

References

1. *Am. Rev. Tuberc.* 1952, **65**, 376.
2. *Arzneim.-Forsch.* 1976, **26**, 409.
3. *J. Pharmacol. Exp. Ther.* 1958, **122**, 110.
4. *IARC Monograph* 1987, **Suppl. 7**, 65, 227.
5. *IARC Monograph* 1974, **4**, 159-172.
6. *Martindale. The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
7. Menon, M. M. et al *Indian J. Exp. Biol.* 1980, **18**, 1104-1106.
8. Renault, J. Y. et al *Teratog., Carcinog., Mutagen.* 1989, **9**, 83-96.
9. Dawson, D. A. et al *Ecotoxicol. Environ. Saf.* 1991, **21**(2), 215-226.
10. Peretti, E. et al *Eur. J. Clin. Pharmacol.* 1987, **33**(3), 283-286.
11. Neis, J. M. et al *Cancer Lett. (Shannon, Irel.)* 1986, **30**, 103-111.
12. Wade, D. R. et al *Mutat. Res.* 1981, **89**, 9-20.
13. Gatehouse, D. et al *Carcinogenesis (London)* 1984, **5**(3), 391-397.
14. Parodi, S. et al *Cancer Res.* 1981, **41**, 1469-1482.
15. Menon, M. M. et al *Indian J. Exp. Biol.* 1981, **19**, 939-942.
16. Malca-Mor, L. et al *Appl. Environ. Microbiol.* 1982, **44**, 801-808.
17. Herbold, B. A. et al *Mutat. Res.* 1976, **40**, 73-84.
18. Probst, G. S. et al *Environ. Mol. Mutagen.* 1981, **3**, 11-32.
19. Mori, H. et al *Jpn. J. Cancer Res.* 1988, **79**(2), 204-211.
20. Speit, G. et al *Hum. Genet.* 1980, **54**, 155-158.
21. MacRae, W. D. et al *Mutat. Res.* 1979, **68**, 351-365.
22. Whiting, R. F. et al *Mutat. Res.* 1979, **62**, 505-515.
23. Yanagisawa, K. et al *Mutat. Res.* 1987, **183**, 89-94.
24. Schroeder, T. M. et al *Hum. Genet.* 1979, **52**, 309-321.
25. Basler, A. *Hum. Genet.* 1978, **42**, 26-27.
26. Manna, G. K. et al *Nucleus (Quezon City, Philipp.)* 1979, **22**, 96-103.
27. Moss, J. D. et al *Am. Rev. Respir. Dis.* 1972, **106**, 849-856.
28. Rubin, D. H. et al *Clin. Pediatr. (Philadelphia)* 1983, **22**, 518-519.
29. Terman, D. S. et al *Neurology* 1970, **20**, 299-304.
30. Sodhi, C.P. et al *Drug Chem. Toxicol.* 1997, **20**(3), 255-269.
31. Yamamoto, T. *Tan, Sui* 1989, **19**(4), 813-818.
32. Steele, V. E. et al *Fundam. Appl. Toxicol.* 1988, **11**(4), 673-684

I110 isophorone



$C_9H_{14}O$ **Mol. Wt.** 138.21 **CAS Registry No.** 78-59-1

Synonyms isoacetophorone; 1,1,3-trimethyl-3-cyclohexen-5-one; isooctaphenone; 3,5,5-trimethyl-2-cyclohexen-1-one

EINECS No. 201-126-0 **RTECS No.** GW 7700000

Uses Solvent. Intermediate for synthesis of alcohols. Raw material for 3,5-dimethylaniline. In pesticide lacquers and finishes manufacture.

Physical properties

M. Pt. –8°C **B. Pt.** 213-214°C **Flash point** 84°C (open cup) **Specific gravity** 0.9229 **Volatility** v.p. 1 mmHg at 38°C ; v.den. 4.77

Solubility Water: 12,000 mg l^{-1}

Occupational exposure

DE-MAK 2 ppm (11 mg m^{-3})

FR-VLE 5 ppm (25 mg m^{-3})

SE-CEIL 5 ppm (30 mg m^{-3})

UK-STEL 5 ppm (29 mg m^{-3})

US-STEL ceiling limit 5 ppm (28 mg m^{-3})

Supply classification irritant

Risk phrases Irritating to eyes, respiratory system and skin (R36/37/38)

Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S26)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 145-255 mg l^{-1} (1).

LC_{50} (96 hr) bluegill sunfish 220 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 120 mg l^{-1} (3).

EC_{50} (24 hr) *Tetrahymena pyriformis* 420 mg l^{-1} (4).

LC_{50} (96 hr) mysid shrimp 12.9 mg l^{-1} (5).

EC_{50} (96 hr) *Selenestrum capricornutum* 126 mg l^{-1} (5).

Environmental fate

Degradation studies

Activated sludge adsorbability 0.193 g g^{-1} C; 96.6% reduction, influent 1000 mg l^{-1}, effluent 34 mg l^{-1} (6).

Activated sludge EC_{50} (3 hr) 100 mg l^{-1}; EC_{50} (24 hr) *Tetrahymena pyriformis* 420 mg l^{-1} (7).

Abiotic removal
Adsorbability 0.193 g g^{-1} carbon 96.6% reduction (8).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2330 mg kg^{-1} (8).
LC_{Lo} (4 hr) inhalation rat 1840 ppm (9).
LD_{50} dermal rabbit 1500 mg kg^{-1} (10).

Sub-acute and sub-chronic data
Kidney tubule injury not reported in ♀ rats exposed to 5 intraperitoneal injections wkly for 2 wk of 5-20% the LD_{50} (11).

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice via gavage. Some evidence of carcinogenicity in ♂ rats, equivocal evidence in ♂ mice, no evidence in ♀ mice or rats. Increased incidence of kidney tubular cell adenoma and adenocarcinoma occurred in ♂ rats fed 250-500 mg kg^{-1}, 5 days wk^{-1} for 103 wk; evidence for preputial gland carcinoma in ♂ rats was equivocal, as was liver adenoma/carcinoma, integumentary system tumours and haematopoeitic system malignant tumours in ♂ mice (12,13).
Neither isophorone nor its metabolites showed covalent binding to DNA in liver and kidneys of rats and mice, hence tumours reported in ♂ rats and mice after long-term oral administration are not likely to be caused by genotoxic mechanisms (14).

Metabolism and toxicokinetics
After oral administration to rabbits and rats, the urinary metabolites included: isophorol, *cis/trans*-3,5,5-trimethyl-2-cyclohexen-1-one, dihydroisophorone, diisophorone glucuronide, and 5,5-dimethyl-3-oxocyclohex-1-ene carboxylic acid (15-17).

Irritancy
100 mg applied to rabbits' skin for 24 hr caused mild irritation (18).
920 µg applied to rabbits' eyes caused severe irritation (10).
25 ppm caused eye, nose and throat irritation in humans (19).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (20).
Induced sister chromatid exchanges but not chromosome aberrations in Chinese hamster ovary cells *in vitro* (21).
L5178Y tk^+/tk^- mouse lymphoma cell forward mutation assay without metabolic activation positive (22).

Other comments

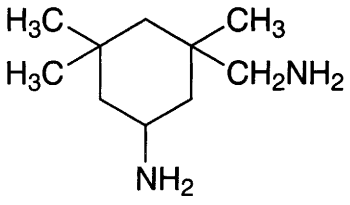
Reviews on human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels, epidemiology, workplace experience, hazard assessment and physico-chemical properties listed (23).
Physico-chemical properties, toxicity, hazards and French regulations of isophorone reviewed (24).
Toxicology reviewed (25,26).

References

1. Cairns, M. A. et al *Arch. Environ. Contam. Toxicol.* 1982, **11**, 703-707.
2. Buccafusco, R. J. et al *Bull. Environ. Contam. Toxicol.* 1981, **26**, 446.
3. LeBlanc, G. A. *Bull. Environ. Contam. Toxicol.* 1980, **24**, 684-691.
4. Yoshioka, Y. et al *Sci. Total Environ.* 1985, **43**, 149.
5. *US EPA Contract No. 68-01-4646* 1978.
6. Guisti, D. M. et al *J. Water Pollut. Control. Fed.* 1974, **46**(5), 947-965.
7. Yoshioka, Y. et al *Ecotoxicol. Environ. Saf.* 1986, **12**, 206-212.
8. *Toxicol. Appl. Pharmacol.* 1970, **17**, 498.
9. *J. Ind. Hyg. Toxicol.* 1940, **22**, 477.

10. *Union Carbide Data Sheet* 1971, Union Carbide Corp., New York, NY, USA.
11. Bernard, A. M. et al *Toxicol. Lett.* 1989, **45**(2-3), 271-280.
12. *National Toxicology Program Research and Testing Division* 1992, Report No.TR-291, NIEHS, Research Triangle Park, NC, USA.
13. Bucher, J. R. et al *Toxicology* 1986, **39**, 207-219.
14. Thier, R. et al *Arch. Toxicol.* 1990, **64**(8), 684-685.
15. *Chemical Safety Data Sheets 1 Solvents* 1988, The Royal Society of Chemistry, London, UK.
16. Dutertue, L. *Toxicol. Eur. Res.* 1978, **1**(4), 209.
17. Truhort, R. C. R. *Acad. Sci. Ser. 7* 1970, **271**, 1333.
18. *J. Eur. Toxicol.* 1972, 5, 31.
19. Patty, F. A. *Industrial Hygiene and Toxicology* 1967, Interscience Publishers, New York, NY, USA.
20. Mortelmans, K. et al *Environ. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
21. Buzzi, R. et al *Mutat. Res.* 1990, **234**, 269-288.
22. McGregor, D. B. et al *Environ. Mol. Mutagen.* 1988, **12**, 85-154.
23. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
24. *Cah. Notes Doc.* 1989, **134**, 175-178.
25. *Gov. Rep. Announce. Index (U. S.)* 1990, **90**(11), Abstr. No.028,423.
26. *Gov. Rep. Announce. Index (U. S.)* 1988, **88**(13), Abstr. No.833,883

I111 isophorone diamine



$C_{10}H_{22}N_2$ **Mol. Wt.** 170.30 **CAS Registry No.** 2855-13-2

Synonyms 3-aminomethyl-3,5,5-trimethylcyclohexylamine; 5-amino-1,3,3-trimethyl-cyclohexanemethylamine; Vestamin IPD; Degamin IPDA

EINECS No. 220-666-8

Uses Synthesis of diisocyanate plastics.

Physical properties

B. Pt. 247°C
Solubility Organic solvents: hydrocarbons

Occupational exposure

UN No. 2289 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Harmful in contact with skin and if swallowed – Causes burns – May cause sensitisation by skin contact – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21/22, R34, R43, R52/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S26, S36/37/39, S45, S61)

Genotoxicity

Salmonella typhimurium TA98 and TA100 with and without metabolic activation negative (1).

Other effects

Other adverse effects (human)

A man handling epoxy resins and wood in a shipyard experienced chronic itching, fissured dermatitis of the fingertips and palms. Similarly, a man employed in an electronics company using epoxy resins, metals, plastics and varnishes suffered from chronic itching and scaly contact dermatitis on the hands and fingers. Patch-tests were positive for isophorone diamine (2).

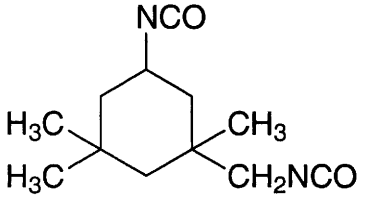
Other comments

Reviews on physico-chemical properties, human health effects and experimental toxicology listed (3).

References

1. Takahashi, A. et al *Chem. Express* 1993, **8**(9), 785-788.
2. Camarasa, J. G. et al *Contact Dermatitis* 1989, **20**(5), 382-383.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I112 isophorone diisocyanate



$C_{12}H_{18}N_2O_2$ **Mol. Wt.** 222.29 **CAS Registry No.** 4098-71-9

Synonyms isophorone diamine diisocyanate; 3-isocyanatomethyl-3,5,5-trimethylcyclohexylisocyanate; 5-isocyanate-1-(isocyantomethyl)-1,3,3-trimethylcyclohexane; Vestanat IPDI

EINECS No. 223-861-6 **RTECS No.** NQ 9370000

Uses Cross-linking and curing agent.

Physical properties

M. Pt. –60°C (approx.) **B. Pt.** 158-159°C at 15 mmHg **Flash point** >110°C **Specific gravity** 1.049

Occupational exposure

DE-MAK 0.01 ppm (0.092 mg m^{-3})
FR-VME 0.01 ppm (0.09 mg m^{-3}) **FR-VLE** 0.02 ppm (0.18 mg m^{-3})
SE-LEVL 0.005 ppm (0.05 mg m^{-3}) **SE-CEIL** 0.01 ppm (0.09 mg m^{-3})
UK-LTEL MEL 0.02 mg m^{-3} (as NCO) **UK-STEL** MEL 0.07 mg m^{-3} (as NCO)
US-TWA 0.005 ppm (0.045 mg m^{-3})

UN No. 2290 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification toxic
Risk phrases Toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by inhalation and skin contact (R23, R36/37/38, R42/43)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S28, S38, S45)

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) inhalation rat 260 mg m^{-3} (1).
LD_{50} dermal rabbit 1060 mg kg^{-1} (1).

Other effects

Other adverse effects (human)
A study of exposed workers showed that concentrations of 0.54 mg m^{-3} caused local irritation to eyes and respiratory tract (2).

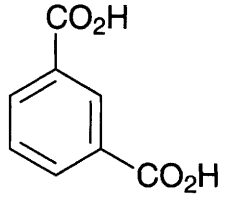
Other comments

Reviews on human health effects, experimental toxicity, physicochemical effects, epidemiology, workplace experience and ecotoxicology listed (3).

References

1. *Documentation of Threshold Limit Values in Workroom Air* 1980, ACGIH, Cincinnati, OH, USA.
2. Qin, C. W. D. et al *Gongye Weisheng Yu Zhiyebing* 1994, **20**(3) (Chinese) (*Chem. Abstr.* **122** 297754).
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I113 isophthalic acid



$C_8H_6O_4$ **Mol. Wt.** 166.13 **CAS Registry No.** 121-91-5
Synonyms *m*-benzenedicarboxylic acid; *m*-phthalic acid; PIA
EINECS No. 204-506-4 **RTECS No.** NT 2007000

Physical properties

M. Pt. 345-348°C **B. Pt.** sublimes
Solubility Water: 130 mg l^{-1} at 25°C. Organic solvents: acetic acid, ethanol

Environmental fate

Anaerobic effects

Anaerobically metabolised by *Pseudomonas* sp. strain P136 (1).

Degradation studies

Biodegradable (2).

Decomposed by a soil microflora in 8 days (3).

95% COD removal at 76 mg COD g^{-1} O_2 dry inoculum hr^{-1}; adapted activated sludge at 20°C, product is sole carbon source (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 10400 mg kg^{-1} (5).

LD_{50} intraperitoneal mouse 4200 mg kg^{-1} (6).

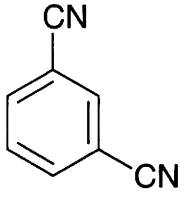
Irritancy

100 mg instilled into rabbit eyes for 24 hr caused mild irritation (5).

References

1. Nozawa, T. et al *J. Bacteriol.* 1988, **170**(12), 5778-5784.
2. *List of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* 1987, Chemicals Inspection and Testing Institute, Japan.
3. Alexander, M. et al *J. Agric. Food Chem.* 1966, **14**, 410.
4. Pitter, P. *Water Res.* 1976, **10**, 231-235.
5. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
6. *C. R. Seances Acad. Sci., Ser. 3* 1958, **246**, 851

I114 isophthalonitrile



$C_8H_4N_2$ **Mol. Wt.** 128.13 **CAS Registry No.** 626-17-5

Synonyms *m*-phthalodinitrile; 1,3-benzenedicarbonitrile; *m*-dicyanobenzene; 1,3-dicyanobenzene

EINECS No. 210-933-7 **RTECS No.** CZ 1900000

Physical properties

M. Pt. 160-162°C **B. Pt.** sublimes **Volatility** v.den. 4.42

Occupational exposure

FR-VME 5 mg m^{-3}

US-TWA 5 mg m^{-3}

Ecotoxicity

Invertebrate toxicity

EC_{50} (5-30 min) *Photobacterium phosphoreum* 107 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 180 mg kg^{-1} (2).
LD_{50} oral rat 1860 mg kg^{-1} (3).
LD_{50} oral rabbit, guinea pig 350-370 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 480 mg kg^{-1} (5).

Irritancy

500 mg instilled into rabbit eyes for 24 hr caused mild irritation (3).

Other comments

Reviews on human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (6).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. *J. Med. Chem.* 1978, **21**, 906.
3. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
4. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
5. *Ind. Health* 1966, **4**, 11.
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I115 isoprene

$$CH_2=C(CH_3)CH=CH_2$$

C_5H_8 **Mol. Wt.** 68.12 **CAS Registry No.** 78-79-5

Synonyms 2-methylbivinyl; 2-methylbutadiene; 2-methyl-1,3-butadiene

EINECS No. 201-143-3 **RTECS No.** NT 4037000

Uses Monomer for polyisoprene manufacture; manufacture of butyl rubber.
Occurrence Isolated from pyrolysis products of natural rubber.

Physical properties

M. Pt. –146.7°C **B. Pt.** 34°C **Flash point** –54°C **Specific gravity** 0.681 at 20°C with respect to water at 4°C
Volatility v.p. 400 mmHg at 15.4°C ; v.den. 2.35
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1218 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid
Supply classification extremely flammable
Risk phrases Extremely flammable – Harmful to aquatic organisms, may cause long-term adverse efffects in the aquatic environment (R12, R52/53)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not empty into drains – Take precautionary measures against static discharges – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S9, S16, S29, S33, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, fathead minnow and goldfish 43, 74, 180 mg l^{-1}, respectively (1).

Environmental fate

Degradation studies

Degraded by *Nocardia* strains (2).

Abiotic removal

Activated carbon 10×, 89% reduction, influent 1000 ppm, effluent 110 ppm; 78% reduction, influent 500 ppm, effluent 110 ppm (3).

Mammalian & avian toxicity

Acute data

LC_{50} (2 hr) inhalation mouse 140 g m^{-3} (4).

LC_{50} (4 hr) inhalation rat 180 g m^{-3} (5).

Sub-acute and sub-chronic data

No-effect level inhalation rat 1670 ppm 16 × 6 hr (1).

National Toxicology Program short term inhalation study in rats and mice scheduled for peer review (6).

Haematological changes and microscopic lesions including testicular atrophy, olfactory epithelial degeneration, and forestomach epithelial hyperplasia observed in mice, but not rats, exposed to 7000 ppm for 2 wk (7).

Carcinogenicity and chronic effects

The National Toxicology Program tested rats via inhalation. Clear evidence of carcinogenicity in ♂s, some evidence of carcinogenicity in ♀s (8).

♂ Sprague-Dawley or Wistar rat liver microsomes metabolised isoprene *in vitro* into 2-(1-methylethenyl)oxirane with an approximately 2:1 preference for the (*S*)- over the (*R*)-enantiomer. No enantioselectivity was observed for mouse or rabbit or ♀ human livers, but dog, monkey, or ♂ human livers preferentially formed the (*R*)-enantiomer (9).

Metabolism and toxicokinetics

In ♂ mice and rats, rate of metabolism was directly proportional to concentration below 300 ppm, small amounts were exhaled unchanged (25% and 15% respectively) and $t_{1/2}$ was 4.4 and 6.8 min, respectively (10).

In ♂ rats exposed to 8-8200 ppm, 75% excretion of total metabolites was via urine (11).

Metabolised *in vitro* by rabbit, mouse and rat liver microsomes to 3,4-epoxy-3-methyl-1-butene and 3,4-epoxy-2-methyl-1-butene, which are not mutagenic. Formation of the mutagenic, and presumably carcinogenic, isoprene diepoxide is possible, hence genotoxicity in rodents or other species cannot be eliminated (12).

Irritancy

Irritating to skin and mucous membranes (species unspecified) (13).

Genotoxicity

Induced sister chromatid exchanges in bone marrow cells, increased levels of micronucleated polychromatic and normochromatic erythrocytes, but did not induce chromosomal aberrations or alter mitotic index in ♂ mice exposed to 438, 1750 or 7000 ppm for 12 days (14,15).

Other effects

Any other adverse effects

Narcotic in high concentrations (species unspecified) (13).

Legislation

Reportable quantity listed in US Federal Comprehensive Environmental Response, Compensation and Liability Act (16).

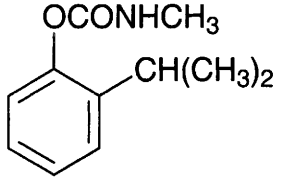
Other comments

Reviews on human health effects, experimental toxicity, ecotoxicology, workplace experience and physicochemical effects listed (17).
Future directions in toxicology research on isoprene reviewed (18).
Slight inhibition of microbial growth after 24 hr at saturation concentration (19).

References

1. Cage, J. C. *Br. J. Ind. Med.* 1970, **27**.
2. Van Ginkel, C. G. et al *FEMS Microbiol. Ecol.* 1987, **45**(5), 275-279.
3. Dahm, D. B. et al *Environ. Sci. Technol.* 1974, **8**(13).
4. *Gig. Tr. Prof. Zabol.* 1965, **9**(1), 36.
5. *Russ. Pharmacol. Toxicol.* 1968, **31**, 162.
6. *National Toxicology Program Research and Testing Division* 1999, Report No. TOX31, NTIS No. PB95-226486, Management Status Report, NIEHS, Research Triangle Park, NC 27709, USA.
7. Melnick, R. L. et al *Environ. Health Perspect.* 1990, **86**, 93-98.
8. *National Toxicology Program Research and Testing Division* 1999, Report No. TR-486, NIEHS, Research Triangle Park, NC 27709, USA.
9. Small, R. D. et al *Xenobiotica* 1997, **27**(11), 1155-1164.
10. Peter, H. et al *Toxicol. Lett.* 1987, **36**(1), 9-14.
11. Dahl, A. R. et al *Toxicol. Appl. Pharmacol.* 1987, **89**(2), 237-248.
12. Gervasi, P. G. et al *Environ. Health Perspect.* 1990, **86**, 85-87.
13. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
14. Tice, R. R. et al *Mutagenesis* 1988, **3**(2), 141-146.
15. Shelby, M. D. et al *Environ. Health Perspect.* 1990, **86**, 71-73.
16. US EPA *Fed. Regist.* 1989, **54**(155), 33426-33484.
17. *ECETOC Technical Report No. 71*, 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
18. Bird, M. G. *Environ. Health Perspect.* 1990, **86**, 99-102.
19. Cabridenc. R. et al *Etude des possibilities de biodegradation d'un effluent de fabrication d'isoprene* 1968, IRCHA, France

I116 isoprocarb



$C_{11}H_{15}NO_2$ **Mol. Wt.** 193.25 **CAS Registry No.** 2631-40-5

Synonyms 2-isopropylphenyl methylcarbamate; 2-(1-methylethyl)phenyl methylcarbamate; MIPC; MIPCIN; MIPSIN; *o*-cumenyl methylcarbamate; Etrofolan; Hytox; Mipcin

EINECS No. 220-114-6 **RTECS No.** FB 7880000

Uses Contact insecticide.

Physical properties

M. Pt. 93-96°C **B. Pt.** 128-129°C at 20 mmHg **Specific gravity** 0.62 **Partition coefficient** log P_{ow} 0.36 at 25°C
Volatility v.p. 2.85 mmHg at 20°C
Solubility Water: 0.265 g l^{-1}. Organic solvents: acetone, methanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 4.2 mg l^{-1} (1).
LC_{50} (96 hr) carp, golden orfe 10-20, 20-40 mg l^{-1} (2).

Invertebrate toxicity
Inhibited ammonium oxidisers, nitrate reducers and denitrifying soil bacteria (3).
EC_{50} (3 hr) *Daphnia* 0.30 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 150-180 mg kg^{-1} (4,5).
LD_{50} dermal mouse 7600 mg kg^{-1} (4).
LD_{50} intraperitoneal rat 142 mg kg^{-1} (6).

Sub-acute and sub-chronic data
No-effect level in 90-day feeding studies in rats 300 mg kg^{-1} (1).

Irritancy
Non-irritating to rabbit eye and skin (dose and duration unspecified) (1).

Genotoxicity

Questionable positive results for induction of sister chromatid exchanges and chromosome aberrations in Chinese hamster ovary cells (7).

Legislation

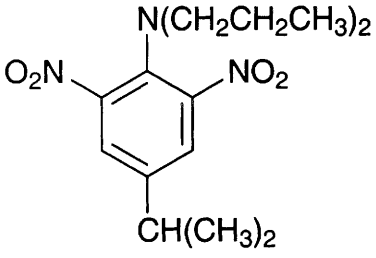
WHO Toxicity Class II (8).
EPA Toxicity Class II (2).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Lee, K. B. et al *Han'guk T'oyang Piryo Hakhoechi* 1988, **21**(2), 149-159 (Kor.) (*Chem. Abstr.* **110**, 2520h).
4. *Guide to the Chemicals used in Crop Protection* 1968, Information Canada, Ottawa, Ontario, Canada.
5. *Special Publication of the Entomological Society of America* 1978, College Park, MD, USA.
6. *Bull. WHO* 1971, 44(1-3), 241.
7. Wang, T. C. et al *Bull. Inst. Zool. Academia Sinica* 1987, **26**(4), 317-329.
8. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.

9. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

I117 isopropalin



$C_{15}H_{23}N_3O_4$ **Mol. Wt.** 309.37 **CAS Registry No.** 33820-53-0

Synonyms 4-(1-methylethyl)-2,6-dinitro-*N*,*N*-dipropylbenzenamine; 2,6-dinitro-*N*,*N*-dipropylcumidine; 4-isopropyl-2,6-dinitro-*N*,*N*-dipropylaniline

EINECS No. 251-690-7 **RTECS No.** BX 9286000

Uses Superseded selective pre-plant herbicide.

Physical properties

Flash point 40.6°C **Volatility** v.p. 1.4×10^4 mmHg at 30°C
Solubility Water: 0.1 mg l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, benzene, chloroform, diethyl ether, *n*-hexane, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow, goldfish 0.1-0.15 mg l^{-1} (1).

Invertebrate toxicity
LD_{50} honeybees, 0.011 mg bee^{-1} (1).

Environmental fate

Degradation studies
Microorganisms may play a role in degradation as well as loss from volatilisation and photodecomposition (2).

Abiotic removal
Decomposed by UV light (3).

Adsorption and retention
Strongly adsorbed in soil with negligible leaching (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral quail, mallard duck, chicken >1000, >2000, >2000 mg kg^{-1}, respectively (1).
LD_{50} oral rat 5000 mg kg^{-1} (3).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
No-effect level in 90-day feeding trials in dogs and rats >250 mg kg^{-1} diet (1).

Irritancy
Slightly irritating to rabbits' skin and eyes (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
WHO Toxicity Class Table 5 (5).

Other comments

Hazards reviewed (6).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Romanowski, R. *Weed Sci.* 1978, **26**, 258.
3. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
6. *Dangerous Prop. Ind. Mater. Rep.* 1990, **10**(4), 68-71

I118 isopropenyl acetate

$$CH_3C(O)OC(CH_3)=CH_2$$

$C_5H_8O_2$ **Mol. Wt.** 100.12 **CAS Registry No.** 108-22-5

Synonyms 1-propen-2-ol acetate; acetic acid, isopropenyl ester; 2-acetoxypropene; 1-methylvinyl acetate; propen-2-yl acetate

EINECS No. 203-562-7 **RTECS No.** UD 4200000

Uses Reagent for acylation in organic synthesis.

Physical properties

M. Pt. –92.9°C **B. Pt.** 96.6°C at 746 mmHg **Flash point** 18°C (closed cup) **Specific gravity** 0.9 at 20°C **Volatility** v.den. 3.45

Occupational exposure

UN No. 2403 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3000 mg kg^{-1} (1).

References

1. Smyth et al *J. Ind. Hyg. Toxicol.* 1949, **31**, 60

I119 2-isopropoxyethanol

$$HOCH_2CH_2OCH(CH_3)_2$$

$C_5H_{12}O_2$ **Mol. Wt.** 104.15 **CAS Registry No.** 109-59-1

Synonyms ethylene glycol isopropyl ether; isopropyl cellosolve; isopropyl glycol; 2-(1-methylethoxy)ethanol

EINECS No. 203-685-6 **RTECS No.** KL 5075000

Uses Animal repellent. Solvent.

Physical properties

B. Pt. 143°C; 42-44°C at 13 mmHg **Flash point** 45°C (open cup) **Specific gravity** 0.9030 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.092 (1) **Volatility** v.p. 5.2 mmHg at 25°C ; v.den. 3.6
Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (22 mg m^{-3})
FR-VME 25 ppm (105 mg m^{-3})
SE-LEVL 10 ppm (45 mg m^{-3}) **SE-STEL** 20 ppm (90 mg m^{-3})
US-TWA 25 ppm (106 mg m^{-3})
Supply classification harmful
Risk phrases Harmful by inhalation and in contact with skin – Irritating to the eyes (R20/21, R36)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 5470 mg l^{-1} (1).
LC_{50} (14 day) guppy 5460 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 3610 mg l^{-1} (3).

Environmental fate

Degradation studies
COD 2.08 mg l^{-1} O_2; BOD_5 0.18 mg l^{-1} O_2 (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 4900, 5660 mg kg^{-1}, respectively (5,6).
LC_{50} (7 hr) inhalation rat 1930 ppm (7).
LD_{50} dermal rabbit 1600 mg kg^{-1} (5).
LD_{50} intraperitoneal rat, mouse 800, 1860 mg kg^{-1}, respectively (6).

Sub-acute and sub-chronic data
Inhalation rat, no-adverse effect level 100 ppm 6 hr day^{-1} for 15 days (8).

Metabolism and toxicokinetics
Rapidly metabolised in rats, and dogs, 89% being excreted in the urine within 24 hr, 73% and 11% via the lungs as carbon dioxide. Major urinary metabolites are isopropoxyacetic acid (30%) *N*-isopropoxyacetylglycine (46%) and ethylene glycol (13%) (9).

Irritancy
Dermal rabbit (24 hr) 20 mg caused moderate irritation and 500 mg instilled into rabbit eye for 24 hr caused mild irritation (10).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

References

1. Lipnick, R. L. et al *Xenobiotica* 1987, **17**(8), 1011-1075.
2. Leegcrater, D. C. *Aquat. Toxicol.* 1989, **15**(2), 157-168.
3. Hermens, J. et al *Aquat. Toxicol.* 1984, **5**(2), 143-154.
4. *Shell Industrie Chemicalien Gids* 1975, Shell Nederland Chemie, 's-Gravenhage, Netherlands.
5. *Am. Ind. Hyg. Assoc. J.* 1969. **30**;470.
6. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals Under Single Exposure* 1982, 67, CIP, Moscow, USSR.
7. *J. Ind. Hyg. Toxicol.* 1943, **25**, 157.
8. Cage, J. C. *Br. J. Ind. Med.* 1970, **27**.
9. Hutson, D. H. et al *Xenobiotica* 1971, **1**, 105.
10. Marhold, J. V. *Prehled Prumyslove Toxikologie; Organicke Latky* 1986, 627, Prague, Czechoslovakia.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I120 isopropyl acetate

$$CH_3CO_2CH(CH_3)_2$$

$C_5H_{10}O_2$ **Mol. Wt.** 102.13 **CAS Registry No.** 108-21-4

Synonyms 1-methylethyl acetate; 1-methylethyl ethanoate

EINECS No. 203-561-1 **RTECS No.** AI 4930000

Uses Used in perfumery, and as a solvent for cellulose derivatives, plastics, oils and fats.

Physical properties

M. Pt. -73°C **B. Pt.** 87-89°C **Flash point** 4°C (closed cup) **Specific gravity** 0.871 at 20°C with respect to water at 4°C **Volatility** v.p. 40 mmHg at 17°C ; v.den. 3.52
Solubility Water: 40 ml l^{-1} at 27°C. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

DE-MAK 200 ppm (850 mg m^{-3})
FR-VME 250 ppm (950 mg m^{-3}) **FR-VLE** 300 ppm (1140 mg m^{-3})
UK-STEL 200 ppm (849 mg m^{-3})
US-TWA 250 ppm (1040 mg m^{-3}) **US-STEL** 310 ppm (1290 mg m^{-3})

UN No. 1220 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)

Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Do not breathe vapour – Do not empty into drains – Take precautionary measures against static discharges (S2, S16, S23, S29, S33)

Ecotoxicity

Bioaccumulation

The calculated bioconcentration factor of 1.8 indicates that environmental accumulation is unlikely (1).

Environmental fate

Degradation studies

BOD_5 61% reduction in dissolved oxygen using a settled domestic wastewater seed (2).

The calculated soil adsorption coefficient of 14.8 indicates that isopropyl acetate will be highly mobile in soil (3).

Evaporation was significant in both dry and wet soil (4).

Abiotic removal

Low atmospheric reactivity (5).

Resistant to hydrolysis under acidic conditions (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3-7 g kg^{-1} (7,8).

LC_{Lo} (4 hr) inhalation rat 32,000 ppm (7).

LD_{50} gavage rat, mouse (duration unspecified) 10.9, 6.6 g kg^{-1} respectively. Increased motor activity, interrupted respiration and death within 1-3 days reported (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, with metabolic activation negative (10).

Other effects

Other adverse effects (human)

12 human subjects of both sexes were exposed to isopropyl acetate for 15 min. Majority of subjects experienced some degree of eye irritation at 200 ppm. Highest concentration which majority of subjects estimated satisfactory for 8-hr exposure (11).

Other comments

Reviews on experimental toxicology, epidemiology and human health effects listed (12).

References

1. Stephan, H. et al *Solubilities of Inorganic and Organic Compounds in Binary Systems* 1963, **1**, 1-79.
2. Price, K. S. et al *J. Water Pollut. Contr. Fed.* 1974, **46**, 63-77.
3. Swann, R. L. et al *Res. Rev.* 1983, **85**, 17-28.
4. Ambrose, D. et al *J. Chem. Therm.* 1981, **13**, 795-802.
5. Farley, F. F. *Int. Conf. Photochem. Oxid. Pollut. Control Proc.* 1977, **2**, 713-726.
6. Elam, E. U. *Kirk-Othmer Enc. Chem. Tech.* 3rd ed., 1978, **9**, 311-337.
7. Smyth H. F. et al *Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
8. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, **2**, Clayton, G. D. et al (Eds.), John Wiley, New York, NY, USA.
9. Guseinov, V. G. et al *Azerb. Med. Zh.* 1988, **63**(5), 41-45, (Russ.) (*Chem. Abstr.* **106**, 79939b).
10. Zeiger, E. et al *Environ. Mol. Mutagen.* 1992, **19**(Suppl. 21), 2-141.
11. Silverman, L. et al *J. Ind. Hyg. Toxicol.* 1946, **28**, 262.
12. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I121 isopropylamine

$$CH_3CH(NH_2)CH_3$$

C_3H_9N **Mol. Wt.** 59.11 **CAS Registry No.** 75-31-0

Synonyms 2-aminopropane; 1-methylethylamine; 2-propylamine; 2-propanamine; *sec*-propylamine

EINECS No. 200-860-9 **RTECS No.** NT 8400000

Uses Solvent and chemical intermediate.

Physical properties

M. Pt. -101.2°C **B. Pt.** 33-34°C **Flash point** -2°C (open cup) **Specific gravity** 0.694 at 15°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.26 **Volatility** v.p. 579.6 mmHg at 25°C ; v.den. 2.03
Solubility Water: miscible. Organic solvents: soluble in acetone, benzene, chloroform; miscible with diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (12 mg m^{-3})
FR-VME 5 ppm (12 mg m^{-3})
SE-LEVL 5 ppm (12 mg m^{-3}) **SE-STEL** 10 ppm (25 mg m^{-3})
US-TWA 5 ppm (12 mg m^{-3}) **US-STEL** 10 ppm (24 mg m^{-3})

UN No. 1221 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive
Supply classification extremely flammable, irritant
Risk phrases Extremely flammable – Irritating to eyes, respiratory system and skin (R12, R36/37/38)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Do not empty into drains (S2, S16, S26, S29)

Ecotoxicity

Fish toxicity
No malformations were seen in zebrafish embryos following exposure of fertilised eggs to 2-aminopropane; the hatched fish developed normally. The concentrations producing 50 and 100% embryo lethality were 91.2 and 200 mmol l^{-1}, respectively, and the no-observed-effect level was 10 mmol l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 91.6 mg l^{-1} (2).
EC_{50} (96 hr) *Selenastrum capricornutum* 120.3 mg l^{-1} (pH adjusted) (2).

Bioaccumulation
Calculated bioconcentration factor 0.43 (3).

Environmental fate

Adsorption and retention
Very mobile in soil (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 820 mg kg^{-1} (5).
LC_{50} (4 hr) inhalation rat 4000 ppm (6,7).
LD_{50} dermal rabbit 380-550 mg kg^{-1} (7).

Irritancy
Dermal rabbit (24 hr) 10 mg caused severe irritant effects; 50 μg instilled into rabbit eye (24 hr) caused severe irritant effects (2,8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 with and without metabolic activation negative (9).

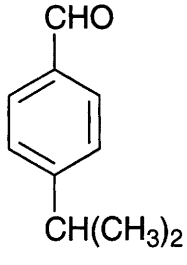
Other comments

Detected in tobacco leaves and cigarette smoke. Emitted to the air from decomposing manure in animal feed lots (10).
Physical properties, chemical properties, experimental toxicology, environmental effects, ecotoxicology, workplace experience, epidemiology, human health effects and hazards reviewed (11,12).

References

1. Groth, G. et al *Bull. Environ. Contam. Toxicol.* 1993, **50**(6), 878-882.
2. Chester, N. A. et al *Environ. Sci. (Tokyo)* 1992, **17**(3), 117-126.
3. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1982, **5, 4**, McGraw-Hill, New York, NY, USA.
4. Swann, R. L. et al *Res. Rev.* 1983, **85**, 16-28.
5. Smyth, H. F. et al *Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119-122.
6. *Interagency Collaborative Group on Environmental Carcinogenesis* 17 Jun 1974.
7. Sax, N. I. et al *Dangerous Properties of Industrial Materials* 7th ed., 1989, Van Nostrand Reinhold, New York, NY, USA.
8. Marhold, J. V. *Sbornik Vysleaku Toxixogickeho Bystreni Latek A Priprauku* 1972, **62**, Prague, Czechoslovakia.
9. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
10. Mosier, A. R. et al *Environ. Sci. Technol.* 1973, **7**, 642-644.
11. *Cah. Notes Doc.* 1990, **141**, 875-878 (Fr.) (*Chem. Abstr.* **114**, 233948c).
12. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I122 4-isopropylbenzaldehyde



$C_{10}H_{12}O$ **Mol. Wt.** 148.20 **CAS Registry No.** 122-03-2

Synonyms 4-(1-methylethyl)benzaldehyde; cumic aldehyde; *p*-isopropylbenzaldehyde

EINECS No. 204-516-9 **RTECS No.** CU 7000000

Uses Perfumery.

Occurrence In essential oils of eucalyptus, myrrh and cassia.

Physical properties

B. Pt. 235-236°C **Flash point** 93°C **Specific gravity** 0.978 at 20°C
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
50% inhibitory growth concentration *Tetrahymena pyriformis* GL-C 32.5 g m^{-3} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 1390, 2440 mg kg^{-1}, respectively (2-4).
LD_{50} dermal rabbit 2800 mg kg^{-1} (5).

Metabolism and toxicokinetics
Oral ♂ rabbits 12 g with 20 ml water, the rabbits were then allowed food and water *ad. lib.*, urine was collected for 3 days. Metabolites in urine were *p*-cumyl alcohol, *o*-cumyl alcohol, 8-hydroxycuminic acid, 9-hydroxycuminic acid, and 2-(*p*-carboxyphenyl) propinoic acid (6).

Irritancy
Dermal rabbit (24 hr) 500 mg caused irritation (5).

References

1. Schultz, T. W. et al *ASTM Spec. Tech. Publ.* 1988, **1007**(Aquat. Toxicol. Environ. Fate: 11th Vol.), 410-423.
2. Madhyasha, X. M. et al *Indian J. Biochem.* 1968, **5**, 161.
3. Rachwell, P. et al *Nutr. Cancer* 1979, **1**, 10.
4. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1964, **2**, 395.
5. Opdyke, D. L. J. *Food Cosmet. Toxicol.* 1974, **12**, 395.
6. Ishida, T. et al *Xenobiotica* 1989, **19**(8), 843-855

I123 isopropyl butyrate

$$CH_3CH_2CH_2CO_2CH(CH_3)_2$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 638-11-9
Synonyms butanoic acid,1-methylethyl ester; butyric acid, isopropylester; isopropyl butanoate
EINECS No. 211-320-7

Physical properties

M. Pt. -95°C **B. Pt.** 130-131°C **Flash point** 30°C **Specific gravity** 0.859 at 15°C with respect to water at 4°C
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 2405 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 15000 mg kg^{-1} (1).

References

1. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1964, **2**, 327

1124 isopropyl chloroformate

$ClCO_2CH(CH_3)_2$

$C_4H_7ClO_2$ **Mol. Wt.** 122.55 **CAS Registry No.** 108-23-6

Synonyms carbonochloridic acid,1-methylethyl ester; isopropyl chlorocarbonate; chloroformic acid isopropyl ester

EINECS No. 203-563-2 **RTECS No.** LQ 6475000

Physical properties

B. Pt. 105°C **Flash point** 20°C (closed cup) **Specific gravity** 1.078 at 20°C with respect to water at 4°C
Volatility v.den. 4.2
Solubility Organic solvents: acetone, chloroform, ethyl ether

Occupational exposure

UK-LTEL 1 ppm (5.1 mg m^{-3})

UN No. 2407 **Conveyance classification** toxic substance, danger of fire (flammable gas), corrosive

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1070 mg kg^{-1} (1).
LD_{50} oral mouse 178 mg kg^{-1} (2).
LD_{50} dermal mouse 12 mg kg^{-1} (2).
LD_{50} dermal rabbit 11,300 mg kg^{-1} (1).

Irritancy
500 mg (duration unspecified) instilled into rabbit eye caused severe irritation (1).

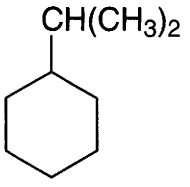
Other effects

Any other adverse effects
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 μg l^{-1} (3).
Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472 1991 (4).

References

1. *Ind. Hyg. Found. Am., Chem. Toxicol. Series, Bull.* 1967, **6**, 1, Pittsburgh, PA, USA.
2. Eckroth, D. & Grayson, M. (Eds.) *Kirk-Othmer Encyclopedia of Chemical Technology* 3rd ed., 1978, Wiley, New York, NY, USA.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

I125 isopropylcyclohexane



C_9H_{18} **Mol. Wt.** 126.24 **CAS Registry No.** 696-29-7

Synonyms 1-methylethylcyclohexane

EINECS No. 211-792-4

Physical properties

B. Pt. 155°C **Flash point** 35°C **Specific gravity** 0.802 at 20°C

Occupational exposure

UN No. 1993

Mammalian & avian toxicity

Metabolism and toxicokinetics

Oral gavage rats (concentration unspecified) experienced moderate kidney damage similar to that produced by acyclic, branched chain hydrocarbons. The urinary metabolites identified included: *cis*-4-isopropylcyclohexanol, *trans*-4-isopropylcyclohexanol, 2-cyclohexylpropanoic acid, 2-cyclohexyl-1,3-propanediol, 2-*trans*-hydroxy-4-*trans*-isopropylcyclohexanol, 2-*cis*-hydroxy-4-*cis*-isopropylcyclohexanol, and 2-*cis*-hydroxy-4-*trans*-isopropylcyclohexanol (1).

References

1. Henningsen, G. M. *J. Toxicol. Environ. Health* 1988, **24**(1), 19-25

I126 isopropyl formate

$$HCO_2CH(CH_3)_2$$

$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 625-55-8

Synonyms formic acid, 1-methylethyl ester; formic acid, isopropyl ester

EINECS No. 210-901-2 **RTECS No.** LQ 8750000

Physical properties

B. Pt. 68.3°C **Flash point** 12.2°C (closed cup) **Specific gravity** 0.873 at 20°C **Volatility** v.den. 3.03

Occupational exposure

UN No. 1281 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig 1400 μg kg^{-1} (1).

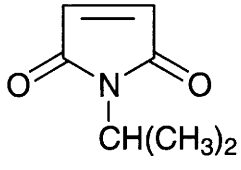
Other comments

Reviews on experimental toxicology, human health effects and physico-chemical properties listed (2).

References

1. Frear, E. H. (Ed.) *Pesticide Index* 1969, **4**, 256, College Science Publication, State College, PA, USA.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I127 *N*-isopropylmaleimide



$C_7H_9NO_2$ **Mol. Wt.** 139.15 **CAS Registry No.** 1073-93-4

Synonyms 1-(1-methylethyl)-1*H*-pyrrole-2,5-dione

RTECS No. ON 5550000

Physical properties

M. Pt. 27.5°C **B. Pt.** 85°C at 17 mmHg

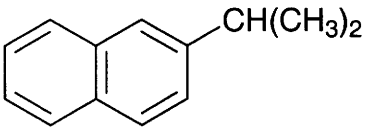
Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 18 mg kg^{-1} (1).

References

1. *US Army Armament Research and Development Command Report* Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD, USA

I128 2-isopropylnaphthalene



$C_{13}H_{14}$ **Mol. Wt.** 170.25 **CAS Registry No.** 2027-17-0

Synonyms 2-(1-methylethyl)naphthalene; β-isopropylnaphthalene

EINECS No. 217-976-0

Physical properties

M. Pt. 10.5-11°C **B. Pt.** 268°C **Specific gravity** 0.9762 at 20°C **Volatility** v.p. 5.18×10^{-3} mmHg at 25°C
Solubility Water: 0.9 mg l^{-1}

Environmental fate

Abiotic removal

Photodegradability in aquatic systems studied, $t_{1/2}$ 22.3 hr in distilled water. Photolysis rate (4hr) 93.7% in 14 g l^{-1} NaCl solution (1).

Mammalian & avian toxicity

Acute data

Intraperitoneal (24 hr) mice 3000 mg kg^{-1} no pulmonary damage. No affect on the lipid peroxidation or phospholipid contents in the lung. Maxiumum levels detected in the lung, liver and kidney 6 hr after administration (2,3).

References

1. Fukuda, K. *Chemosphere* 1988, **17**(4), 651-659.
2. Honda, T. et al *Chem. Pharm. Bull.* 1990, **30**(11), 3130-3135.
3. Honda, T. et al *Eisei Kagaku* 1990, **37**(4), 300-306 (Japan.) (*Chem. Abstr.* **115**, 225651t)

I129 isopropyl nitrate

$$(H_3C)_2CHONO_2$$

$C_3H_7NO_3$ **Mol. Wt.** 105.09 **CAS Registry No.** 1712-64-7

Synonyms nitric acid, 1-methylethyl ester; propane-2-nitrate

EINECS No. 216-983-6 **RTECS No.** QU 8930000

Uses Fuel ignition promoter in rocket fuel. Organic intermediate.

Physical properties

B. Pt. 102°C **Flash point** 12°C (closed cup) **Specific gravity** 1.036 at 20°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

SE-LEVL 10 ppm (45 mg m^{-3}) **SE-STEL** 15 ppm (70 mg m^{-3})

UN No. 1222 **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LC_{50} (2 hr) inhalation mouse 65 g m^{-3} (1).

Metabolism and toxicokinetics

Four human volunteers were exposed to 45.8 mg m^{-3} for 60 min. Expired air, blood and urine of the volunteers contained isopropyl nitrate. Respiratory $t_{1/2}$ 98 min. 0.02% of the estimated intake was excreted in the urine within 6-hr post-exposure (2).

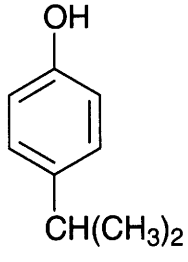
Legislation

Included in Schedule 6 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, 78, CIP, Moscow, USSR.
2. Ahonen, I. *Toxicol. Lett.* 1989, **47**(2), 205-211.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

I130 4-isopropylphenol



$C_9H_{12}O$ **Mol. Wt.** 136.19 **CAS Registry No.** 99-89-8

Synonyms 4-(1-methylethyl)phenol; *p*-cumenol; *p*-isopropylphenol; Australol

EINECS No. 202-798-8 **RTECS No.** SL 5950000

Physical properties

M. Pt. 59-61°C **B. Pt.** 212-212.5°C **Specific gravity** 0.990 at 20°C

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2430

Ecotoxicity

Fish toxicity

Steelhead trout 3 mg l^{-1} caused death within 4 hr (1).

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 0.25 mg l^{-1}, Microtox test (2).

Bioaccumulation

Accumulates in *Acinetobacter calcoacetius anitratus* grown on media containing 26-105 μg ml^{-1} *p*-isopropylphenol. There was a direct relationship between bioaccumulation and incubation time (3).

Environmental fate

Abiotic removal

Photooxidation $t_{1/2}$ of alkyl phenols in middle latitude shallow surface waters ranged from 1 day to several months (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 875 mg kg^{-1} (5).
LD_{50} intravenous mouse 40 mg kg^{-1} (6).
LD_{Lo} intraperitoneal mouse 250 mg kg^{-1} (7).

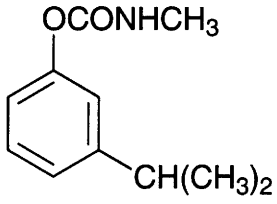
Other comments

A potential method for treating chemical pollution with phenoloxidases has been tried on *p*-isopropylphenol. Phenoloxidase activity was differently inhibited by the presence of clays and clay-humus complexes; pH and temperature also influenced activity (8).
Air pollution emission factors reviewed (9).

References

1. MacPhee, C. et al *Lethal Effects of 2014 Chemicals Upon Sockeye Salmon, Steelhead Trout and Three-Spine Stickleback* 1989, 77, EPA 560/6-89-001, PB890156715, Washington, DC, USA.
2. Heil, T. P. et al *J. Environ. Sci. Health, Part B* 1989, **B24**(4), 349-360.
3. Zaim, K. K. *Doga: Turk Mehendislik Cevre Bilimleri Derg* 1991, **15**(1), 39-53.
4. Faust, B. C. et al *Environ. Sci. Technol.* 1987, **21**(10), 957-964.
5. *Hyg. Sanit. (USSR)* 1980, **46**(1), 94.
6. *J. Med. Chem.* 1980, **23**, 1350.
7. *Summary of Tables of Biological Tests* 1953, **5**, 339, National Research Council Chemical-Biological Coordination Center, Washington, DC, USA.
8. Claus, H. et al *Water Sci. Technol.* 1990, **22**(26), 69-77.
9. Pope, A. A. et al *U.S. Environ. Prot. Agency Off. Air. Qual. Plann. Strand. [Tech. Rep.]* 1988, EPA-450/2-88-006a, EPA, Research Triangle Park, NC, USA

I131 3-isopropylphenyl methylcarbamate



$C_{11}H_{15}NO_2$ **Mol. Wt.** 193.25 **CAS Registry No.** 64-00-6

Synonyms 3-(1-methylethyl)phenyl methylcarbamate; methylcarbamic acid, *m*-cumenyl ester; *m*-cuminyl methylcarbamate; *m*-isopropylphenyl methylcarbamate

EINECS No. 200-572-3 **RTECS No.** FB 7875000

Uses Superseded insecticide (1).

Physical properties

M. Pt. 72-74°C

Solubility Water: 85 ppm at 30°C. Organic solvents: acetone, dimethylformamide, isopropanol, toluene, xylene

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 3.16-10.0 mg kg^{-1}, starling 17.0 mg kg^{-1} (2).
LD_{50} oral rat, mouse, guinea pig, chicken 10-29 mg kg^{-1} (3-6).
LD_{50} dermal rabbit, rat 40, 113 mg kg^{-1}, respectively (7,5).
LD_{50} intraperitoneal rat 14.2 mg kg^{-1} (8).
LD_{50} intravenous mouse, rat 1.4-3.2 mg kg^{-1} (9,10).
LD_{50} intramuscular dog, rat 13-14 mg kg^{-1} (10).

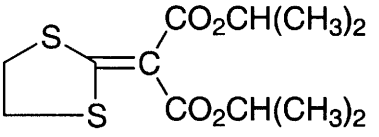
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

References

1. *The Pesticide Manual* 9th ed., 1991, British Crop Protection Council, Farnham, UK.
2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355382.
3. *Toxicol. Appl. Pharmacol.* 1972, **21**, 315.
4. *J. Agric. Food Chem.* 1970, **18**, 793.
5. *The Pesticide Manual* 1968, British Crop Protection Council, Worcestershire, UK.
6. *Toxicol. Appl. Pharmacol.* 1967, **11**, 49.
7. *Farm Chemicals Handbook* 1980, Meister Publishing Co., Willoughby, OH, USA.
8. *Bull. WHO* 1971, **44**(1-3), 241.
9. US Army Armament Research and Development Command, Report NX02085, Chemical Systems Laboratory, Aberdeen Proving Ground, MD, USA.
10. *Br. J. Ind. Med.* 1965, **22**, 317.
11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

I132 isoprothiolane



$C_{12}H_{18}O_4S_2$ **Mol. Wt.** 290.40 **CAS Registry No.** 50512-35-1

Synonyms 1,3-dithiolan-2-ylidenepropanedioic acid bis(1-methylethyl) ester; Fuji-one

RTECS No. TY 1846000

Uses Fungicide. Control of rice blast (*Pyricularia oryzae*), rice stem rot and *Fusarium* leaf spot on rice. Also reduces insect population on rice.

Physical properties

M. Pt. 54-54.5°C **B. Pt.** 167-169°C at 0.5 mmHg **Specific gravity** 1.044 **Volatility** v.p. 1.4×10^{-4} mmHg at 25°C

Solubility Water: 48 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform, dimethyl sulfoxide, hexane, methanol, xylene

Occupational exposure

JP-OEL 5 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 6.7 mg l^{-1} (1).

Medaka fry (HO5 strain) sensitive to isoprothiolane toxicity (2).

In vitro GF-scale cells (derived from goldfish scales) midpoint cytotoxicity value 253 mg kg^{-1} (3).

Invertebrate toxicity

EC_{50} *Chlamydomonas reinhardti* growth 3.4 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂ rat, ♂ mouse 1190, 1340 mg kg^{-1}, respectively (1).

LD_{50} dermal rat >10.25 g kg^{-1} (1).

Genotoxicity

Not toxic and not mutagenic in *Salmonella typhimurium* test strains, metabolic activation not specified (5).

Salmonella typhimurium TA98, TA100, TA102, TA1535, TA1538 with and without metabolic activation negative, *Saccharomyces cerevisiae* without metabolic activation negative (6).

In vitro Syrian hamster embryo morphological transformation negative. High concentrations were cytotoxic (7).

In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations equivocal (8).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).

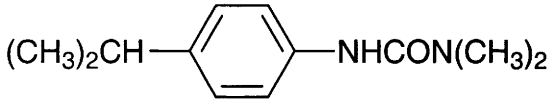
WHO Toxicity Class III (11).

EPA Toxicity Class III (12).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Miyashita, M. et al *Kokuritsu Kogai Kenkyusho Kenkyu Hokoku* 1988, **114**, 137-145 (Japan.) (*Chem. Abstr.* **109**, 33309e).
3. Saito, H. et al *Chemosphere* 1991, **23**(4), 525-527.
4. Lee, E. K. *Sikmul Hakhoe Chi* 1982, **25**, 113 (Korea.), (*Chem. Abstr.* **109**, 157691x).
5. Rusina, O. Y. et al *Gig. Sanit.* 1990, (3), 59-60 (Russ.).
6. Choi, E. J. et al *Environ. Mutagen. Carcinog.* 1985, **5**(1), 11-18.
7. Zhany, Z. et al *Huaxi Yike Daxue Xuebao* 1989, **20**(1), 96-98 (Ch.) (*Chem. Abstr.* **110** 226951n.
8. Wang, T. C. et al *Bull. Inst. Zool., Acad. Sin.* 1987, **26**(4), 317-329.
9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
12. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

I133 isoproturon



$C_{12}H_{18}N_2O$ **Mol. Wt.** 206.29 **CAS Registry No.** 34123-59-6

Synonyms *N,N*-dimethyl-*N'*-[4-(1-methylethyl)phenyl]urea; 3-(4-isopropylphenyl)-1,1-dimethylurea; 3-*p*-cumenyl-1,1-dimethylurea; Auger; Aciron; Barclay Guideline; Dinex; Graminon; Herpron; Ipon; Matin; Tolkan

EINECS No. 251-835-4 **RTECS No.** YT 0170000

Uses Herbicide, control of annual grasses and broad-leaved weeds.

Physical properties

M. Pt. 158°C **Specific gravity** 1.16 at 20°C **Partition coefficient** log P_{ow} 2.25 (pH 7, 22°C) (1)
Volatility v.p. 2.33×10^{-8} mmHg at 20°C
Solubility Water: 72 mg l^{-1} at 20°C. Organic solvents: benzene, dichloromethane, hexane, methanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Possible risk of irreversible effects (R22, R40)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) guppy, goldfish, bluegill sunfish, rainbow trout 90-240 mg l^{-1} (1).

Toxicity to other species
0.125 kg hg^{-1} sprayed onto black grass at the 2-3 leaf stage resulted in a decrease in the mean fresh weight of plants (2).

Environmental fate

Nitrification inhibition

Effect of 0.0001-0.1% isoproturon on the nitrification of ammonium nitrate. 0.0001-0.001% had no inhibitory effect; nitrification was 85-90% in the first 16 days and the process was completed by 16-24 days. 0.01% depressed nitrification; 27-38% in 32 days, completed over 32-64 days; 0.1% only 36% nitrification was observed by 64 days (3).

Nitrification by two concentrations *Azotobacter* strains was not influenced by 15 and 300 ppm doses (4).

Degradation studies

Undergoes enzymic and microbial demethylation at the nitrogen and hydrolysis of the phenylurea to 4-isopropylaniline. $t_{1/2}$ 12-29 days in soil (1).

Laboratory incubation with soil from a field that had received four doses over a 12-month period. Degradation rates of isoproturon were the same in pretreated and control soil samples (5).

Arthrobacter sp., *Bacillus* sp. and *Pseudomonas* sp. were unable to utilise isoproturon as carbon or nitrogen sources. Had no significant effect on bacterial, actinomycetes and fungal populations (6).

Aerobic soil bacteria *Pseudomonas convexa* and *Bacillus* sp. and nitrogen fixers *Rhizobium phaseoli* and *Azotobacter chroococcum* exposed 0-50 μg ml^{-1} in shake cultures did not show any adverse effect on growth; higher concentrations were inhibitory to growth. 10-20 μg ml^{-1} caused stimulation of growth in *Rhizobium phaseoli* and *Azotobacter chroococcum* (7).

In both sandy and clay soil exposed to isoproturon the metabolite 4-(2-hydroxyisopropylphenyl) urea was identified (8).

Adsorption and retention

Degradation of isoproturon in sand clay and clay loam soils demonstrated an apparent increase in the strength of adsorption with time (9).

Studied on homoionic clays at 10°C and 26°C containing Cu^{2+}, Ca^{2+} and K^{+} cations. Cationic adsorption pattern was Cu^{+}, Ca^{2+} and K^{+} in decreasing order in all three clays. Adsorption increased at lower temperatures (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral Japanese quail, pigeon >3000, >5000 mg kg^{-1}, respectively (1).

LD_{50} oral mouse, rat 3350, 3600 mg kg^{-1}, respectively (11).

LC_{50} (4 hr) inhalation ♀ rat >0.67 mg 1 air^{-1} (1).

LD_{50} intraperitoneal sheep (death after 48-56 hr) 3.6 g kg^{-1}. Heart rate increased above controls and body temperature and respiration rate decreased below controls 1-24 hr after administration (12).

Oral goat 500 mg kg^{-1} moderate cellular changes (e.g. fatty degeneration) in the liver and kidney and emphysema in the lung at 7 days (13).

Sub-acute and sub-chronic data

Oral (90 day) dog, rat no-effect level 50, 400 mg kg^{-1}, respectively (14).

Dermal (21 days) ♂ ♀ rats repeated application (unspecified dose) of technical grade and powder formulation caused mild to moderate toxic effects. Technical grade was more toxic to ♂ rats as evidenced by animal mortality and haematological enzymic changes (15).

Metabolism and toxicokinetics

Oral rat 50% is eliminated within 8 hr, predominantly in urine (14).

Following administration to goats of a single oral dose of 500 mg kg^{-1}, the compound was rapidly absorbed and appeared in the blood within 15 min. The kinetic behaviour followed a two-compartment open model with a high elimination half-life (9.87 hr) and volume of distribution (4.49 l kg^{-1}) associated with low total body clearance (0.32 l kg^{-1} hr^{-1}), suggesting slow elimination from the blood. Excretion of isoproturon in the faeces was maximum at 48 hr and approximately 56% of the total dose was recovered from the faeces. Approximately 11% of the dose was excreted in the urine. Maximum residues were detected in all tissues on day-4 after administration, declining rapidly by day-5. No residues were detected after day-7 (13).

Genotoxicity

In vivo mammalian chromosomal aberration, micronucleus and sperm-shape abnormality assays. Dose-dependent mutagenic effect in chromosomal aberrations and sperm-shape abnormality tests, micronucleus assay only significant effects seen at highest dose (200 mg kg^{-1}) (species unspecified) (16).
Mouse bone marrow micronucleus test negative in ♂ and ♀ mice (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (18).
WHO Toxicity Class III (19).
ADI 0.0062 mg kg^{-1} body weight (14).

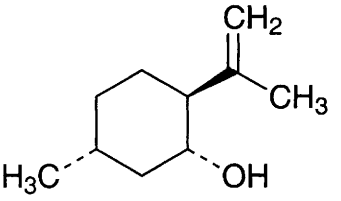
Other comments

Bioconcentration factors in the stems and leaves of two freshwater rooted macrophytes *Elodea densa* and *Ludwigia nadans* were ~ 10 and 13 after exposure to 30 and 60 μg l^{-1} isoprofuron, respectively (20).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (21).
Biodegradation reviewed (22).
Stable to light, alkali and acid.
Metabolic pathways reviewed (23).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Blair, A. M. *Weed Res.* 1978, **18**(6), 381-387.
3. Haleemi, M. A. et al *Pak. J. Sci. Ind. Res.* 1988, **31**(11), 798-800.
4. Gudkari, D. *Zentralbl. Mikrobiol.* 1987, **142**(4), 283-291.
5. Walker, A. et al *Weed Res.* 1991, **31**(1), 49-57.
6. Kapur, R. et al *Asian Environ.* 1986, **8**(4), 24-26.
7. Gupta, R. et al *J. Res. (Punjab Agric. Univ.)* 1987, **24**(3), 464-468.
8. Berger, B. et al *Fresenius' Z. Anal. Chem.* 1989, **334**(4), 360-362 (*Chem. Abstr.* **111**, 110898s).
9. Blair, A. M. et al *Crop Prot.* 1990, **9**(4), 289-294.
10. Kumar, Y. et al *J. Indian Soc. Soil. Sci.* 1987, **35**(3), 394-399.
11. Thizy, A. et al *C. R. Ser. D* 1972, **274**, 2053.
12. Mikhailov, G. et al *Vet.-Med. Nauki* 1987, **24**(2), 30-35 (Bulg.) (*Chem. Abstr.* **108**, 162978a).
13. Juliet, S. et al *J. Agric. Food Chem.* 1998, **46**(1), 178-183.
14. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
15. Dikshith, T. S. et al *Vet. Hum. Toxicol.* 1990, **32**(5), 432-434.
16. Behera, B. C. et al *Indian J. Exp. Biol.* 1990, **28**(9), 826-827.
17. Gebel, T. et al *Arch. Toxicol.* 1997, **71**(3), 193-197.
18. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
19. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
20. Grollier, T. et al *Ecotoxicol. Environ. Saf.* 1997, **36**(3), 205-212.
21. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
22. Frimmel, F. H. *Vom Wasser* 1989, **73**, 273-286 (Ger.) (*Chem. Abstr.* **112**, 104455z).
23. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

I134 isopulegol



$C_{10}H_{18}O$ **Mol. Wt.** 154.25 **CAS Registry No.** 89-79-2

Synonyms 5-methyl-2-(1-methylethenyl)cyclohexanol, [1*R*-(1α,2β,5α)]-; (1*R*,3*R*,4*S*)-(–)-*p*-menth-8-en-3-ol

EINECS No. 201-940-6 **RTECS No.** OT 0190000

Physical properties

B. Pt. 268°C; 91°C at 12 mmHg **Flash point** 78°C **Specific gravity** 0.911 at 20°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity

5 ppm (24 hr) caused no toxic effects to trout, bluegill sunfish, yellow perch and goldfish (1).
Stickleback 10 mg l^{-1} caused the death of 50% of the fish within 1 hr. The remaining fish remained alive for the duration of the experiment (48 hr) (2).

Environmental fate

Degradation studies

Bacterium (species unspecified) from sewage isolated by enrichment on (–)-methanol will utilize (–)-isopulegol as a sole carbon source, but not (+)-isopulegol (3).

Mammalian & avian toxicity

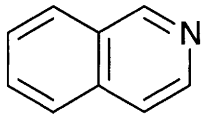
Metabolism and toxicokinetics

In vitro rat liver microsomes, major metabolite is the allylic alcohol with menthofuran as a minor metabolite (4).

References

1. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, PB87-200-275, Washington, DC, USA.
2. MacPhee, C. et al *Lethal Effects of 2014 Chemicals upon Sockeye Salmon, Steelhead Trout and Three-Spine Stickleback* 1989, EPA 560/6-89-001, PB89-156715, Washington, DC, USA.
3. Shukia, O. P. et al *Can. J. Microbiol.* 1987, **33**(6), 489-497.
4. Madyastha, K. M. *Biochem. Biophys. Res. Commun.* 1990, **173**, 1086

I135 isoquinoline



C_9H_7N **Mol. Wt.** 129.16 **CAS Registry No.** 119-65-3

Synonyms 2-azanaphthalene; 2-benzazine; benzopyridine; benzo[*c*]pyridine; leucoline; β-quinoline

EINECS No. 204-341-8 **RTECS No.** NW 6825000

Uses In the synthesis of insecticides, antimalarials and dyes.

Occurrence In coal tar. Component of creosote.

Physical properties

M. Pt. 26-28°C **B. Pt.** 242°C **Flash point** >107°C **Specific gravity** 1.099 at 30°C with respect to water at 4°C

Partition coefficient log P_{ow} 2.08

Solubility Organic solvents: miscible with acetone, benzene, diethyl ether

Ecotoxicity

Fish toxicity

5 ppm (24 hr) caused no toxic effects on trout, bluegill sunfish, yellow perch and gold fish (1).

Invertebrate toxicity

LC_{50} (24 hr) *Daphnia pulex* 39.9 mg l^{-1} (2).

LC_{50} (24 hr) *Tetrahymena pyriformis* 0.8 g l^{-1} (3).

EC_{50} (5, 15 min) *Photobacterium phosphoreum* 1.7, 2.2 mg l^{-1}, respectively, Microtox test (4).

Environmental fate

Degradation studies

Anaerobically degradable to methane and carbon dioxide (5).

Transformed by microbial action to oxygenated analogue (6).

Microbial community of Gram-negative rods isolated from sewage utilised isoquinoline as sole nitrogen and carbon source. 1-Hydroxyisoquinoline was identified as the major transformation-product. Transformation via dihydroxyisoquinoline was suggested by the accumulation of a pink product in the reaction mixture (7).

Acinetobacter sp. isolated from oil- and creosotecontaminated soils utilised isoquinoline as sole carbon and nitrogen source. Degradation was associated with the build up of the pigment 1-hydroxyisoquinoline, which was further degraded to unknown intermediate ring cleavage products and carbon dioxide (8).

Alcaligenes faecalis and *Pseudomonas diminuta* will utilise isoquinoline as sole carbon source. Both excreted the metabolite 1-oxo-1,2-dihydroisoquinoline (9).

1.5 μg ml^{-1} mixed with ground water and microorganisms from creosote-contaminated soil (27 μg bacterial protein added) incubated 30°C for 14 days. Samples at 1, 3, 5, 8, and 14 days contained 0.9, 0.3, 0.3, 0.1, and undetectable μg ml^{-1}, respectively. The sterile control contained 1.4 μg after 14 days (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 360 mg kg^{-1} (11).

LD_{50} dermal rabbit 590 mg kg^{-1} (11).

LD_{Lo} intraperitoneal mouse 128 mg kg^{-1} (12).

Irritancy
Dermal rabbit (24 hr) 10 mg (uncovered) caused severe irritation and 250 μg instilled into the eye (duration unspecified) caused severe irritation (11).

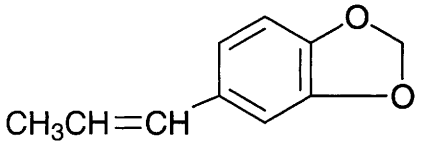
Genotoxicity

A CASE study reported isoquinoline to have marginal genotoxic potential (13).

References

1. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, PB87-200-275, Washington, DC, USA.
2. Southwold, G. R. et al *Environm. Sci. Technol.* 1978, **12**(9), 1062-1066.
3. Schultz, T. W. et al *Arch. Environ. Contam. Toxicol.* 1978, **7**, 457-463.
4. Birkholz, D. A. et al *Water Res.* 1990, **24**(1), 67-73.
5. Pereira, W. E. et al *Water Sci. Technol.* 1988, **20**(11-12), 17-23.
6. Gobsy, E. M. et al *U.S. Environ. Prot. Agency Res. Dev.* [Rep.] EPA 1990, EPA-600/9-90/401, 39-42.
7. Shukla, O. P. *Microbiol. Lett.* 1990, **45**(178), 89-96.
8. Aislabie, J. et al *Appl. Environ. Microbiol.* 1989, **55**(12), 3247-3249.
9. Roeger, P. et al *Biol. Chem. Hoppe-Seyler* 1990, **371**(6), 511-13.
10. Muller, J. K. et al *Appl. Environ. Microbiol.* 1991, **57**(5), 1277-1286.
11. Smyth et al *Arch. Ind. Occup. Med.* 1951, **4**, 119.
12. *Summary Tables of Biological Tests* 1950, **2**, 189, National Research Council Chemical-Biological Coordination Centre, Washington, DC, USA.
13. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50

I136 isosafrole



$C_{10}H_{10}O_2$ **Mol. Wt.** 162.19 **CAS Registry No.** 120-58-1

Synonyms 5-(1-propenyl)-1,3-benzodioxole; 1,2-(methylenedioxy)-4-propenylbenzene

EINECS No. 204-410-2 **RTECS No.** DA 5950000

Uses Modification and strengthening of perfumes. Manufacturing of heliotropin.

Physical properties

M. Pt. 8.2°C (*trans* form), –21.5°C (*cis* form) **B. Pt.** 253°C (*trans* form), 77-79°C at 3.5 mmHg (*cis* form)
Flash point 104°C **Specific gravity** 1.1206 at 20°C with respect to water at 4°C (*trans* form), 1.1182 with respect to water at 4°C (*cis* form)
Solubility Organic solvents: soluble in 8 parts of 90% ethanol; miscible with benzene, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 1340, 2470 mg kg^{-1}, respectively (1,2).
LD_{50} oral redwing blackbird >1000 mg kg^{-1} (3).
LD_{Lo} intraperitoneal, intravenous mouse, rabbit 256, 300 mg kg^{-1}, respectively (4,5).
LD_{Lo} subcutaneous cat 2 g kg^{-1} (5).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3. Degree of evidence not previously categorised; evaluation based on criteria in Monograph 10, 1976 (6).

Oral ♂, ♀ rat, mouse maximum tolerated dose continuous administration from 7 days of age caused no neoplasms of the forestomach (7).

Oral (82 wk) mouse 215 mg kg^{-1} daily in distilled water induced lung and liver tumours (8).

Irritancy

Dermal rabbit (24 hr) caused moderate irritation (9).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation negative (10).

CASE structural activity methodology, based on qualitative chemical structural features to predict mutagenic potential, classified isosafrole as being marginally active (11).

In vitro rat hepatocytes unscheduled DNA synthesis negative. Cytotoxic at concentrations between 10^{-3} and 10^{-2} M (12).

♀ CD-1 mice injected intraperitoneally with [^{32}P]-isosafrole showed a low level of radiolabel binding to liver-DNA (13).

Other effects

Any other adverse effects

In vitro (72 hr) rat hepatocytes induced several cytochrome P_{450} isoenzymes, demonstrated by increased catalytic activity by western blotting and by immunocytochemistry (14).

Other comments

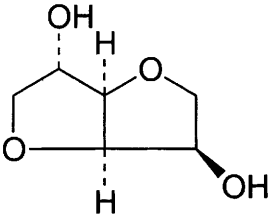
Pretreatment of mice with isosafrole is highly effective at preventing CCl_4-induced liver damage *in vivo*, probably by forming metabolic intermediate complexes with cytochrome P_{450}, and also protects against ferric nitrilotriacetate-induced renal necrosis and lipid peroxidation. In the latter case, metabolic activation by cytochrome P450 is not involved (15,16).

Reviews on human health effects and experimental toxicology listed (17).

References

1. *Toxicol. Appl. Pharmacol.* 1965, 7, 18.
2. *Food Cosmet. Toxicol.* 1964, **2**, 327.
3. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
4. *Summary Tables of Biological Tests* 1949, **1**, 45, National Research Council Chemical-Biological Coordination Centre.
5. *Arch. Exp. Pathol. Pharmakol.* 1895, **35**, 342 (Ger.).
6. *IARC Monograph* 1987, **Suppl. 7**, 65.
7. Reuber, M. D. et al *Digestion* 1979, **19**(1), 42-47.
8. Innes, J. R. M. *J. Natl. Cancer Inst.* 1969, **42**, 1101-1114.
9. *Food Cosmet. Toxicol.* 1976, **14**, 307.
10. Wislocki, P.G. et al *Cancer Res.* 1977, **37**(6), 1883-1891.
11. Klopman, G. et al *Mutat. Res.* 1990, **228**(1), 1-50.
12. Howes, A. J. *Food Chem. Toxicol.* 1990, **28**(8), 537-542.
13. Randerath, K. et al *Carcinogenesis (London)* 1984, **5**(12), 1613-1622
14. Bars, R. G. *Biochem. J.* 1989, **262**(1), 151-158.
15. Zhao, Z. S. et al *Toxicol. Appl. Pharmacol.* 1996, **140**, 411-421.
16. Zhao, Z. S. et al *Chem.-Biol. Interact.* 1997, **108**(1,2), 107-118.
17. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.

I137 isosorbide



$C_6H_{10}O_4$ **Mol. Wt.** 146.14 **CAS Registry No.** 652-67-5

Synonyms 1,4:3,6-dianhydro-D-glucitol; Devicorun; Hydronol; Isobide, 1,4:3,6-dianhydrosorbitol; Ismotic

EINECS No. 211-492-3 **RTECS No.** LZ 4380000

Uses As a diuretic

Physical properties

M. Pt. 61-64°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 24,150 mg kg^{-1} (1).

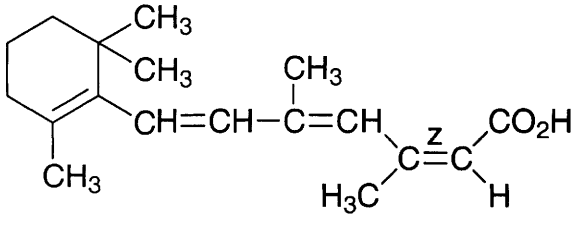
LD_{50} intravenous mouse, rat 6870 and 11,300 mg kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal mouse 13,600 mg kg^{-1} (3).

References

1. *Pharmacometrics* 1969, **3**, 15.
2. *Jpn. J. Pharmacol.* 1982, **6**, 71.
3. *Drugs in Japan. Ethical Drugs* 6th ed., 1982, Edo Japan Pharmaceutical Information Centre, Yukugyo Jiho Co. Ltd., Tokyo, Japan

I138 isotretinoin



$C_{20}H_{28}O_2$ **Mol. Wt.** 300.44 **CAS Registry No.** 4759-48-2

Synonyms 13-*cis*-retinoic acid; neovitamin A acid; 13-*cis*-vitamin A acid; Accutane

EINECS No. 225-296-0 **RTECS No.** VH 6440000

Uses Treatment of severe acne and other skin disorders.

Physical properties

M. Pt. 174-175°C
Solubility Organic solvents: ethanol

Ecotoxicity

Invertebrate toxicity
Interferes with final differentiation of hydra buds, *in vitro* Hydra Assay (duration, dose unspecified) (1).
American sea urchin, isotretinoin induced a dose-related delay in development. Isotretinoin metabolites, 4-oxoisotretinoin and 4-oxotretinoin, and the isomer tretinoin induced strikingly dysmorphic development. It is suggested that it is the metabolites rather than the parent compound which are responsible for foetal abnormalities observed in higher animals (2).

Toxicity to other species
Frog embryo teratogenesis assay, small cell frog blastulae exposed 96 hr. Scored as having strong teratogenic potential (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, mouse 1960, 3389 mg kg^{-1}, respectively (4).
LD_{50} intraperitoneal mouse 138 mg kg^{-1} (4).

Teratogenicity and reproductive effects
Teratogenicity of single oral dose 200 mg kg^{-1} to pregnant ICR mice on days 7, 8 or 9 of gestation on craniofacial development was tested. Day-8 of gestation was the most sensitive period; resorption rates were 46%; 88% of embryos and 100% of litters developed malformations. Treatment on day-9 of gestation, resorption rates normal but 9/10 litters and 75% of embryos had malformations, mostly of their palate and ear auricle. This indicates a strong developmental stage-dependent susceptibility to the drug and stage-specific pattern of malformations. The target of the drug appears to be the neural crest and developing neuroepithelium (5).
Oral TO mice were administered 100, 150, or 200 mg kg^{-1} on one of gestion days 8-12. A large number of the mice dosed at any of the three levels on days 8 or 9 suffered caudal regression syndrome. The data suggest that the highest dose caused caudal agenesis and the lower doses caudal regression due to a combination of vascular disruption, oedema, and cell death (6).
Postnatal mouse screening test 85 mg kg^{-1} per day (duration not specified). Caused no effect on maternal mortality, the number of viable litters, litter size or pup birth weight (7).
Pregant cynomolgus macaque oral, four dose regimes: dose A: 2, 10, 25 mg kg^{-1} on gestation days (GD) 18-28; dose B: 5 mg kg^{-1} as an equally divided dose twice daily, GD 21-24; dose C: 5 mg kg^{-1} as an equally divided dose twice daily GD 25-27 and dose D: 2.5 mg kg^{-1} daily GD 10-25 and then twice (2×2.5 mg kg^{-1}) daily GD 26-27. Dose A caused maternal death and toxicity indicated by a reduction in weight and food consumption and diarrhoea at all dose levels. No significant maternal toxicity observed in dose regimes B-D. Dose regimes A and B were embryo lethal, embryonic death was not significant in dose C. Examination of GD 100 embryos showed no malformations in doses A-C, dose D resulted in embryo malformations of 71% with malformed external ears, 57% with hypoplasia or aplasia of the thymus and 29% with malformations of the heart (8).
Chick embryos were injected via the yolk sac with single 15 µl doses of either 1.5 µg, 15 µg or 150 µg on embryonic days 2, 3, 4, 5 or 6. Examination on day-14 of incubation showed mortality and total malformations were dose and developmental-stage responsive. Defects occurred in mesenchymal tissues derived from the cranial neural crest ectomesenchyme which are analogous to those observed in animal models and in human foetuses exposed during maternal therapy for cystic acne. The greatest incidence of malformations occurred when isotretinoin was given after cranial neural crest cell migration was complete (9).
In vitro 9.5-day rat embryo grown in culture for 48 hr with serum concentration of 500 ng ml^{-1} induced defects in visceral arch development. Embryos must be exposed for a minimum period of time, regardless of the concentration of isotretinoin above the 500 ng ml^{-1} threshold (10).

Oral 40-80 mg day^{-1} during the 1st month of human pregnancy can induce severe congenital malformation. The human accutane dysmorphic syndrome is characterised by rudimentary external ears, absent or imperforate auditory canals, cleft palate, depressed midface, abnormalities of brain jaw and heart. Humans are ~16 × more sensitive to the teratogenic effects of oral isotretinoin than hamsters (11).

Metabolism and toxicokinetics

Percutaneous absorption *in vivo* monkey and exposure to light caused 60% degradation on the surface of the skin but did not change the amount penetrating the epidermis. On human skin the amount penetrating the epidermis did not increase over a 25-fold range of dose (12).

Oral pregnant hamster single dose 35 μg kg^{-1} administered during primitive streak stage of embryo development. Found distributed in all tissues sampled (including placenta and foetus) the largest accumulation was in the liver with the least in fat. Isotretinoin had a slower clearance and the longest elimination ($t_{1/2}$) time of the acidic retinoids tested (13).

Human oral 80 mg (single dose), excreted 17-23% of drug by 4 days. Major metabolites in bile were glucuronide conjugates of 4-oxoisotretinoin and 16-hydroxyisotretinoin. Minor metabolites were glucuronide conjugates of isotretinoin and 18-hydroxyisotretinoin (14).

Single 100 mg kg^{-1} and multiple 3 × 100 mg kg^{-1} 4 hr apart, given to NMRI mice on day-10 of gestation. Major plasma metabolite was 13-*cis*-retinoyl-β-glucuronide followed by 4-oxo-metabolites and all-*trans*-retinoic acid. Transfer to the mouse embryo was very efficient for all-*trans*-retinoic acid and 10-fold less efficient for 13-*cis*-retinoic acid (15).

Metabolised by mouse liver, but not skin, microsomes *in vitro* to *cis*- and *trans*-4-hydroxy-13-retinoic acid and 4-oxo-13-retinoic acid as major metabolites (16).

Genotoxicity

In vitro human embryonic palatal mesenchymal (HEPM) cells with and without metabolic activation interferes with DNA synthesis and decreases HEPM cell proliferation (17).

Other effects

Other adverse effects (human)

Healthy human volunteers dermal 1.5% solution, dose-related exfoliative effects, expressed by an increase of cell counts (number of corneocytes cm^{-2} skin surface) and a decrease of corneocyte area (18).

In vitro human teratocarcinoma-derived cell line, PA-1, 10^{-6} to 10^{-8} M did not significantly alter the log-phase growth rate but did decrease the saturation cell density and mitotic indexes. Also induced changes in cell morphology which appear to be related to reorganisation of microtubules and microfilaments (19).

Any other adverse effects

Systemic administration (dose unspecified) hamster caused a reduction of acinar tissue in the meibomiam gland. Clinical observations included alopecia and weight loss. Ocular complications included crusting of the eyelid margin and the external surface of the lid and erythema of the conjunctiva (20).

Oral mice (dose, duration unspecified), mice killed and examined at 4, 7 and 12 wk. Effects on *in vivo* immune regulation were characterised by expansion of the splenic marginal zone and the paracortical region of the lymph nodes (21).

Oral (in food) rat 45 mg kg^{-1} increased total serum triacylglycerol and cholesterol concentrations after 3 days. Higher doses (≥450 mg kg^{-1}) did not increase triacylglycerol earlier (22).

Other comments

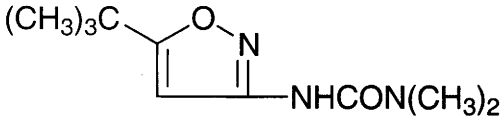
A significant delay in tumour onset was observered in rats pretreated with isotretinoin, 300 mg kg^{-1} in diet, 1 wk prior to tumour induction with 1,2-dimethylhydrazine (20 mg kg^{-1} each wk for 20 wk) (23).

Effects on epidermal proliferation, mechanisms of action, antitumour pharmacology and anti-inflammatory action reviewed (24-26).

References

1. Johnson, E. M. et al *Teratology* 1989, **39**(4), 349-361.
2. Kahn, T. A. et al *Fundam. Appl. Toxicol.* 1988, **11**(3), 511-518.
3. DeYoung, D. J. et al *Drug Chem. Toxicol.* (1977) 1991, **14**(1-2), 127-141.
4. Sporn, M. B. et al (Ed.) *The Retinoids* Volume 2, 1984, Academic Press, New York, NY, USA.
5. Park, S. H. et al *Koryo Taehakkyo Uikwa Taehalz Nonmunjip* 1986, **23**(3), 145-156 (Korean) (*Chem. Abstr.* **107**, 51983h.
6. Padmanabhan, R. *Reprod. Toxicol.* 1998, **12**(2), 139-151.
7. *Environmental Health Research and Testing Inc., Report* 1987, Order No.PB89-139075, Avail. NTIS (*Chem. Abstr.*, **111**, 1483269).
8. Hummler, H. et al *Teratology* 1990, **42**(3), 263-272.
9. Hart, R. C. et al *Teratology* 1990, **41**(4), 463-472.
10. Ritchie, H. et al *Teratology* 1991, **43**(1), 71-81.
11. Willhite, C. G. et al *J. Craniofacial Genet. Dev. Biol.* 1986 (Suppl.2), 193-209.
12. Lehman, P. A. et al *J. Invest. Dermatol.* 1988, **91**(1), 56-61.
13. Howard, W. B. et al *Arch. Toxicol.* 1989, **63**(2), 112-120.
14. Vane, F. M. et al *Xenobiotica* 1990, **20**(2), 193-207.
15. Kraft, J. C. et al *Teratog., Carcinog., Mutagen.* 1991, **11**(1), 21-30.
16. Oldfield, N. *Drug Metab. Dispos.* 1990, **18**(6), 1105-1107.
17. Watanabe, T. et al *J. Nutr. Sci. Vitaminol.* 1990, **36**(4), 311-325.
18. Haidl, G. et al *J. Soc. Cosmet. Chem.* 1988, **39**(1), 53-67.
19. Taylor, D. D. et al *Differentiation* 1990, **43**(2), 123-130.
20. Lumbert, R. W. et al *J. Invest. Dermatol.* 1989, **92**(3), 321-325.
21. Kutz, D. R. et al *Br. J. Exp. Pathol.* 1987, **68**(3), 343-350.
22. McMaster, J. et al *Arch. Dermatol. Res.* 1989, **281**(2), 116-118.
23. O'Dwyer, P. J. et al *Surg. Forum* 1986, **37**, 436-438.
24. Lever, L. R. et al *Retinoids: 10 years on, Retinoid Symp. 1990* Pub. 1991, Ed., Saurat, J. H., Karger, Basel, Switzerland.
25. Chomienne, C. *Pathol. Biol.* 1989, **37**(8), 865-867 (Fr.) (*Chem. Abstr.* **111**, 224695a).
26. Coffey, J. W. et al *Int. Congr. Ser. – Excerpta Med.* 1987, **750**, 705-708

I139 isouron



$C_{10}H_{17}N_3O_2$ **Mol. Wt.** 211.26 **CAS Registry No.** 55861-78-4

Synonyms *N'*-[5-(1,1-dimethylethyl)-3-isoxazolyl]-*N,N*-dimethylurea; isuron; Isoxyl; SSH

RTECS No. YT 0058000

Uses Pre- and post-emergence control of broad-leaved and grass weeds in sugar cane and pineapples. Also used for total weed control on non-crop land.

Physical properties

M. Pt. 119-120°C **Specific gravity** 1.23 at 20°C **Partition coefficient** log P_{ow} 1.98 (1)
Volatility v.p. 3.8×10^{-7} mmHg at 25°C
Solubility Water: 790 mg l^{-1} at 25°C. Organic solvents: acetone, ethanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp, Japanese killifish 78.7, 173.0 mg l^{-1}, respectively (1).
LC_{50} (96 hr) rainbow trout, bluegill sunfish 110-140 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} (72 hr) acute oral honeybee 1600 mg kg^{-1} (2).

Environmental fate

Degradation studies

In soil $t_{1/2}$ 22 days, some microbial degradation can occur (1).

Biodegradation in sewage and river water, incubation period of 120 days 0.01, 0.1 ppm added to samples. In sewage 31 and 25%, respectively, were mineralised whereas only 7% was mineralised in river water, although the amount of isouron decreased to 66-68% the original amount. Metabolites identified in the aqueous environment were: *N,N*-dimethyl-*N'*- [5-(1,1-dimethyl-2-formylethyl)-3-isoxazolyl]urea, *N*-methyl-*N'*-[5-(1,1-dimethylpropyl)-3-isoxazolyl]urea, *N*-[5-(1,1-dimethylpropyl)-3-isoxazolyl]urea, *N,N*-dimetyl-*N'*-[5-(1,1-dimethyl-3-hydroxypropyl)-3-isoxazoly]urea and *N*-methyl-*N'*-[5-(1,1-dimethyl-3-hydroxypropyl)-3-isoxazolyl]urea (3).

Degradation of 4 ppm applied to soils followed 1st order kinetics. $t_{1/2}$ 42-203 days at 10-40°C with water contents adjusted to 20-90% of the field capacity. The rate of degradation was correlated with temperature between 20-40°C. The same metabolites as above were formed (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 520, 760 mg kg^{-1} (1).

LD_{50} oral bobwhite quail >2000 mg kg^{-1} (1).

LC_{50} (8 hr) inhalation rat >0.415 mg 1 air^{-1} (1).

LD_{50} dermal rat 5000 mg kg^{-1}.

LD_{50} intraperitoneal rat 270 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral (2 yr) rat no-effect level 7.26-8.77 mg kg^{-1} day^{-1}, mice 3.42-16.6 mg kg^{-1} day^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

WHO Toxicity Class III (7).

ADI 0.0342 mg kg body weight (2).

Metabolic pathways reviewed (8).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Wang, Y. S. et al *Nippon Noyaku Gakkaishi* 1991, **16**(1), 19-25.
4. Wu, T. C. et al *Nippon Noyaku Gakkaishi* 1991, **16**(2), 195-200.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
8. Roberts, T.R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

I140 isovaleraldehyde

$(CH_3)_2CHCH_2CHO$

$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 590-86-3

Synonyms 3-methylbutanal; 3-methylbutyraldehyde; isoamyl aldehyde; isopentanal; isovaleric aldehyde; 3-methylbutyraldehyde

EINECS No. 209-691-5 **RTECS No.** ES 3450000

Uses Flavour/perfume manufacture, pharmaceuticals and synthetic resins.
Occurrence Orange, peppermint, lemon, eucalyptus and other oils.

Physical properties

M. Pt. −51°C **B. Pt.** 90°C **Flash point** −1°C **Specific gravity** 0.785 at 20°C with respect to water at 20°C
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 2058 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity
LC_{50} (14 day) guppy 2.19 μg l^{-1} (1).

Environmental fate

Degradation studies
Waste water treatment (activated sludge): 6 hr, 9.2% of ThOD; 12 hr, 14.2% of ThOD; 24 hr, 16.1% of ThOD (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 8.91 g kg^{-1} (3).
LC_{Lo} (4 hr) inhalation rat 16,000 ppm (3).
LD_{50} dermal rabbit 3.18 g kg^{-1} (3).

Metabolism and toxicokinetics
Metabolised *in vitro* by cytochrome P_{450} rabbit liver isoenzymes by oxidative cleavage and olefin formation (4).

Genotoxicity

Bacillus subtilis H17 with and without metabolic activation positive (5).

Other comments

Recommended for testing for health effects, environmental and ecological fate by the US Federal Toxic Substances Control Act March 1991 (6).

References

1. Deneer, J. W. *Aquat. Toxicol.* 1988, **12**(2), 185-192.
2. Gerhold, R. M. et al *J. Water Pollut. Control Fed.* 1966, **38**(4), 562.
3. *Toxicol. Appl. Pharmacol.* 1974, **28**, 313.
4. Roberts et al *Proc. Nat. Acad. Sci. U.S.A.* 1991, **88**(20), 8963-8966.
5. Matsui, S. et al *Water Sci. Technol.* 1989, **21**(8-9), 875-887.
6. *Fed. Regist.* 06 Mar 1991, **56**(44), 9534-9572

I141 isovaleric acid

$$(CH_3)_2CHCH_2CO_2H$$

$C_5H_{10}O_2$ **Mol. Wt.** 102.13 **CAS Registry No.** 503-74-2

Synonyms 3-methylbutanoic acid; isopropylacetic acid; delphinic acid

EINECS No. 207-975-3 **RTECS No.** NY 1400000

Uses Used in flavours and perfumes. Intermediate in organic synthesis.

Occurrence Natural substance in hop oil, tobacco and valerian.

Physical properties

M. Pt. –37°C **B. Pt.** 175-177°C **Specific gravity** 0.931 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 0.93 (calculated)

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Bioaccumulation

Enters surface waters in the effluents from sewage works; typical concentrations range from 0.8 to 574 μg l^{-1} in the effluent, but because the log P_{ow} for the acid is only 0.93 it is improbable that aquatic fauna would be exposed to appreciable concentrations (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2000 mg kg^{-1} (2).

LD_{50} dermal rabbit 310 mg kg^{-1} (2).

LD_{50} intravenous mouse 1120 mg kg^{-1} (3).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation and 940 μg instilled into rabbit eye caused mild irritation (2,4).

Other comments

Reviews on experimental toxicology and human health effects listed (5).

References

1. Murtaugh, J. J. et al *J. Water Pollut. Control Fed.* 1965, **37**, 410-415.
2. *Union Carbide Safety Data Sheets* 31 Jan 1972, Union Carbide Corp., New York, NY, USA.
3. Ore, L. et al *Acta Pharmacol. Toxicol.* 1961, **18**, 141.
4. Opdyke, D. C. J. *Food Cosmet. Toxicol.* 1979, **17**, 841.
5. *ECETOC Technical Report No. 30(5)* 1994, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

I142 isovaleronitrile

$CH_3CH(CH_3)CH_2CN$

C_5H_9N **Mol. Wt.** 83.13 **CAS Registry No.** 625-28-5

Synonyms 3-methylbutanenitrile; isoamyl cyanide; 3-methylbutyronitrile; 2-methylbutane-*sec*-mononitrile

EINECS No. 210-884-1 **RTECS No.** NY 1750000

Uses Organic synthesis.

Occurrence Aroma component in tomatoes.

Physical properties

M. Pt. –100.9°C **B. Pt.** 130.3°C **Specific gravity** 0.795 at 15°C with respect to water at 4°C

Partition coefficient log P_{ow} 0.85

Mammalian & avian toxicity

Acute data

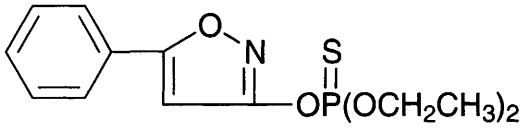
LD_{50} oral mouse 230 mg kg^{-1} (1).

LD_{Lo} subcutaneous rabbit 43 mg kg^{-1} (2).

References

1. *Nippon Eiseigaku Zasshi* 1984, **39**, 423.
2. *Arch. Int. Pharmacodyn. Ther.* 1899, **5**, 161

I143 isoxathion



$C_{13}H_{16}NO_4PS$ **Mol. Wt.** 313.31 **CAS Registry No.** 18854-01-8

Synonyms phosphorothioic acid, *O,O*-diethyl *O*-(5-phenyl-3-isoxazolyl) ester; Karphos

EINECS No. 242-624-8 **RTECS No.** TF 5600000

Uses Control of scale insects, aphids, hoppers, beetles and caterpillars on citrus fruit, tea, tobacco, garden trees, rice, sugarcane and vegetables.

Physical properties

B. Pt. 160°C at 0.15 mmHg **Partition coefficient** log P_{ow} 0.589 (1) **Volatility** v.p. 1.0×10^{-6} mmHg at 25°C

Solubility Water: 1.9 mg l^{-1} at 25°C

Occupational exposure

Supply classification toxic

Risk phrases Toxic in contact with skin and if swallowed (R24/25)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with

skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S36/37, S45)

Ecotoxicity

Fish toxicity

In vitro GF-scale cells (derived from goldfish scales) midpoint cytotoxicity value 14.7 mg l^{-1} (2).

LC_{50} (48 hr) carp 2.1 mg l^{-1} (2).

Environmental fate

Degradation studies

$t_{1/2}$ 9-40 days in soils (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken, mouse 21.6, 79.1 mg kg^{-1}, respectively (3).

LD_{50} oral rat 112 mg kg^{-1} (4).

LD_{50} dermal mouse, rat 193, 450 mg kg^{-1}, respectively (4).

LD_{50} intraperitoneal mouse 105 mg kg^{-1} (3).

LD_{50} subcutaneous mouse 720 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Oral (2 yr) rat no-effect level 1.2 mg kg^{-1} (1).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances)Statutory Instrument No. 472, 1991 (5).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).

WHO Toxicity Class Ib (7).

EPA Toxicity Class II (formulation) (8).

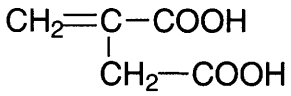
Other comments

Unstable in alkalis. Decomposes at 160°C.

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Saito, H. et al *Chemosphere* 1991, **23**(4), 525-537.
3. *Annual Report of Sankyo Research Laboratories* 1977, **29** 1, Tokyo 140.
4. *Bull. Entomol. Soc. Am.* 1969, **15**, 121.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
8. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

I144 itaconic acid



$C_5H_6O_4$ **Mol. Wt.** 130.10 **CAS Registry No.** 97-65-4

Synonyms methylenesuccinic acid; propylenedicarboxylic acid; methylenebutanedioic acid

EINECS No. 202-599-6

Uses Co-monomer in the synthesis of acrylic fibres and latex. Aluminium anodising reagent.

Physical properties

M. Pt. 162-164°C (with decomp.), also reported as 172°C **B. Pt.** 268°C **Specific gravity** 1.63 at 20°C
Partition coefficient log P_{ow} –0.4 at 25°C
Solubility Water: 83 g l^{-1} at 20°C. Organic solvents: alcohol

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) *Salmo gardineri* 190 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (24 hr) *Daphnia magna* 240 mg l^{-1} (1).
ECb_{50} (72 hr) *Scenedesmus subspicatus* 47 mg l^{-1} (1).

Environmental fate

Degradation studies
Readily biodegradable under aerobic conditions in water; 96% biodegradation after 13 days (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2969 mg kg^{-1} (1).
LD_0 dermal rat >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Gavage Sprague-Dawley rats (4 wk) 80, 200, 500 mg kg^{-1} day^{-1}. No toxic effects were observed at any dose level (1).
Oral Sprague-Dawley rats (13 wk) 0, 1500, 4700, 14000 ppm daily in diet. NOEL 14,000 ppm daily (1050 mg kg^{-1} day^{-1}) (1).

Teratogenicity and reproductive effects
Gavage CD rats 250-1000 mg kg^{-1} day^{-1} on gestation days 6-15. All animals were killed on gestation day-20 and foetuses were examined. NOAEL for pregnant rats 1000 mg kg^{-1} day^{-1}. NOEL for offspring 1000 mg kg^{-1} day^{-1} (1).

Irritancy
Rabbit eye irritant (1).

Sensitisation
Not a skin sensitiser in guinea pigs (1).

Genotoxicity

Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100 with and without metabolic activation negative (1).
Chinese hamster V79 lung fibroblasts with and without metabolic activation non-mutagenic (1).
CHO cells with and without metabolic activation non-clastogenic (1).
Non-genotoxic *in vivo* to Swiss mice (1).

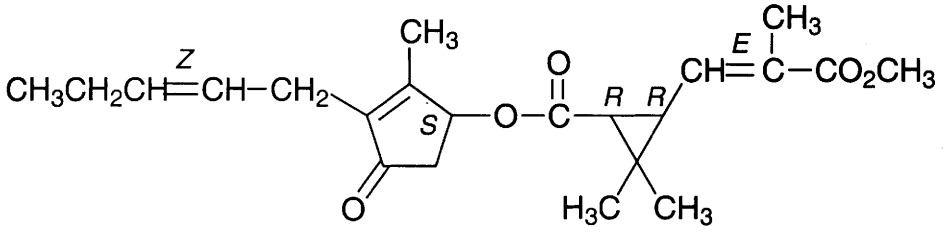
Other comments

Worldwide production of itaconic acid in 1998 ~15,000 tonnes (1).
Itaconate is a potent inhibitor of isocitrate lyase in *Pseudomonas indigofera* (2).
Itaconic acid was formed from citramalate in cell-free enzyme extracts of *Aspergillus terreus* (3).
The methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *sec*-butyl, and benzyl esters of *cis*-itaconic acid have growth-retarding and chloropyll-destroying properties in green plants (4).

References

1. *Organisation for Economic Cooperation and Development, Screening Information Data Set of High Production Chemicals* OECD Chemicals Programme, OECD Paris Centre, 2 rue Andre Pascal, 75775 Paris Cedex 16, France.
2. McFadden, B. A. et al *J. Bacteriol.* 1977, **131**(1), 136-144.
3. Jakubowska, J. et al *Acta Microbiol. Pol., Ser. B* 1974, **6**(2), 51-61.
4. Karanov, E. N. et al *Dokl. S-kh. Akad. Sofia* 1975, **8**(2), 15

J1 jasmolin I



$C_{21}H_{30}O_3$ **Mol. Wt.** 330.47 **CAS Registry No.** 4466-14-2

Synonyms cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-, 2-methyl-4-oxo-3-(2-pentenyl)-2-cyclopenten-1-yl ester, [1*R*-[1α[*S**(*Z*],3β(*E*)]]-; jasmoline I

Uses Insecticide and acaricide.

Occurrence An active insecticidal constituent of pyrethrum flowers.
One of the family of pyrethrin insecticides (1).

Environmental fate

Abiotic removal

Oxidation and loss of insecticidal activity can occur in air and light. In the presence of alkalis is rapidly hydrolysed causing loss of activity. Synergists have a stabilising effect (1).
For pyrethrins in general, degradation is promoted by sunlight and UV light. Degradation begins at the alcohol group and involves the formation of numerous cleavage products (1).

Mammalian & avian toxicity

Metabolism and toxicokinetics

In mammals, pyrethrins are rapidly degraded in the stomach by hydrolysis of the ester bonds to form harmless metabolites (1).

Irritancy

Pyrethrins may cause dermatitis in sensitised persons. Slightly irritating to skin and eyes (1).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances)Statutory Instrument No. 472, 1991 (2). Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (3).

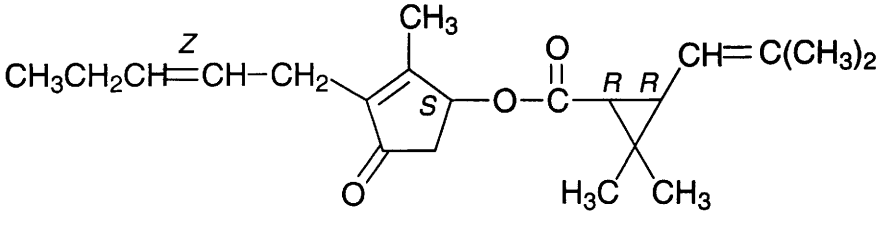
Other comments

Toxicity and metabolism reviewed (4).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. Timofiyevskaya, L. A. et al *Scientific Literature in Russian on Selected Hazardous Chemicals. Pyrethroids* 1993, **119**, UNEP/IRTPC, Eng. Transl. (Ed.) Richardson, M. L., Geneva, Switzerland

J2 jasmolin II



$C_{22}H_{30}O_5$ **Mol. Wt.** 374.48 **CAS Registry No.** 1172-63-0

Synonyms 3-(3-methoxy-2-methyl-3-oxo-1-propenyl)-2,2-dimethylcyclopropanecarboxylic acid 2-methyl-4-oxo-3-(2-pentenyl)-2-cyclopenten-1-yl ester, [1*R*-[1α[*S**(*Z*)],3β(*E*)]]-

Uses Insecticide and acaricide.

Occurrence In extracts from the plant *Pyrethrum (Chrysanthemum) cinerariaefolium* and its flowers.

One of the family of pyrethrin insecticides (1).

Physical properties

Solubility Water: practically insoluble. Organic solvents: readily soluble in organic solvents.

Environmental fate

Abiotic removal

Oxidation and loss of insecticidal activity can occur in air and light. In the presence of alkalis is rapidly hydrolysed causing loss of activity. Synergists have a stabilising effect (1).

For pyrethrins in general, degradation is promoted by sunlight and UV light. Degradation begins at the alcohol group and involves the formation of numerous cleavage products (1).

Mammalian & avian toxicity

Metabolism and toxicokinetics

In mammals, pyrethrins are rapidly degraded in the stomach by hydrolysis of the ester bonds to harmless metabolites (1).

Irritancy

Slightly irritating to skin and eyes.

Pyrethrins may cause dermatitis in sensitised persons.

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances)Statutory Instrument No. 472, 1991 (2). Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).

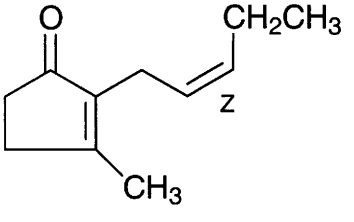
Other comments

Toxicity and metabolism of pyrethroids reviewed (4).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. Timofiyevskaya, L. A. et al *Scientific Literature in Russian on Selected Hazardous Chemicals. Pyrethroids* 1993, **119**, UNEP/IRPTC, Eng. Transl. (Ed.) Richardson, M. L., Geneva, Switzerland

J3 jasmone



$C_{11}H_{16}O$ **Mol. Wt.** 164.25 **CAS Registry No.** 488-10-8

Synonyms 3-methyl-2-(2-pentenyl)-(Z)-2-cyclopenten-1-one; *cis*-jasmone

EINECS No. 207-668-4 **RTECS No.** GY 7301000

Uses In perfumery.

Occurrence Volatile portion of jasmin flower oil.

Physical properties

B. Pt. 146°C at 27 mmHg **Flash point** 107°C **Specific gravity** 0.904

Genotoxicity

In vitro Chinese hamster ovary K-1 cells, sister chromatid exchanges induced with mitomycin C were investigated for modifying effects by jasmone. Post-treatment with jasmone significantly increased the frequency of sister chromatid exchanges (1).

References

1. Sasaki, Y. F. et al *Mutat. Res.* 1989, 226 (2), 103-110

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