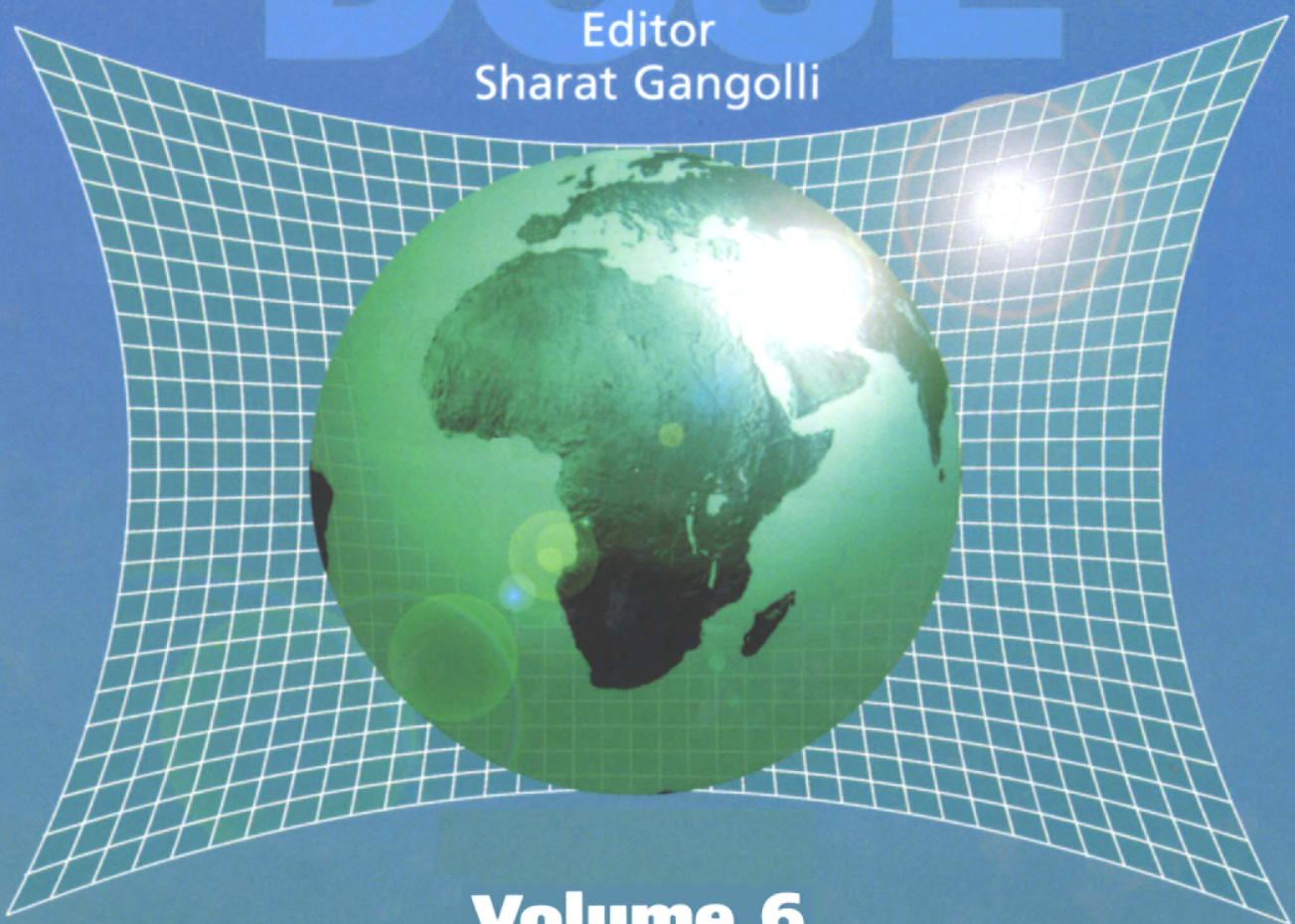
The Dictionary of Substances and their Effects

DOSE

Second Edition

Editor
Sharat Gangolli



Volume 6
O–S

The Dictionary of Substances and their Effects

Second Edition

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RS•C
ROYAL SOCIETY OF CHEMISTRY

PRODUCTION TEAM

Ken Wilkinson (Staff Editor)
Richard Ellis
Sally Faint
Julie Hetherington
Alan Skull

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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:

Chemical Databank Production
Royal Society of Chemistry
Thomas Graham House
Science Park
Cambridge CB4 0WF
UK
Telephone: +44 (0)1223 420066
Fax: +44 (0)1223 423429

Document Delivery

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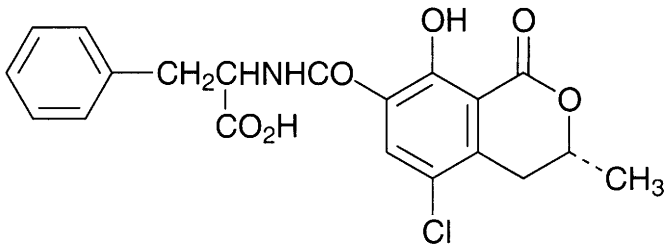
Fax: + 44 (0)20 7287 9798
Email: library@rsc.org

01 ochratoxin A



$C_{20}H_{18}ClNO_6$ **Mol. Wt.** 403.82 **CAS Registry No.** 303-47-9

Synonyms (–)-ochratoxin A; (*R*)-*N*-[(5-chloro-3,4-dihydro-8-hydroxy-3-methyl-1-oxo-1*H*-2-benzopyran-7-yl)carbonyl]phenylalanine; *N*-[[(3*R*-5-chloro-8-hydroxy-3-methyl-1-oxo-7-isochromanyl]carbonyl]-3-phenyl-L-alanine; (–)-*N*-[(5-chloro-8-hydroxy-3-methyl-1-oxo-7-isochromanyl)carbonyl]-3-phenylalanine

EINECS No. 206-143-7 **RTECS No.** AY 4375000

Occurrence Toxic metabolite produced by *Aspergillus* and *Penicillium* species. Residues have been identified in cereals and other foods and feeds of plant origin and some cured meats (1).

Physical properties

M. Pt. 169°C

Solubility Organic solvents: chloroform, diethyl ether, ethanol, methanol, xylene

Occupational exposure

UN No. 3172

Ecotoxicity

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 16 ppm, Microtox test (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral duck, chicken, turkey, quail 0.3, 3.3, 5.9, 16.5 mg kg^{-1}, respectively (3-5).

LD_{50} oral rat, mouse 20, 46 mg kg^{-1}, respectively (6,7).

LD_{50} intraperitoneal rat, mouse 13, 40 mg kg^{-1}, respectively (8).

LD_{50} intravenous rat, mouse 13, 30 mg kg^{-1}, respectively (8).

In rats, mice, dogs and pigs both acute and chronic effects are localised to the kidney, in which necrosis of the proximal tubular epithelium occurs (9).

Sub-acute and sub-chronic data

Intramuscular chicken (24 day) 0.25 or 0.5 mg kg^{-1} day^{-1} for 10 days induced an increase in urine flow rate, decreased urine osmolarity, increased excretion of sodium, potassium, calcium and phosphorus, increased water consumption and faecal moisture, and caused a relative alkalosis when measured immediately after 10 days of administration. These effects were not observed 2 wk later (10).

Oral dog (14 day) 0.1 or 0.2 mg kg^{-1} day^{-1} caused necrosis of the lymphoid tissues in the lymph nodules of the ileum, colon and rectum (11).

Oral rat (17 day) 1 mg kg^{-1} diet significantly decreased cytochrome P_{450} in the kidney after 17 days. This effect was not observed after 7 days treatment. Cytochrome P_{450} was not affected in the liver (12).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (13).

Oral mouse (49 wk) 40 mg kg^{-1} diet for 44 wk. Hepatic-cell tumours (well-differentiated trabecular adenomas) were found in 5/9 treated mice compared with 0/10 among controls. Hyperplastic liver nodules were found in 1/9 treated mice and 2/10 controls. Solid renal-cell tumours occurred in 2/9 treated mice and 0/10 controls. Cystic adenomas of the kidney were found in cell-treated mice and 0/10 controls (14).

Subcutaneous mouse (81 wk) 10 µg $animal^{-1}$ 2 × wk^{-1} for 36 wk. No tumour was observed in treated or control mice (15).

Subcutaneous rat (87 wk) 2.5 mg kg^{-1} 2 × wk^{-1} for 17 wk; 2/10 treated rats and 2/10 controls developed fibrosarcomas at the site of injection (16).

Gavage rat (2 yr) 0, 21, 70 or 210 µg kg^{-1} 5 day wk^{-1} for 9, 15 or 24 months. Clear evidence of carcinogenic activity was shown by substantially increased incidences of uncommon tubular cell adenomas and tubular cell carcinomas of the kidney in ♂ and ♀ rats. Increased incidences and multiplicity of fibroadenomas of the mammary gland were also observed in ♀ rats. Ochratoxin A administration also caused non-neoplastic renal changes including tubular cell hyperplasia, tubular cell proliferation, cytoplasmic alteration, karyomegaly, and degeneration of the renal tubular epithelium (17).

Teratogenicity and reproductive effects

Subcutaneous rat, single dose of 0.5-5.0 mg kg^{-1} on 1 of day 4-10 of gestation. The minimum toxic dose was 1.75 mg kg^{-1}, which caused decreased foetal weight and various foetal malformations. Higher doses caused foetal resorption. Ochratoxin A was most effective when given on day 5 or 6 of gestation (18).

Intraperitoneal mouse, 2 mg kg^{-1} induced craniofacial malformations when administered on day 8 of gestation but not when given on day 10 (19).

Oral or intraperitoneal mouse, 3-5 mg kg^{-1} day^{-1} on days 15-17 of gestation caused cerebral necrosis in most foetuses (20).

Intraperitoneal mouse, single dose 5 mg kg^{-1} on 1 of days 7-12 of gestation caused increases in prenatal mortality and in foetal malformations and a decrease in foetal weight. The highest number of malformations was seen in foetuses of animals treated on day 8 of gestation (35% dead or absorbed, 58% grossly malformed, 87% with skeletal malformations) (21).

Intraperitoneal mouse single dose of 0-7 mg kg^{-1} on 1 day between days 8 and 13 of gestation. The newborn mice with severe microcephaly died a short time after birth. The surviving offspring were examined at 6 wk of age. In all treated groups, body and brain weights were reduced in a dose-dependent manner. Administration on days 9, 10 and 11 of gestation had the greatest effect (22).

Metabolism and toxicokinetics

In rats, ochratoxin A is absorbed through the stomach wall and jejunum. It is distributed principally to the liver, muscle and kidneys (23-27).

Ochratoxin A is metabolised to phenylalanine and a less toxic isocoumarin derivative (ochratoxin-α) by the microbial flora of the colon and by carboxypeptidase A and α-chymotrypsin (27-29).

Plasma $t_{1/2}$ ~60 hr. Excretion occurs via the faeces and urine (species unspecified) (30).

Following oral or intraperitoneal administration to mice, biliary excretion and enterohepatic circulation of ochratoxin A was demonstrated (31).

Genotoxicity

CASE structure-activity methodology predicted it to be marginally positive for mutagenicity to *Salmonella typhimurium* (32).

Bacillus subtilis rec assay negative (33).

In vitro primary rat hepatocytes, unscheduled DNA synthesis negative (34).

In vitro Chinese hamster L5178Y cells, tk^+/tk^- negative (34).

In vitro human lymphocytes, chromosomal aberrations positive (35).

In vitro mouse mammary carcinoma cells, induction of mutations negative (36).

Other effects

Other adverse effects (human)

The geographical distribution of Balkan endemic nephropathy in Bulgaria and the former Yugoslavia correlates with the incidence of mortality due to urothelial urinary tract tumours (31,37,38).

In an endemic area for Balkan nephropathy, 7% of the population had ochratoxin A in the blood compared with none in control group from another area (39).

Ochratoxin A has been reported to affect immune function both at the level of antibody synthesis and Natural Killer cell activity (40).

Any other adverse effects

In vitro hepatoma cells, ochratoxin A inhibited nucleic acid and protein synthesis by competing with phenylalanine at the phenylalanyl-tRNA-synthetase active site (41).

Aspartame, at tenfold higher concentrations than ochratoxin A (100-1000 μM) was found partially to protect against the ochratoxin A-induced inhibition of protein synthesis in monkey kidney cells (Vero cells), and more efficiently when added 24 hr prior to the toxin (IC_{50} 34 μM) than together (IC_{50} 22 μM) (42).

When incubated with fresh renal cortex slices from rats, ochratoxin A inhibited *p*-aminohippurate uptake, thus altering renal formation (43).

Other comments

Physical properties, occurrence, analysis, carcinogenicity, mammalian toxicity and mutagenicity reviewed (1).

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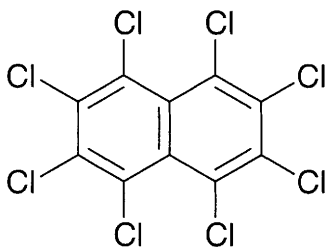
02 octachloronaphthalene



$C_{10}Cl_8$ **Mol. Wt.** 403.73 **CAS Registry No.** 2234-13-1

Synonyms perchloronaphthalene; Pepna

EINECS No. 218-778-7 **RTECS No.** QK 0250000

Uses Waterproofing agent. Fireproof additive in plastics. Additive for cutting oils.

Physical properties

M. Pt. 197.5°C **B. Pt.** 440°C **Specific gravity** 2.00 **Partition coefficient** log P_{ow} 8.4 (1)
Volatility v.p. 1×10^{-8} mmHg at 25°C ; v.den. 13.9
Solubility Water: 0.08 µg l^{-1} at 22°C. Organic solvents: benzene, cyclohexane, carbon tetrachloride, ethanol

Occupational exposure

FR-VME 0.1 mg m^{-3}
SE-LEVL 0.2 mg m^{-3} **SE-STEL** 0.6 mg m^{-3}
UK-LTEL 0.1 mg m^{-3} **UK-STEL** 0.3 mg m^{-3}
US-TWA 0.1 mg m^{-3} **US-STEL** 0.3 mg m^{-3}

Ecotoxicity

Bioaccumulation
Bioconcentration factors for guppy and trout 0 and 330, respectively. The large molecular size may inhibit membrane permeation resulting in low bioaccumulation (1,2).

Environmental fate

Abiotic removal

Estimated volatilisation $t_{1/2}$ 43 hr for model river water, 19.5 days for model pond water (3,4).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ ~440 days (5).

Adsorption and retention

Estimated K_{oc} of 750,000-1,600,000 indicated the octachloronaphthalene will be essentially immobile in soil and will partition to sediment and be suspended in water (3).

Other effects

Other adverse effects (human)

Exposure may cause acne-like skin rash. It may also cause liver injury, resulting in such effects as fatigue, dark urine, yellow jaundice and possibly death (6).

Any other adverse effects

Single dose of 44 mg kg^{-1} to ♂ rats (route unspecified) induced 1.5-fold increase in hepatic cytochrome P_{450}, 18-fold increase in benzo[*a*]pyrene hydroxylase and 18-fold increase in 9-chlorobiphenyl hydroxylase activities (7).

Legislation

The log P_{ow} value exceeds the European Community recommended level of 3.0 (6th and 7th Amendments) (8).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (9).

Other comments

Contaminant of polychlorinated biphenyls. Detected in wastewater from aluminium smelting plant (10,11).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

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03 1-octadecanethiol

$$CH_3(CH_2)_{16}CH_2SH$$

$C_{18}H_{38}S$ **Mol. Wt.** 286.57 **CAS Registry No.** 2885-00-9

Synonyms 1-mercaptooctadecane; octadecyl mercaptan

EINECS No. 220-744-1 **RTECS No.** RG 0500000

Uses In manufacture of electrodes. Chain-transfer agent in preparation of acrylic polymers. Lubricating oil additive.

Physical properties

M. Pt. 29-31°C **B. Pt.** 204-210°C at 11 mmHg **Flash point** 185°C **Specific gravity** 0.8475 at 20°C
Solubility Organic solvents: diethyl ether

Mammalian & avian toxicity

Irritancy
Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (1).

Other comments

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

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04 octadecyltrichlorosilane

$$CH_3(CH_2)_{17}SiCl_3$$

$C_{18}H_{37}Cl_3Si$ **Mol. Wt.** 387.94 **CAS Registry No.** 112-04-9

Synonyms trichlorooctadecylsilane

EINECS No. 203-930-7 **RTECS No.** VV 4680000

Uses In preparation of silica gel-based stationary phase for chromatography.

Physical properties

B. Pt. 380°C **Flash point** 89°C **Specific gravity** 0.984 at 25°C

Occupational exposure

UN No. 1800 **HAZCHEM Code** 4X **Conveyance classification** corrosive substance

Other effects

Other adverse effects (human)

Extremely destructive to tissue of the mucous membrane 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).

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05 octafluoro-2-butene

$$CF_3CF{=}CFCF_3$$

C_4F_8 **Mol. Wt.** 200.03 **CAS Registry No.** 360-89-4

Synonyms octafluorobut-2-ene; 1,1,1,2,3,4,4,4-octafluoro-2-butene; perfluorobut-2-ene; perfluoro-2-butene; RC-318

EINECS No. 206-640-9 **RTECS No.** EM 8980000

Uses Manufacture of polymers. Refrigerant.

Physical properties

M. Pt. –135°C **B. Pt.** 1.2°C **Specific gravity** 1.5297

Occupational exposure

UN No. 2422 **Conveyance classification** non-flammable non-toxic gas

Mammalian & avian toxicity

Acute data

LC_{Lo} (4 hr) inhalation rat 6100 ppm (1).

Genotoxicity

Drosophila melanogaster sex-linked recessive lethal assay positive (2).

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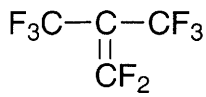
O6 octafluoroisobutene



C_4F_8 **Mol. Wt.** 200.03 **CAS Registry No.** 382-21-8

Synonyms perfluoroisobutylene; octafluoro-*sec*-butene; octafluoroisobutylene

Mammalian & avian toxicity

Acute data

LC_{50} (0.25 minutes) nose-only inhalation rats 361 ppm (1).
LC_{50} (10 minutes) nose-only inhalation rats 17 ppm (1).
LC_{50} (6 hr) inhalation rat 500 ppb (2).
LC_{50} (2 hr) inhalation rabbit 1200 ppb (3).
LC_{50} (2 hr) inhalation guinea pig 1050 ppb (3).
LC_{Lo} (2 hr) inhalation mouse 10 mg m^{-3} (4).
A post-exposure latency period of ~8 hr exists in rats exposed by inhalation for 10 minutes to 100 mg m^{-3} before the onset of overt pulmonary oedema. Exercise performed during the post-perfluoroisobutylene period did not potentiate the toxic response, but when overt pulmonary oedema was pre-existent, exercise had a potentiating effect (5).

Irritancy

Marked irritation of conjunctivae, throat, and lungs in human acute exposure (6).

Other effects

Other adverse effects (human)

Deadly poison by inhalation. May cause pulmonary oedema or death after a latent period of 6-8 hr (7,5).

Other comments

Perfluoroisobutylene is a pyrolysis product of polytetrafluoroethene (7).
In rats exposed to inhalation exposures of 10-250 μg l^{-1}, doubling the inhaled dose produced a 1.3-1.8-fold increase in uptake, with a corresponding decrease in percentage retained (5).
N-Acetylcysteine administered orally to rats 4-8 hr before exposure to perfluoroisobutylene protects against the toxic effects of this gas. The duration of protection *in vivo* has been related to the duration of increased plasma thiol levels (7).
Respirators containing activated carbon filters remove perfluoroisobutylene from workplace air (8).

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07 octafluoropropane

$$CF_3CF_2CF_3$$

C_3F_8 **Mol. Wt.** 188.02 **CAS Registry No.** 76-19-7

Synonyms Freon 218; Genetron 218; perfluoropropane; profluorane; R 218

EINECS No. 200-941-9

Uses Blowing agent. Etchant in manufacturing semi-conductors. Propellant. Working fluid for heat pumps and refrigerators.

Physical properties

M. Pt. –183°C **B. Pt.** –36°C

Occupational exposure

UN No. 2424 **HAZCHEM Code** 2RE **Conveyance classification** non-flammable non-toxic gas

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Injection of 0.15 ml of gas into the anterior chamber of rabbits and cats eyes produced an octafluoropropane bubble that persisted for 22 days. Corneal oedema was induced which persisted after the gas bubble disappeared (1).

References

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08 octanal

$$CH_3(CH_2)_6CHO$$

$C_8H_{16}O$ **Mol. Wt.** 128.21 **CAS Registry No.** 124-13-0

Synonyms C-8 aldehyde; capryl aldehyde; caprylic aldehyde; *n*-octyl aldehyde; octanaldehyde

EINECS No. 204-683-8 **RTECS No.** RG 7780000

Uses Organic synthesis. In perfumery. Flavouring agent.

Occurrence In plant oils, cooked meat and fish, milk and dairy products. Residues have been identified in drinking water (1).

Physical properties

M. Pt. 12-15°C **B. Pt.** 171°C **Flash point** 51°C (closed cup) **Specific gravity** 0.821 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.65 (2) **Volatility** v.p. 850 mmHg at 25°C ; v.den. 4.41

Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol, propylene glycol, fixed oils

Ecotoxicity

Fish toxicity

LC_{50} (14 day) guppy 230 mg l^{-1} (2).

Environmental fate

Degradation studies

Biodegradability 2.4% of ThOD in activated sludge in 24 hr (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >110 mg kg^{-1} (4).
LD_{50} oral rat 5600 mg kg^{-1} (5).
LD_{50} dermal rat 6400 mg kg^{-1} (5).

Teratogenicity and reproductive effects

Low teratogenicity when injected suprablastodermally (72 hr) in chick embryos (6).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation, 100 mg instilled into rabbit eye caused mild irritation (exposure unspecified) (7,8).

Other effects

Other adverse effects (human)

High degree of membrane-damaging activity to human lung lymphoblasts (9).

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09 octane

$$CH_3(CH_2)_6CH_3$$

C_8H_{18} **Mol. Wt.** 114.23 **CAS Registry No.** 111-65-9

Synonyms *n*-octane

EINECS No. 203-892-1 **RTECS No.** RG 8400000

Uses Solvent. Organic synthesis. Fuel additive. Blowing agent.
Occurrence Aroma component of plant oils, cooked meat and fish, and dairy products. In paraffin fraction of petroleum. Residues have been detected in natural and drinking waters and in human milk (1).

Physical properties

M. Pt. -57°C **B. Pt.** 125-127°C **Flash point** 22°C (open cup) **Specific gravity** 0.7036 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 5.15 **Volatility** v.p. 10 mmHg at 19.2°C ; v.den. 3.86
Solubility Water: 0.7 mg l^{-1} at 20°C. Organic solvents: benzene, diethyl ether, ethanol, petroleum ether

Occupational exposure

DE-MAK 500 ppm (2350 mg m^{-3})
FR-VME 300 ppm (1450 mg m^{-3})
JP-OEL 300 ppm (1400 mg m^{-3})
SE-LEVL 200 ppm (900 mg m^{-3}) **SE-STEL** 300 ppm (1400 mg m^{-3})
US-TWA 300 ppm

UN No. 1262 **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 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)

Ecotoxicity

Fish toxicity
Coho salmon (96 hr) no mortality at 100 ppm in artificial sea water (2).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 890 ppm, Microtox test (3).
EC_{50} (48 hr) *Daphnia magna* 0.38 mg l^{-1} (4).

Bioaccumulation
Calculated bioconcentration factors of 780-5100 indicate that environmental accumulation would be significant (5).

Environmental fate

Nitrification inhibition
50% inhibition of ammonia consumption (25 days) *Nitrosomonas* sp. 45 mg l^{-1} (6).

Anaerobic effects
50% toxic inhibition (50 days) methanogenic bacterial culture 2 mg l^{-1} (6).

Degradation studies
Catabolised by *Pseudomonas* sp. PG-I at substrate concentrations up 0.3%. Growth was inhibited at higher concentrations (7).
ThOD 3.5 (8).
BOD_{35} 2.33 mg O_2 l^{-1} in hydrocarbon oxidising bacteria culture in seawater at 25°C (9).

Abiotic removal
Estimated volatilisation $t_{1/2}$ 5.6 hr in model river water at 25°C and for model pond water 30 days (10,11).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 1.8 days (12).

Adsorption and retention
Estimated K_{oc} of 5500-15,600 indicate that adsorption to soil and sediments would be significant (5).

Mammalian & avian toxicity

Acute data
LC_{50} (90 min) inhalation mouse >13,700 ppm (13).
Inhalation mouse 6000-13,700 ppm caused central nervous system depression in 30-90 min, 16,000 ppm caused respiratory arrest in 1/4 animals within 5 min, and 32,000 ppm caused respiratory arrest in 4/4 animals in 3 min (13).
LD_{Lo} intravenous mouse 430 mg kg^{-1} (14).

Sub-acute and sub-chronic data
Intraperitoneal rat 1 ml kg^{-1} day^{-1} for 7 days resulted in decreased body weight, liver enlargement and loss of drug metabolising capacity (15).

Metabolism and toxicokinetics

Following inhalation, exposure of rats to ^{14}C-octane at concentrations up to 350 ppm for 2 hr resulted in >95% of the absorbed octane being excreted about equally via the kidneys and as exhaled $^{14}CO_2$ within 20 hr (16).
Poorly absorbed through rat skin (17).
The greatest affinity for octane was seen in the adipose tissue (18).
Metabolised to 1-octanol through a cytochrome P_{450} oxidase system. Undergoes further metabolism by oxidation to a 1-octanoic acid or by conjugation to form glucuronide (19).

Irritancy

Irritating to the eyes, upper respiratory tract and mucous membranes (20,21).

Other effects

Other adverse effects (human)

Acts as a simple asphyxiant (22).
Aspiration of the liquid into the lungs caused convulsion and rapid death from asphyxiation, respiratory paralysis or cardiac arrest (23).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (24).
The log P_{ow} value exceeds the European community recommended level of 3.0 (6th and 7th Amendments) (25).

Other comments

Physical properties, occurrence and environmental fate reviewed (1).
Physical properties, use, toxicity and safety precautions reviewed (26-28).
Autoignition temperature 206°C.

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O10 1-octanethiol

$$CH_3(CH_2)_6CH_2SH$$

$C_8H_{18}S$ **Mol. Wt.** 146.30 **CAS Registry No.** 111-88-6

Synonyms 1-mercaptooctane; 1-octyl thiol; *n*-octyl mercaptan

EINECS No. 203-918-1 **RTECS No.** RG 9740000

Uses Polymerisation chain transfer agent. Organic synthesis.

Physical properties

M. Pt. –49.2°C **B. Pt.** 197-200°C **Flash point** 69°C (open cup) **Specific gravity** 0.8433 at 20°C with respect to water at 4°C **Volatility** v.p. 1.55 mmHg at 37.7°C ; v.den. 5.0
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Dermal mouse (2 wk) direct application 3 × wk^{-1} caused an increase in epidermal weight and thickness (1).

Sensitisation
Reported to be a moderate skin sensitiser in guinea pigs (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3).

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O11 *tert*-octanethiol

$$(CH_3)_2C(SH)CH_2C(CH_3)_3$$

$C_8H_{18}S$ **Mol. Wt.** 146.30 **CAS Registry No.** 141-59-3

Synonyms *tert*-octyl mercaptan; 2,4,4-trimethyl-2-pentanethiol

EINECS No. 205-490-1 **RTECS No.** SA 3260000

Uses Organic synthesis.

Physical properties

B. Pt. 154-166°C **Flash point** 40.5°C **Specific gravity** 0.848 **Volatility** v.den. 5.0

Occupational exposure

UN No. 3023 **HAZCHEM Code** 3WE **Conveyance classification** toxic substance, danger of fire (flammable liquid)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 85 mg kg^{-1} (1).

LC_{50} inhalation rat, mouse 47, 51 ppm, respectively (exposure unspecified) (1).

LD_{50} intraperitoneal rat 13 mg kg^{-1} (1).

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O12 octanoic acid

$$CH_3(CH_2)_6CO_2H$$

$C_8H_{16}O_2$ **Mol. Wt.** 144.21 **CAS Registry No.** 124-07-2

Synonyms caprylic acid; 1-heptanecarboxylic acid; *n*-octanoic acid; octanylic acid; octic acid; octylic acid

EINECS No. 204-677-5 **RTECS No.** RH 0175000

Uses Manufacture of dyestuffs, drugs, fungicides, perfumes and flavours.

Occurrence Aroma component of plants, cooked meat and fish, wines, milk and dairy products. Secondary product in ethanolic fermentation.

Physical properties

M. Pt. 16-16.5°C **B. Pt.** 237°C **Flash point** 132°C **Specific gravity** 0.910 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 3.05 **Volatility** v.p. 1 mmHg at 92°C ; v.den. 5.0

Solubility Water: 0.0689 g 100 ml^{-1}. Organic solvents: glacial acetic acid, acetone, carbon disulfide, chloroform, diethyl ether, ethanol, petroleum ether

Ecotoxicity

Fish toxicity

Not toxic to bluegill sunfish at saturated concentrations at ambient temperature (1).

LC_{50} (48 hr) red killifish 47 mg l^{-1} in fresh water, 150 mg l^{-1} in seawater (2).

Invertebrate toxicity

LC_{50} (48 hr) *Hyale plumulosa* 130 mg l^{-1} (2).

Decreased growth rate of *Saccharomyces cerevisiae* and *Kluyveromyces marxianus* during ethanolic fermentation at 16 mg l^{-1} at 30°C (3).

Environmental fate

Degradation studies

BOD_5 1.28 mg l^{-1} O_2 for substrate concentration of 2.9 mg l^{-1} (4).

Biodegradation in activated sludge 9.8% of ThOD after 6 hr, 20% of ThOD after 12 hr, 33% of ThOD after 24 hr (5).

Abiotic removal

Adsorption by powdered activated carbon 50 mg g^{-1} carbon at 100 mg l^{-1} (sodium salt) (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 10,000 mg kg^{-1} (7).

LD_{Lo} dermal rabbit 650 mg kg^{-1} (8).

LD_{50} intravenous mouse 600 mg kg^{-1} (9).

Sub-acute and sub-chronic data

Oral (duration unspecified) dog, 1-5% diet caused diarrhoea (10).

Teratogenicity and reproductive effects

Subcutaneous mouse, 0 or 600 mg kg^{-1} on day 8 of gestation did not cause any foetotoxic or teratogenic effects (11).

Metabolism and toxicokinetics

Lactate precursor in suckling rat liver but not in rat muscle in *in vitro* studies (12).

Irritancy

Dermal rabbit (24 hr) 10 mg caused severe irritation (8).

Rated 9, on numerical scale of 1-10, in 24 hr rabbit eye irritancy test (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (14,15).

Saccharomyces cerevisiae with and without metabolic activation negative (15).

Triturus helveticus chromosomal aberrations positive (16).

Other effects

Other adverse effects (human)

Extremely destructive to tissue of the mucous membranes and upper respiratory tract (17).

Legislation

The log P_{ow} value exceeds the European Community recommended level of 3.0 (6th and 7th Amendments) (18).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (19).

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013 1-octanol

$$CH_3(CH_2)_6CH_2OH$$

$C_8H_{18}O$ **Mol. Wt.** 130.23 **CAS Registry No.** 111-87-5

Synonyms alcohol C-8; caprylic alcohol; Dytomol M-83; Epal 8; heptyl carbinol; 1-hydroxyoctane; octilin; octyl alcohol; Lipol L8

EINECS No. 203-917-6 **RTECS No.** RH 6550000

Uses Solvent. Anaesthetic. Plant growth regulation. Manufacture of perfumes.
Occurrence Aroma component of plants, cooked meat and fish, milk and dairy products.

Physical properties

M. Pt. –16°C **B. Pt.** 196°C **Flash point** 81°C **Specific gravity** 0.827 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.07 **Volatility** v.p. 1 mmHg at 54°C ; v.den. 4.48
Solubility Water: 300 mg l^{-1} at 20°C. Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) fathead minnow, golden orfe 6, 16 mg l^{-1}, respectively (1-3).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 23 mg l^{-1} (3).
LC_{50} (48 hr) *Nitocra spinipes* 60 mg l^{-1} (3).
EC_{50} (30 min) *Photobacterium phosphoreum* 3.7-7.3 ppm Microtox test (4).
Toxicity threshold for *Microcystis aeruginosa* 1.9 mg l^{-1}, *Scenedesmus quadricauda* 6.3 mg l^{-1}, *Entosiphon sulcatum* 44 mg l^{-1} (5,6).

Bioaccumulation
The calculated bioconcentration factor is 18-110 (7).

Environmental fate

Nitrification inhibition
IC_{50} (25 days) *Nitrosomonas* 67 mg l^{-1} (2).

Carbonaceous inhibition
IC_{50} (5 days) aerobic heterotrophs isolated from activated sludge 200 mg l^{-1} (2).

Anaerobic effects
IC_{50} (50 days) methanogenic bacterial culture 370 mg l^{-1} (2).

Degradation studies
ThOD 2.95 mg O_2 l^{-1}, BOD_5 1.088 mg O_2 l^{-1} (8).
COD 98% of ThOD (9).

Abiotic removal
Estimated volatilisation $t_{1/2}$ 1.8 days in model river water, 82 days in model pond water (7,10).
68% removal by reverse osmosis from waste water at a concentration of 1.3 mg l^{-1} (11).
Reaction with photochemically produced hydroxyl radicals in the atmosphere $t_{1/2}$ ~1.3 days (12).

Adsorption and retention
Calculated K_{oc} of 137-983 indicate that 1-octanol will adsorb moderately to some soils and sediments (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 1800 mg kg^{-1} (13).
LC_{Lo} (4 hr) inhalation rat 5600 mg m^{-3} (14).
LD_{50} intravenous mouse 69 mg kg^{-1} (15).

Teratogenicity and reproductive effects
Inhalation rat, 150 mg m^{-3} 7 hr day^{-1} on days 1-19 produced no teratogenic effects, no maternal toxicity and no foetotoxicity (16).
Gavage rats (6-15 days gestation) 0, 1, 5 and 10 mmol kg^{-1}, maternal but no developmental toxicity observed (17).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation (18).
Irritating to the mucous membranes and upper respiratory tract (19).

Sensitisation
Reported to cause allergic skin reaction in man (19).

Genotoxicity

In vivo rat bone marrow, chromosomal aberrations and polyploidy positive (20).

Other effects

Any other adverse effects
EC_{50} *in vitro* rat heart cells, inhibition of sodium-calcium exchange 23 mg l^{-1} (21).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (22).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).
The log P_{ow} value exceeds the European Community recommended level of 3.0 (6th and 7th Amendments) (24).

Other comments

Residues have been identified in drinking water (25).
Used as a plant growth regulator in combination with 1-decanol (26).

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014 2-octanol

$$CH_3(CH_2)_5CH(OH)CH_3$$

$C_8H_{18}O$ **Mol. Wt.** 130.23 **CAS Registry No.** 123-96-6

Synonyms capryl alcohol; *sec*-caprylic alcohol; 1-methyl-1-heptanol; methylhexylcarbinol; 2-hydroxy-*n*-octane; 2-octyl alcohol; *sec*-octyl alcohol

EINECS No. 204-667-0 **RTECS No.** RH 0795000

Uses Organic synthesis. Solvent. Fragrance ingredient. Anti-foaming agent

Occurrence Isolated from geranium oil. Traces have been identified in some dairy products and in natural waters (1).

Physical properties

M. Pt. –38.6°C **B. Pt.** 178.5°C **Flash point** 60°C **Specific gravity** 0.8264 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.90 **Volatility** v.p. 1 mmHg at 32.8°C ; v.den. 4.49
Solubility Water: 0.96 ml l^{-1}. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} rainbow trout <100 µg l^{-1} (exposure unspecified) (2).

Bioaccumulation
Calculated bioconcentration factors of 12-70 indicate that environmental accumulation should not be significant (3).

Environmental fate

Degradation studies
Biodegradation by activated sludge 1.1% of ThOD after 6 hr, 2.9% of ThOD after 12 hr, 2.7 of ThOD after 24 hr (4).

Abiotic removal
Volatilisation $t_{1/2}$ 1.3 days from model river water 46 days from model pond water (3,5).
Reaction with hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ ~1.1 days (6).

Adsorption and retention
Calculated K_{oc} of 92-720 indicate 2-octanol may adsorb to some sediments and soils (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse >3200 and 4000 mg kg^{-1}, respectively (7,8).
LD_{50} intravenous mouse 66 mg kg^{-1} (9).
Immersion of mouse tails into the liquid for 3 hr caused some deaths due to absorption (8).

Sub-acute and sub-chronic data
Inhalation rat (4.5 month) 180-350 mg m^{-3} 2 hr day^{-1} 6 days wk^{-1} caused mild reversible central nervous system disorders, depression of haemoglobin and erythrocyte count, and minor changes in the liver, kidneys and myocardium (8).
Dermal rabbit, 2 ml day^{-1} for 6 days caused erythema, inflammation and cracking of the skin, which healed in 10-12 days (8).

Metabolism and toxicokinetics
Absorbed by guinea pig skin (7).

Irritancy
Causes severe eye irritation (species unknown) (10).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Physical properties, occurrence and environmental fate reviewed (1).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

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O15 3-octanol

$$CH_3(CH_2)_4CH(OH)CH_2CH_3$$

$C_8H_{18}O$ **Mol. Wt.** 130.23 **CAS Registry No.** 589-98-0

EINECS No. 209-667-4 **RTECS No.** RH 0855000

Uses In some toothpastes (1).

Occurrence In rats, 3-octanol is a metabolite of *n*-octane (2). In aromas of many cooked and prepared foods. In many essential oils, including peppermint.

Physical properties

B. Pt. 174-178°C **Flash point** 65°C **Specific gravity** 0.819

Ecotoxicity

Toxicity to other species

It is capable of blocking conduction of nervous impulses in bundles of a few axons from the sciatic nerves of the toad *Bufo marinus* (3).

Other comments

Can antagonise tremor produced by agents such as harmaline by blocking low threshold calcium channels in the inferior olive region of the rat brain (dose and route unspecified) (4).

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O16 2-octanone

$$CH_3(CH_2)_5C(O)CH_3$$

$C_8H_{16}O$ **Mol. Wt.** 128.21 **CAS Registry No.** 111-13-7

Synonyms hexyl methyl ketone; methyl hexyl ketone

EINECS No. 203-837-1 **RTECS No.** RH 1484000

Uses Chemical intermediate.

Occurrence Contributor to organoleptic properties of many fresh and cooked foods. In cigarette smoke.

Physical properties

M. Pt. −16°C **B. Pt.** 172-173°C **Flash point** 62°C **Specific gravity** 0.820 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 2.37 **Volatility** v.p. 0.75 mmHg at 20°C ; v.den. 4.43

Solubility Water: 900 mg l^{-1}. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 35.9 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 17.7 ppm Microtox test (2).

Environmental fate

Degradation studies

Can be biodegraded by cells in a mixed microbial culture in a saturable, concentration dependent manner (3).

It can be hydroxylated and further oxidised by a thermophilic obligate methane oxidising bacteria H2-(type 1) to a mixture of alcohol, aldehyde, acids and ketones (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 3.2, 3.8 g kg^{-1}, respectively (5,6).

LD_{50} dermal rabbit >5 g kg^{-1} (7).

LD_{50} intraperitoneal rat, mouse 800, 1600 mg kg^{-1}, respectively (5).

Sub-acute and sub-chronic data

Guinea pigs lost weight after receiving the compound dermally for 2 wk by occluded application (dose unspecified) (5).

Oral rats receiving 20 mg kg^{-1} for 16 days showed an increase in serum lipid concentration. The compound has been reported to lower serum cholesterol in both rats and mice (8,9).

Metabolism and toxicokinetics

Compound can be absorbed through guinea pig skin (5).

Irritancy

Slight irritation to rabbit eye, and skin (5,7).

Non-irritant to human skin (7).

Sensitisation

Negative in sensitisation tests (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 without metabolic activation negative (10).
Escherichia coli WP2 and WP2*uvrA* without metabolic activation negative (10).

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O17 4-octanone

$$CH_3(CH_2)_3C(O)(CH_2)_2CH_3$$

$C_8H_{16}O$ **Mol. Wt.** 128.21 **CAS Registry No.** 589-63-9

EINECS No. 209-655-9

Uses Chemical intermediate.
Occurrence Contributor to organoleptic properties of many fresh and prepared foods. A pheromone secreted by species such as blue duiker (1).

Physical properties

M. Pt. 164-167°C **B. Pt.** 165-168°C at 760 mmHg **Specific gravity** 0.819 at 20°C
Solubility Organic solvents: soluble carbon tetrachloride, miscible with diethyl ether, ethanol

Mammalian & avian toxicity

Metabolism and toxicokinetics
It is thought that the compound may be metabolised in a variety of species to 2,5-diketones, which may produce neuropathies (2).

Other comments

A pollutant in river water (3).

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O18 1-octen-3-ol

$$CH_3(CH_2)_4CH(OH)CH{=}CH_2$$

$C_8H_{16}O$ **Mol. Wt.** 128.21 **CAS Registry No.** 3391-86-4

Synonyms amyl vinyl carbinol

EINECS No. 222-226-0 **RTECS No.** RH 3300000

Uses As an attractant of insects including mosquito and tsetse fly (1).

Occurrence Contributor to organoleptic properties of many fresh and prepared foods. In urine of several species.

Physical properties

B. Pt. 84-85°C at 25 mmHg **Flash point** 61°C **Specific gravity** 0.830

Environmental fate

Abiotic removal

Can be removed from brewery waste gases by scrubbing with detergent (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 340 mg kg^{-1} (3).

LD_{50} dermal rabbit 3.3 g kg^{-1} (3).

LD_{50} intravenous mouse 56 mg kg^{-1} (4).

Other comments

Present in mouse urine during pregnancy and lactation (5).

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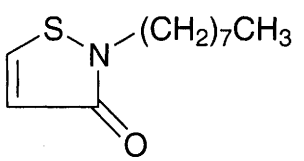
O19 octhilinone



$C_{11}H_{19}NOS$ **Mol. Wt.** 213.34 **CAS Registry No.** 26530-20-1

Synonyms 2-octyl-3(2*H*)-isothiazolone; 2-*n*-octyl-4-isothiazolin-3-one; Kathon; RH-893; Pancil; Skane M-8

EINECS No. 247-761-7 **RTECS No.** NX 8156900

Uses Fungicide, particularly for mildews. Biocide used for wound dressing in trees, in cooling-towers and in leather preparation.

Physical properties

B. Pt. 120°C at 0.01 mmHg **Partition coefficient** log K_{ow} 2.45 at 24°C **Volatility** v.p. 3.675×10^{-5} at 25°C
Solubility Water: 500 mg l^{-1} at 25°C. Organic solvents: ethyl acetate, hexane, methanol, toluene

Occupational exposure

DE-MAK 0.05 mg m^{-3} (inhalable fraction of aerosol)

Supply classification toxic, dangerous for the environment
Risk phrases Harmful if swallowed – Toxic by inhalation and in contact with skin – Causes burns – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R23/24, R34, R43, R50/53)
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) – 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, S26, S36/37/39, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, fathead minnow, channel catfish, bluegill sunfish 0.065, 0.140, 0.177, 0.196 mg l^{-1}, respectively (1).

Invertebrate toxicity
LC_{50} *Daphnia magna* 0.180 mg l^{-1} (1).

Environmental fate

Degradation studies
When present in tannery effluent, the compound can be at least partly degraded by activated sludge over a 72 hr period (2).

Mammalian & avian toxicity

Sub-acute and sub-chronic data
LD_{50} oral rat 550-1470 mg kg^{-1} (1,3).
LD_{50} dermal rabbit 4.22 ml kg^{-1} (1).
LC_{50} (4 hr) inhalation rat 0.58 mg l^{-1} (1).

Irritancy
500 mg (24 hr) applied to rabbit skin caused irritation, 100 mg (duration unspecified) applied to rabbit eye caused severe 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) Statutory Instrument No. 472, 1991 (5).
WHO Toxicity Class III (6).

Other comments

Allergenic properties reviewed (7).

References

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5. *S. I. 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.
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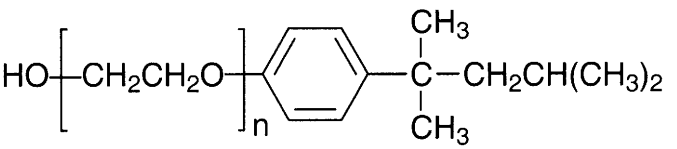
O20 octoxynol



CAS Registry No. 9002-93-1

Synonyms polyethylene glycol mono(4-octylphenyl) ether; α-[4-(1,1,3,3-tetramethylbutyl)phenyl]-ω-hydroxypoly(oxy-1,2-ethanediyl); mono[*p*-(1,1,3,3-tetramethylbutyl)phenyl]ether polyethylene glycol; poly(oxyethylene)*p-tert*-octylphenyl ether; *ortho*-gynol; Triton TX 100; Triton X100; TX 100; Hydrol SW; octoxanil

RTECS No. MD 0907700

Uses Surfactant. Spermatocide.

Physical properties

Specific gravity 1.0595 at 25°C with respect to water at 4°C
Solubility Water: miscible. Organic solvents: acetone, benzene, ethanol, toluene

Environmental fate

Abiotic removal
Removal from wastewater in a two-stage sorption process by filtration through beds of silica gel and activated carbon (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1800 mg kg^{-1} (polymer unspecified) (2).
LD_{50} intravenous mouse 1200 mg kg^{-1} (polymer unspecified) (3).

Teratogenicity and reproductive effects
Gavage mouse 800 mg of Triton X-100 kg^{-1} day^{-1} on days 6-13 of gestation. No maternal or foetal toxicity was observed (4).

Irritancy
1 mg instilled into rabbit eye caused moderate irritation (polymer and exposure unspecified) (2).
Dermal human (3 day) 2 mg caused mild irritation (polymer unspecified) (5).

Sensitisation
In vitro mouse lymphoma cells, DNA damage negative (polymer unspecified) (6).

Other effects

Other adverse effects (human)
Inhibited the E rosetting formed between human T-lymphocytes and sheep red blood cells *in vitro* in a concentration-dependent manner (7).

References

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021 octyl cyanide

$$CH_3(CH_2)_7CN$$

$C_9H_{17}N$ **Mol. Wt.** 139.24 **CAS Registry No.** 2243-27-8

Synonyms nonanenitrile; 1-cyanooctane; pelargononitrile

EINECS No. 218-808-9 **RTECS No.** RA 6606000

Occurrence In shale oil.

Physical properties

M. Pt. -34.2°C **B. Pt.** 224°C **Flash point** 81°C **Specific gravity** 0.8178 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.12 (1)
Solubility Organic solvents: carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

SE-CEIL 5 mg m^{-3} (as CN)
UK-LTEL 5 mg m^{-3} (as CN)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 3600 mg l^{-1} (1).

Environmental fate

Degradation studies
Utilised as sole carbon and nitrogen source by *Pseudomonas fluorescens* (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2060 mg kg^{-1} (3).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (4).

References

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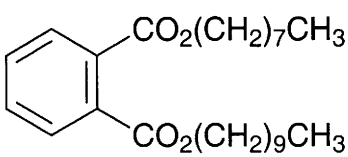
022 octyl decyl phthalate



$C_{26}H_{42}O_4$ **Mol. Wt.** 418.62 **CAS Registry No.** 119-07-3

Synonyms 1,2-benzenedicarboxylic acid, decyl octyl diester; *n*-decyl *n*-octyl phthalate; *n*-octyl *n*-decyl phthalate

EINECS No. 204-295-9 **RTECS No.** TI 0550000

Uses In preparation of plastics.

Occurrence In some plants such as the seeds of *Acanthopax sessiflorus* (1).

Physical properties

M. Pt. –50°C **B. Pt.** 239°C at 4 mmHg **Flash point** 235°C (closed or open cup) **Specific gravity** 0.980 at 20°C with respect to water at 20°C

Occupational exposure

SE-LEVL 3 mg m^{-3} **SE-STEL** 5 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 45 g kg^{-1} (2).

Other comments

As a pollutant of river water and sediment (3,4).

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (5).

References

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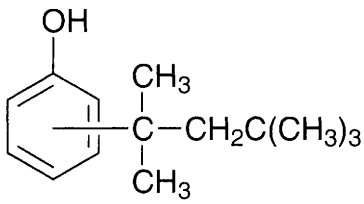
023 *tert*-octylphenol



$C_{14}H_{22}O$ **Mol. Wt.** 206.33 **CAS Registry No.** 27193-28-8

Synonyms (1,1,3,3-tetramethylbutyl)phenol

EINECS No. 248-310-7 **RTECS No.** SM 5775000

Uses Chemical intermediate.

Physical properties

M. Pt. 72-74°C **B. Pt.** 280-283°C **Specific gravity** 0.94 at 24°C with respect to water at 24°C

Ecotoxicity

Fish toxicity

Exposure of maturing ♂ rainbow trout to *tert*-octylphenol (0.5-65 μg l^{-1}) caused a clear dose-related increase in vitellogenin production (a process normally dependent on endogenous oestrogens) (1).

Juvenile ♀ rainbow trout (hatch-day 22) 1-50 μg l^{-1} or (hatch-day 35) 1-30 μg l^{-1}. Significant differences in size of the exposed fish, related to treatment, were still apparent on day-108, 86 days after cessation of treatment in the 1-50 μg l^{-1} experiments. These observations were confirmed in the 1-30 μg l^{-1} experiments in which significant changes in body weight and fork length were observed approximately 15 days after exposure was terminated (2).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 25 mg kg^{-1} (3).

Teratogenicity and reproductive effects

Oral administration to ♀ mice of 2 ng g^{-1} day^{-1} during gestation days 11-17 resulted in a reduction in daily sperm production and efficiency of sperm production in ♂ offspring relative to control males (4).

Subcutaneous neonatal rats (1 day old) received 1 mg 4-*tert*-octylphenol. No effect on the timing of vaginal opening was observed but 9/11 treated rats were in persistent vaginal oestrus at 3 months of age compared with 0/9 controls. Strong evidence was obtained that 4-*tert*-octylphenol has oestrogenic activity (blocking reproductive cyclicity) *in vivo* in both neonatal and adult ♀ rats (5).

Other effects

Any other adverse effects

Oestrogenic activity of 4-octylphenol was demonstrated in a number of *in vitro* assays – proliferation of human breast tumour cells, gene transcription in transfected chicken embryo fibroblasts and vitellogenin gene expression in trout hepatocytes (effective at 2 mg l^{-1} 4-octylphenol). Octylphenol was around 1000× less active than oestradiol in these assays (6).

Other comments

Environmental endocrine disruptor (7).
Occurs in municipal wastewater treatment effluent and sludge (8).
Compound is a product of anaerobic microbial degradation of octylphenol polyethoxylate (9).
The long-term fate of compound in sewage contaminated groundwater has been reviewed (10).

References

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024 octyltin chloride

$$CH_3(CH_2)_7SnCl_3$$

$C_8H_{17}Cl_3Sn$ **Mol. Wt.** 338.29 **CAS Registry No.** 3091-25-6

Synonyms trichlorooctylstannane; octyltrichlorostannane; mono-*n*-octyltin trichloride

EINECS No. 221-435-4 **RTECS No.** WH 8590000

Uses Has antileukaemic and antiviral properties against *Herpes* (1,2).
Chemical intermediate.

Physical properties

B. Pt. 102-110°C at 0.1 mmHg
Solubility Organic solvents: aqueous methanol, ethyl acetate, hexane, trichloromethane

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Sn) (inhalable fraction of aerosol)
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); 3146 (solid) **HAZCHEM Code** 2X (solid) **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4.6 g kg^{-1} (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

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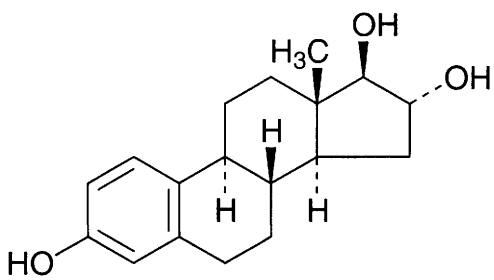
4. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

O25 oestriol



$C_{18}H_{24}O_3$ **Mol. Wt.** 288.39 **CAS Registry No.** 50-27-1

Synonyms 16α,17β-estriol; (16α,17β)-estra-1,3,5(10)-triene-3,16,17-triol; Estriol; follicular hormone hydrate; Ovestin; Theelol; tridestrin; trihydroxyestrin

EINECS No. 200-022-2 **RTECS No.** KG 8225000

Uses Used alone or with estrone and estradiol for treatment of symptoms associated with the climacteric.

Occurrence Widely occurring natural steroid hormone. It has also been isolated from some plants, including flowers of *Salix* (1).

Physical properties

M. Pt. 284-285°C **Specific gravity** 1.27 at 20°C

Solubility Organic solvents: acetone, chloroform, diethyl ether, 1,4-dioxane, ethanol, pyridine, vegetable oils

Mammalian & avian toxicity

Acute data

LD_{50} oral rat > 2000 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (3).

Subcutaneous implant mouse, 0.64-0.85 mg pellet, implanted on day 22-24 of life. Mammary tumours occurred in 18/18 ♀ and 25/30 ♂ mice compared with 28/34 ♀ and 10/83 ♂ controls (4).

Subcutaneous implant hamster, 20 mg pellet reimplanted every 150 days to ensure constant absorption for 318-601 days. After a latent period of 396-593 days 6/11 animals developed kidney tumours. No data on controls were reported (5).

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 cancers occurred up to 370 days in untreated controls or in oestrogen-treated rats. Higher doses of estriol (0.53-0.65 mg pellet^{-1}) had an inhibiting effect on carcinogen-induced tumour development (6).

Teratogenicity and reproductive effects

Administration of 30 μg to rats on days 16-19 of gestation induced partial feminisation of ♂ foetuses (7).

Metabolism and toxicokinetics

Following topical application of 10 μg (on 2 cm^{-2} area skin), 2.45% permeated through mouse skin *in vitro*. Permeation was accompanied by negligible cutaneous first-pass metabolism (8).
Excreted in humans as conjugated and unconjugated 2-hydroxyestriol after 2-hydroxylation (9).

Genotoxicity

In vitro human lymphocytes, aneuploidy negative (10).
In vitro human lymphocytes, sister chromatid exchanges marginally positive (10).
In vitro Chinese hamster ovary cells, sister chromatid exchanges positive (11).
In vitro Chinese hamster Don (22;XY) cells, induction of aneuploidy positive, a dose-response relationship could not be established (12).

Other comments

Use, occurrence, physical properties, analysis, carcinogenicity and mammalian toxicity reviewed (1).
Estriol has about 1/10 the activity of β-estradiol or estrone after subcutaneous administration (1).

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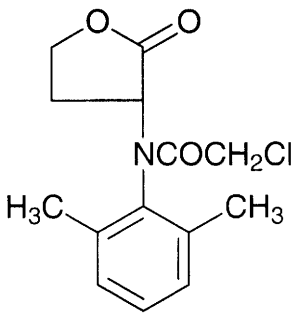
O26 ofurace



$C_{14}H_{16}ClNO_3$ **Mol. Wt.** 281.74 **CAS Registry No.** 58810-48-3

Synonyms (±)-(α)-2-chloro-*N*-2,6-xylylacetamido-γ-butyrolactone; (±)-2-chloro-*N*-(2,6-dimethylphenyl)-*N*-(tetrahydro-2-oxo-3-furanyl)-acetamide

EINECS No. 261-451-9 **RTECS No.** AE 1300200

Uses Systemic fungicide.

Physical properties

M. Pt. 145-146°C **Specific gravity** 1.37 at 20°C **Partition coefficient** log P_{ow} 1.39 at 20°C
Volatility v.p. 1.5×10^{-7} at 20°C
Solubility Water: 146 mg l^{-1} at 20°C. Organic solvents: chloroform, cyclohexane, dimethylformamide, ethyl acetate, isopropanol

Ecotoxicity

Invertebrate toxicity
Inhibits RNA synthesis and consequently DNA synthesis in *Phytophthora nicotiana* (1).
LD_{50} oral > 58 μg bee^{-1} (2).

Environmental fate

Abiotic removal
Decomposed by alkalis, with a hydrolysis $t_{1/2}$ 7 hr at pH 9 and 30°C (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂, ♀ rat 2.6, 3.5 mg kg^{-1}, respectively (3).
LD_{50} dermal rabbit >5 g kg^{-1} (3).

Sub-acute and sub-chronic data
A 90-day feeding study in rats established a NOEL of 20 mg kg $diet^{-1}$ (2).

Irritancy
Caused mild skin irritation and severe eye irritation in rabbits (dose and duration unspecified) (2).

Sensitisation
Not a skin sensitiser in guinea pig (3).

Other effects

Any other adverse effects

When administered at 1-100 mg kg^{-1} intraperitoneally to ♂ rats for 7 days, the compound influenced xenobiotic biotransformation by the liver. 7-Ethoxyresorufin-*O*-deethylase and aniline *p*-hydroxylase activities were reduced, but 7-ethoxycoumarin-*O*-deethylase activity was induced. Cytochrome P_{450} was unaffected (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).
EPA Toxicity Class III (2).
ADI 0.03 mg kg^{-1} body weight (2).

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6. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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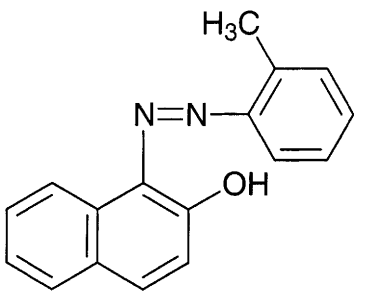
O27 Oil Orange SS



$C_{17}H_{14}N_2O$ **Mol. Wt.** 262.31 **CAS Registry No.** 2646-17-5

Synonyms 1-[(2-methylphenyl)azo]-2-naphthalenol; *o*-tolylazo-β-naphthol; toluene-2-azonaphthol-2; Lacquer Orange V; C.I. 12100; C.I. Solvent Orange 2

EINECS No. 220-162-8 **RTECS No.** QL 5425000

Uses To colour varnishes, oils, fats, waxes and formerly cosmetics (1).

Physical properties

M. Pt. 131°C

Solubility Organic solvents: benzene, chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5 g kg^{-1} (2).
LD_{50} oral rabbit 5 g kg^{-1} (2).
LD_{50} intravenous rabbit 60 mg kg^{-1} (2).
LD_{50} intravenous dog 200 mg kg^{-1} (2).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (3).
Mice fed 1 g kg^{-1} diet for 52 wk at intervals up to 90 wk developed a high incidence of benign intestinal tumours (4).
Rats receiving 300 mg kg $diet^{-1}$ for up to 40 wk developed an incidence of tumours higher than in control (5).
Mice injected subcutaneously twice weekly with 3 mg for 50 wk developed spindle cell sarcomas at the injection site along with intestinal, lung and mammary tumours (6).
Rats receiving subcutaneous injections of 0.5-1 mg once a wk for 13 months did not develop tumours (7).
Bladder carcinomas were produced in mice following implantation into bladder (8).

Other effects

Any other adverse effects

Oral doses of 200 or 400 mg kg^{-1} to rats caused a decrease in haemoglobin production (9).
Doses of 100 or 200 mg kg^{-1} to dogs had a cathartic effect (10).

Other comments

Experimental toxicology reviewed (1).

References

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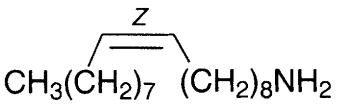
028 oleamine



$C_{18}H_{37}N$ **Mol. Wt.** 267.50 **CAS Registry No.** 112-90-3

Synonyms oleylamine; (Z)-9-octadecen-1-amine; alamine 11; *cis*-9-octadecenylamine; oleinamine; Armeen O

EINECS No. 204-015-5 **RTECS No.** RG 4130000

Uses In liposomes for drug delivery (1).
Chemical intermediate. Lubricating oil additive.

Physical properties

M. Pt. 25°C **B. Pt.** 338-340°C **Flash point** 154°C **Specific gravity** 0.813

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 888 mg kg^{-1} (2).

Teratogenicity and reproductive effects

When administered to mice at 800 mg kg^{-1} orally or 400 mg kg^{-1} intraperitoneally on day 9 of pregnancy, abnormalities were seen in offspring (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

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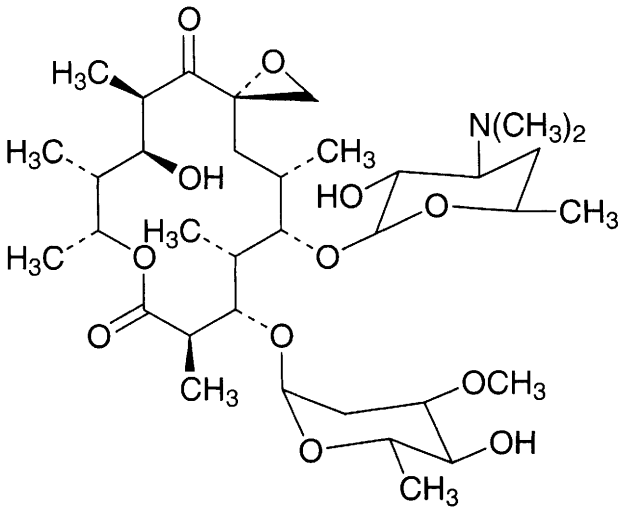
029 oleandomycin



$C_{35}H_{61}NO_{12}$ **Mol. Wt.** 687.87 **CAS Registry No.** 3922-90-5

Synonyms Amimycin; Landomycin; Romicil; Matromycin

EINECS No. 223-495-7 **RTECS No.** RJ 9220000

Uses Antibacterial used orally or intravenously as hydrochloride or phosphate salt.

Occurrence Antibiotic produced by *Streptomyces antibioticus* No. ATCC 11891.

Physical properties

Solubility Organic solvents: acetone, butanol, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 8.2 g kg^{-1} (1).

LD_{50} oral rat >10 g kg^{-1} (1).

LD_{50} intravenous rat 400 mg kg^{-1} (1).

LD_{50} *intravenous* mouse 600 mg kg^{-1} (1).

All as hydrochloride salt.

Teratogenicity and reproductive effects

Rats receiving 20 mg kg^{-1} intraperitoneally on days 8-14 produced offspring with abnormalities of the thymus gland, when sacrificed pre- or post-birth. Abnormalities included inhibition of lymphopoiesis, eosinophilia, neutrophilia and effects on vasculature (2).

Rats receiving the phosphate salts during pregnancy produced offspring with abnormalities of lymph nodes. Numbers of lymphocytes were reduced and barrier filtration and drainage functions of mesenteric lymph nodes were affected (3).

Metabolism and toxicokinetics

When used as the phosphate salt, the compound is well absorbed from the gastro-intestinal tract (4).

Other effects

Any other adverse effects

Ability to induce hepatic cytochrome-P450 has been demonstrated in rats (5).

Ascorbic acid and vitamins of the B group have been shown *in vitro* to reduce the activity of the compound (6).

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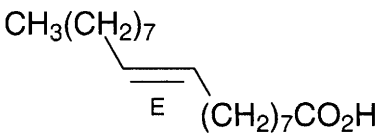
O30 (*E*)-oleic acid



$C_{18}H_{34}O_2$ **Mol. Wt.** 282.47 **CAS Registry No.** 112-79-8

Synonyms elaidic acid; (*E*)-9-octadecenoic acid; *trans*-Δ^9-octadecenoic acid

EINECS No. 204-006-6 **RTECS No.** JX 6125000

Occurrence Formed by isomerisation of oleic acid. Present in butter, margarine and other processed fats (1). Found in sludge following anaerobic treatment of wood processing waste water (2).

Physical properties

M. Pt. 44-45°C **B. Pt.** 288°C at 100 mmHg **Flash point** >110°C **Specific gravity** 0.851 at 79°C

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 512 mg kg^{-1} (3).

LD_{50} intravenous mouse 100 mg kg^{-1} (4).

Metabolism and toxicokinetics

Absorbed from the gastro-intestinal tract after oral administration. 10-17% of an experimental dose to rats of ^{14}C-labelled acid was recovered from the lymphatic drainage of the gastro-intestinal tract (5).

Other comments

Toxic effects on fibroblast biomembranes of the Chinese hamster V79-R reviewed (6).

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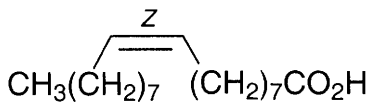
031 (*Z*)-oleic acid



$C_{18}H_{34}O_2$ **Mol. Wt.** 282.47 **CAS Registry No.** 112-80-1

Synonyms (Z)-9-octadecenoic acid; *cis*-Δ^9-octadecenoic acid

EINECS No. 204-007-1 **RTECS No.** RG 2275000

Uses To assist absorption by skin of some medicines (1).
In preparation of soaps and polishes. In myocardial imaging as an ^{131}I-labelled form.
Occurrence Most abundant of the unsaturated fatty acids, present in nearly all natural fats. The most common fatty acid in human milk.

Physical properties

M. Pt. 13.4°C **B. Pt.** 286°C at 100 mmHg **Flash point** >110°C **Specific gravity** 0.895 at 25°C
Volatility v.p. 1 mmHg at 176.5°C
Solubility Organic solvents: miscible diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) fathead minnow 1 g l^{-1} static bioassay at 18-22°C (2).
LC_{50} (96 hr) fathead minnow 205 mg l^{-1} (2).
LC_{50} goldfish 8 mg l^{-1} as sodium salt (duration unspecified) (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 74 g kg^{-1} (4).
LD_{50} intravenous rat 2.4 mg kg^{-1} (5).
LD_{50} intravenous mouse 230 mg kg^{-1} (6).

Metabolism and toxicokinetics
Fatty acid present in fats from many sources and thus a component of diet of man and other species. It is liberated from fat in the course of digestion and taken up into cells of intestinal mucosa by carrier-mediated transport. Main route of metabolism is by the β-oxidation pathway (7).
40-50% of an experimental dose to rats of ^{14}C-oleic acid was recovered from the lymphatic drainage of the gastro-intestinal tract (8).

Irritancy
Non-irritant (9).

Other comments

Must not be used in eye ointments (1).
Chlorinated derivatives are formed during bleaching of wood pulp (10).
Anoxia in myocardial tissue gives rise to accumulation of oleic acid in the tissure (11).
Reviews on human health effects, experimental toxicology, and physico-chemical properties listed (12).
The significance to health of oleic acid intake and its relationship to fats and other fatty acids has been extensively investigated and reviewed (13-15).

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032 omethoate

$$(H_3CO)_2P(O)SCH_2C(O)NHCH_3$$

$C_5H_{12}NO_4PS$ **Mol. Wt.** 213.19 **CAS Registry No.** 1113-02-6

Synonyms *O,O*-dimethyl *S*-(*N*-methylcarbamoyl)methyl phosphorothioate; *O,O*-dimethyl *S*-[2-(methylamino)-2-oxoethyl] phosphorothioate; phosphorothioic acid, *O,O*-dimethyl ester, *S*-ester with 2-mercapto-*N*-methylacetamide; dimethoate *O*-analogue; Dimethoxon; Folimat; dimethoate oxon

EINECS No. 214-197-8 **RTECS No.** TF 8050000

Uses Insecticide. Acaricide.

Physical properties

B. Pt. 135°C (decomp.) **Specific gravity** 1.32 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} –0.754 at 20°C **Volatility** v.p. 2.4×10^{-5} mmHg at 20°C
Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

Supply classification toxic, dangerous for the environment
Risk phrases Harmful in contact with skin – Toxic if swallowed – Very toxic to aquatic organisms (R21, R25, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour

– 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, S23, S36/37, S45, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) goldfish 10-100 mg l^{-1} (1).
LC_{50} (96 hr) golden orfe 30 mg l^{-1}, rainbow trout 9.1 mg l^{-1} (2).

Invertebrate toxicity

EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) 254 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) 295 mg l^{-1} (3).
Caged *Apis mellifera* were provided with 0.25-2.00 ppm in feed for 14 days. 50% mortality was observed with 0.25 ppm doses. This value is less than then corresponding 24 hr LD_{50} (4).
LD_{50} (24 hr) oral bee 40-50 mg bee^{-1} (4).

Environmental fate

Abiotic removal

$t_{1/2}$ for hydrolysis 2.5 day at 24°C, pH 7.0 (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral hen 125 mg kg^{-1} (1).
LD_{50} oral rat, rabbit 30, 50 mg kg^{-1}, respectively (2,5).
LD_{50} oral gavage rat, mouse 19, 54 mg kg^{-1}, respectively (6).
LC_{50} (4 hr) inhalation rat 300 mg m^{-3} (2).
LD_{50} dermal rat 700 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 180 mg kg^{-1} (8).

Sub-acute and sub-chronic data

Oral rat (90 day) no-adverse-effect level 1 mg kg^{-1} diet (1).

Metabolism and toxicokinetics

Following oral administration to mammals, eliminated in the urine within 48 hr (1).

Genotoxicity

In vitro human lymphocytes and mouse spleen cells sister chromatid exchanges, positive (9).
In vitro barley and rye root tip cells, sister chromatid exchanges positive (9).
Induced micronuclei and sperm malformations in mice (6).

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 levels: French chicory and artichokes 0.4 ppm; citrus fruit, strawberries and root vegetables 0.1 ppm; other fruit and vegetables 0.2 ppm (1).
WHO Toxicity Class Ib (12).
EPA Toxicity Class I (formulation) (2).
ADI 0.3 μg kg^{-1} body weight (2).

Other comments

Degradation product of dimethoate (13).
Toxicokinetic parameters in rats discussed (14).

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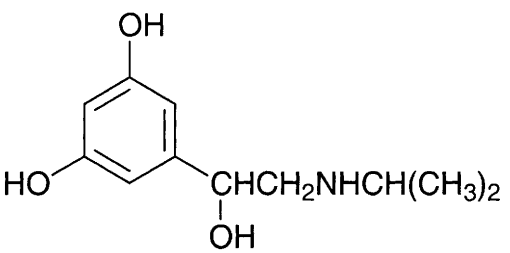
O33 orciprenaline



$C_{11}H_{17}NO_3$ **Mol. Wt.** 211.26 **CAS Registry No.** 586-06-1

Synonyms metaproterenol; 5-[1-hydroxy-2-[(1-methylethyl)amino]ethyl]-1,3-benzenediol; 3,5-dihydroxy-α-[(isopropylamino)methyl]benzyl alcohol; 1-(3,5-dihydroxyphenyl)-1-hydroxy-2-(isopropylamino)ethane; 1-(3,5-dihydroxyphenyl)-2-(isopropylamino)ethanol

EINECS No. 209-569-1 **RTECS No.** DO 1800000

Uses As a bronchodilator in treatment of asthma, and for delay of premature labour. Given orally, by inhalation or by injection, usually as the sulfate salt.

Physical properties

M. Pt. 100°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3.37 g kg^{-1} (1).
LD_{50} oral mouse >8.13 g kg^{-1} (1).
LD_{50} oral rabbit 3.1 g kg^{-1} (1).
LD_{50} intravenous mouse 87.8 mg kg^{-1} (1).
LD_{50} intravenous rabbit 81.3 mg kg^{-1} (1).
LD_{50} intravenous dog 30 mg kg^{-1} (1).

Metabolism and toxicokinetics

When used as the sulfate, it is incompletely absorbed from the gastro-intestinal tract with ~40% reaching the general circulation. It is stereoselectively glucuronidated in hepatic and intestinal cells and excreted in urine, primarily as glucuronide (2,3,4).

Other effects

Other adverse effects (human)

Compound has both anti-bronchospasm and cardiovascular actions in humans (2,5).
At excessively high doses trembling and palpitations are experienced (2,6).

Other comments

Compound exists in D and L forms.
It is an agonist for β-adrenoceptors, primarily of the β2 type, but has some β1 agonist activity (2,7).

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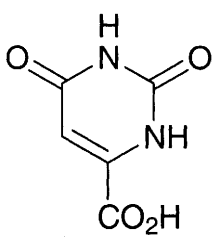
034 orotic acid



$C_5H_4N_2O_4$ **Mol. Wt.** 156.10 **CAS Registry No.** 65-86-1

Synonyms 6-carboxyuracil; whey factor; animal galactose factor; uracil-6-carboxylic acid; 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinecarboxylic acid; Oropur

EINECS No. 200-619-8 **RTECS No.** RM 3180000

Uses In treatment of hyperuricaemia and hypercholesterolaemia. As a feed supplement.
Occurrence Intermediate in biosynthesis of pyrimidine nucleotides and in RNA and DNA synthesis. Normal constituent of some body fluids (1).

Physical properties

M. Pt. 345-346°C

Ecotoxicity

Invertebrate toxicity

Can influence activity of dihydroorotase in *Pseudomonas fluorescens* when incorporated into growing medium (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2 g kg^{-1} (3).

LD_{50} intraperitoneal mouse 841 mg kg^{-1} (3).

LD_{50} intravenous mouse 770 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Mice fed 1% in diet showed no potentiation of tumour production by diethylnitrosamine. Tumour promotion in rats has been reported. Differences are thought to reflect different effects on precursor incorporation into nucleic acids, in the two species (4).

Precursor of pyrimidine nucleotide biosynthesis and promoter for liver carcinogenesis; fed at 1% in diet of rats for 5 wk caused liver DNA damage (5).

Metabolism and toxicokinetics

Competition for renal transport mechanisms between orotate and purine compounds had been demonstrated in sheep (6).

Other effects

Any other adverse effects

Nucleic acid effects are greater in kidney than in liver in the mouse, but greater in liver than in kidney in the rat (7).

Effects on the central nervous system of rats and mice including decreased motor activity, muscle relaxation, potentiation of hexobarbitone sleeping time and an increase in fast β wave activity (8).

An inborn error of metabolism in which there is an absence of orotidine-5'-phosphate pyrophosphorylase and for decarboxylase activities results in accumulation and urinary excretion of excess orotic acid (9).

Other comments

The neurobiological and biochemical basis for the properties of the compound have been reviewed (10).

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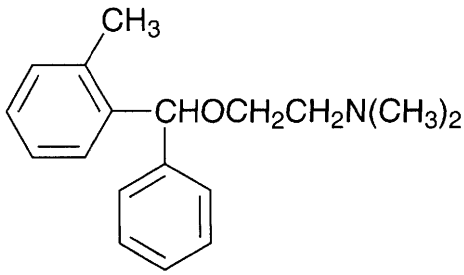
035 orphenadrine



$C_{18}H_{23}NO$ **Mol. Wt.** 269.39 **CAS Registry No.** 83-98-7

Synonyms *N,N*-dimethyl-2-[(2-methylphenyl)phenylmethoxy]ethanamine; *o*-methyldiphenhydramine; 2-methyldiphenhydramine; *N,N*-dimethyl-2-(*o*-methyl-α-phenylbenzyloxy)ethylamine; Disipal; Brocasipil

EINECS No. 201-509-2 **RTECS No.** KR 6120000

Uses To produce muscarinic cholinergic blockade in the treatment of Parkinson's disease and related conditions. Usually used as citrate or hydrochloride salt. Skeletal muscle relaxant.

Physical properties

B. Pt. 195°C at 12 mmHg

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 125 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 80 mg kg^{-1} (1).
LD_{50} intravenous mouse 33 mg kg^{-1} (1).

Teratogenicity and reproductive effects

When New Zealand white rabbits were dosed with the compound at 24 mg kg^{-1} on days 8-15 of pregnancy, concentrations of choline and acetylcholine were reduced in foetus collected on day 16. Placental concentrations of choline were also reduced (2,3).
Foetal malformations were also seen (3).

Metabolism and toxicokinetics

When administered as a salt, the compound is readily absorbed from the gastro-intestinal tract and distributed through the body, including the brain. Most of a dose is eliminated via urine within 3 days, along with some unchanged drug. At least 8 metabolites have been detected in urine (details unspecified) (4,5).
In humans $t_{1/2}$ increases following a multiple-dose regimen (6).

Other effects

Other adverse effects (human)

Adverse effects are those associated with blockade of cholinergic receptor sites and includes dry mouth, loss of pupil accommodation, increase in ocular pressure and palpitations. At high doses hallucination can be experienced. Compound is abused for its euphoriant and hallucinogenic properties (4).

Any other adverse effects

The drug can inhibit oxidative drug metabolism and there is both *in vivo* and *in vitro* evidence for isozyme-specific complexation of a metabolite with cytochrome P_{450} in the rat (6,7).
Anti-hypertonic activity in skeletal muscle is seen in mouse, cat and rabbit and is thought to result from central rather than peripheral actions of the compound (8).

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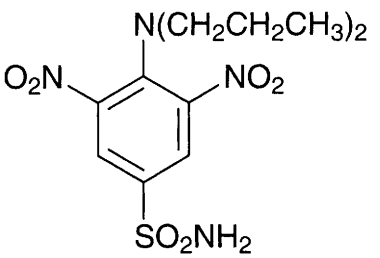
O36 oryzalin



$C_{12}H_{18}N_4O_6S$ **Mol. Wt.** 346.36 **CAS Registry No.** 19044-88-3

Synonyms 3,5-dinitro-*N*,*N*-dipropylsulfanilamide; 4-(dipropylamino)-3,5-dinitrobenzenesulfonamide; EL-119; Dirimal; Ryzelan; Surflan

EINECS No. 242-777-0 **RTECS No.** WO 9350000

Uses Pre-emergence herbicide.

Physical properties

M. Pt. 141-142°C **B. Pt.** 265°C (decomp.) **Partition coefficient** log P_{ow} 3.73 at pH 7 (1)
Volatility v.p. $<10^{-7}$ mmHg at 30°C
Solubility Water: 2.5 mg l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, benzene, dichloromethane, ethanol, methanol, methyl cellosolve

Ecotoxicity

Fish toxicity
LC_{50} bluegill sunfish 2.88 mg l^{-1} (1).
LC_{50} rainbow trout 3.26 mg l^{-1} (1).
LC_{50} (96 hr) goldfish fingerlings >1.4 mg l^{-1} (2).

Invertebrate toxicity
LD_{50} oral honey bee 0.011 mg bee^{-1} (1).

Environmental fate

Degradation studies
In soil microbiological degradation occurs rapidly and involves dealkylation of the amino nitrogen and reduction of the nitro groups (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail, mallard duck >500 mg kg^{-1} (1).

LD_{50} oral rat, mouse >10 g kg^{-1} (3).

LD_{50} oral cat, dog, chicken >1 g kg^{-1} (2).

LD_{50} dermal rabbit >2 g kg^{-1} (2).

Carcinogenicity and chronic effects

2-yr feeding study in rats established a NOEL of 300 mg kg^{-1} diet (2).

Teratogenicity and reproductive effects

Developmental toxicity described as 'suspicious' in humans and negative in rabbit and rat (4).

Irritancy

Slight irritant to skin but not eyes of rabbits (dose, duration unspecified) (1,2).

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).

Log P_{ow} exceeds European Union recommended limit of 3.0 (7).

EPA Toxicity Class IV (8).

EPA Toxicity Class III (formulation) (2).

ADI 0.012 mg kg^{-1} (2).

Other comments

Contaminant of food crops such as apple and lettuce (9).

The biological properties of the compound have been reviewed (3).

Metabolic pathways reviewed (10).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
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3. Decker, O. D. et al *Anal. Methods Pestic. Plant Growth Regul.* 1976, **8**, 433.
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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. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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037 osmium

Os

Os **Mol. Wt.** 190.20 **CAS Registry No.** 7440-04-2

EINECS No. 231-114-0 **RTECS No.** RN 1100000

Uses As an alloy with iridium for pen points and machine bearings. As a catalyst.

Occurrence In the mineral osmiridium and in platinum ores. In Earth's crust at 0.001 ppm.

Physical properties

M. Pt. ~2700°C **B. Pt.** 5027°C **Specific gravity** 22.61 at 20°C with respect to water at 4°C

Ecotoxicity

Invertebrate toxicity

Reported to have a high toxicity to freshwater tubificid worms (1).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous dog 17 mg kg^{-1} (2).

Other effects

Any other adverse effects

Rats receiving 1 ppm in diet showed signs of growth stimulation (3).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

The contribution that osmium makes to the overall inorganic particulate burden in lungs from pneumoconiosis patients had been assessed (5).

The element occurs as seven natural isotopes. In ascending order of occurrence these are: 184, 186, 187, 188, 189, 190, 192. Several artificial radioisotopes have been prepared.

The element is not normally present in animals and is not a requirement for normal growth (6).

References

1. Khangarot, B. S. *Bull. Environ. Contam. Toxicol.* 1991, **46**(6), 906-912.
2. *Scott. Med. Surg. J.* 1926, **26**, 131.
3. Bunyan, J. et al *Nature (London)* 1958, **181**, 1801.
4. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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O38 osmium tetrachloride

$OsCl_4$

Cl_4Os **Mol. Wt.** 332.01 **CAS Registry No.** 10026-01-4

Synonyms osmium chloride

Physical properties

M. Pt. sublimes at 450°C **Specific gravity** 4.38 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Metabolism and toxicokinetics

Inorganic salts of osmium are excreted in faeces after oral administration, but after injection remain at the injection site (1,2).

There are no reports of accumulation (1).

Genotoxicity

In vivo mouse micronucleus test in bone marrow negative (3).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

The compound is soluble in water and hydrolyses into oxides and hydrochloric acid.

References

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3. Liao, M. et al *Weisheng Dulixue Zazhi* 1988, **2**(2), 83-86 (Ch.) (*Chem. Abstr.* **112**, 134189h).
4. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

O39 osmium tetroxide

OsO_4

O_4Os **Mol. Wt.** 254.20 **CAS Registry No.** 20816-12-0

Synonyms osmium oxide (OsO_4), (*T*-4)-; osmic acid

EINECS No. 244-058-7 **RTECS No.** RN 1140000

Uses Oxidising agent, particularly in converting olefins into glycols. Fixing and staining agent for cell tissue studies. Has been given by intra-articular injection in rheumatic disorders of the knee (1).

Physical properties

M. Pt. 39.5-41°C **B. Pt.** 130°C (sublimes) **Specific gravity** 4.906 at 22°C **Volatility** v.p. 11 mmHg at 27°C
Solubility Organic solvents: benzene

Occupational exposure

DE-MAK 0.0002 ppm (0.0021 mg m^{-3})
FR-VME 0.0002 ppm (0.002 mg m^{-3}) (as Os)
UK-LTEL 0.0002 ppm (0.002 mg m^{-3}) (as Os) **UK-STEL** 0.0006 ppm (0.006 mg m^{-3}) (as Os)
US-TWA 0.0002 ppm (0.0016 mg m^{-3}) **US-STEL** 0.0006 ppm (0.0047 mg m^{-3})

UN No. 2471 **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Causes burns (R26/27/28, R34)
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
LD_{50} oral mouse 162 mg kg^{-1} (2).
LC_{Lo} (4 hr) inhalation mouse, rat 40 ppm (2).
LC_{Lo} (30 min) inhalation rabbit 1316 mg m^{-3} (3).
LD_{50} intraperitoneal mouse, rat 13.5, 14.1 mg kg^{-1}, respectively (2).

Teratogenicity and reproductive effects
Antitesticular effects reported at 2 and 7 days following a single intratesticular injection of 0.08 mmol kg^{-1} in rats (4).

Genotoxicity

A small increase in DNA repair synthesis was seen with osmium tetroxide in Syrian hamster embryo cells (5).
Produced positive results in rec assays with *Bacillus subtilis* (6).

Other effects

Other adverse effects (human)
Irritating to nose and throat in humans. Headaches and cough may also occur (7).
Local pain, fever and effusions associated with use for treating rheumatic knee disorders (1).
Lachrymation, visual disturbances such as ground glass and halo effects and conjunctivitis seen in precious metal refining workers exposed to 0.1-0.6 mg m^{-3} (7).
A human fatality was reported following inhalation of osmium tetroxide (8).

Legislation

ACGIH TKV:TWA 0.0002 ppm.
DOT Classification:Poison B; Label: Poison.
Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology, and workplace experience listed (10).

References

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2. *Shell Chemical Co. Unpublished Report* 1961, 8.
3. *J. Ind. Hyg.* 1933, **15**, 136.

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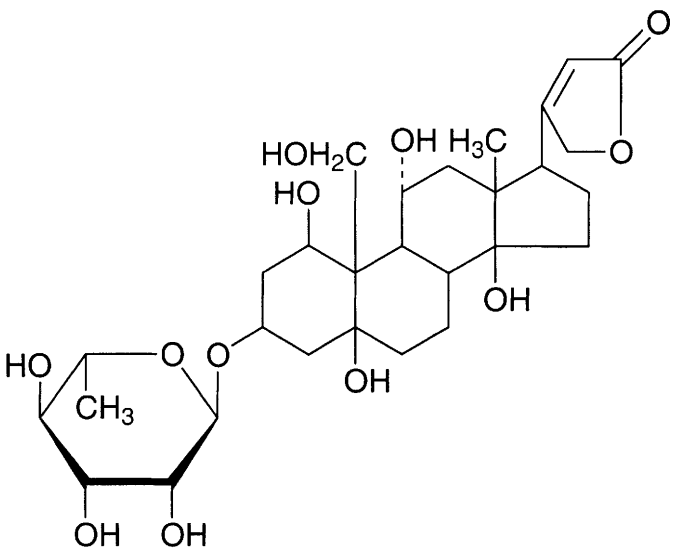
O40 ouabain



$C_{29}H_{44}O_{12}$ **Mol. Wt.** 584.66 **CAS Registry No.** 630-60-4

Synonyms 3-[(6-deoxy-α-L-mannopyranosyl)oxy]-1,5,11α,14,19-pentahydroxycard-20(22)-enolide; acocantherin; Gratibain; Kombetin; Rectobania; Strodival; Strophoperm

EINECS No. 211-139-3 **RTECS No.** RN 3675000

Uses Cardiotonic. Diuretic (veterinary). Inhibitor of K^+-Na^+ dependent ATPase.

Occurrence Obtained from seeds of *Strophanthus gratus* or the wood of *Acokanthera schimperi* or *Acokanthera ouabaio* (1).

Physical properties

M. Pt. 260°C

Occupational exposure

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) – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S45)

Ecotoxicity

Fish toxicity

58.4 mg l^{-1} inhibited K^+ uptake and enhanced intracellular Na^+ accumulation in isolated rainbow trout hepatocytes (2).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral dog, 1.5 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse, rat 11, 47 mg kg^{-1}, respectively (4,5).
LD_{Lo} subcutaneous mouse, rat 8, 50 mg kg^{-1}, respectively (6).
LD_{Lo} intravenous dog, monkey 54, 102 μg kg^{-1}, respectively (7,8).

Metabolism and toxicokinetics

Absorption from the gastro-intestinal tract unpredictable. Plasma $t_{1/2}$ ~21 hr (1).
Ouabain administered orally (8.0 mg) to 33 ♂ human volunteers was absorbed to a minimum of 1.4%. Given intravenously 0.5 mg elimination $t_{1/2}$ was 23 hr, for 33% of the dose, excreted renally. 80% was unchanged ouabain, while the remaining 20% was unidentified conjugated metabolites (9).

Genotoxicity

In vitro mouse lymphoma L5178Y tk^+/tk^- without metabolic activation weakly positive (10).

Other comments

Pharmacology in humans and laboratory animals reviewed (11).

References

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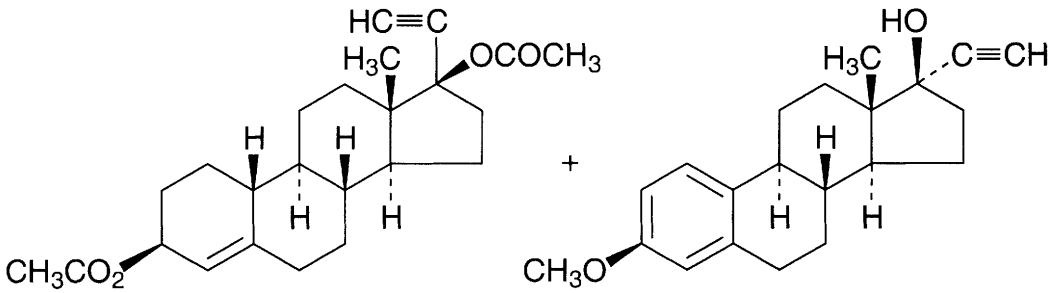
041 ovulen



$C_{45}H_{58}O_6C_{21}$ **Mol. Wt.** 947.18 **CAS Registry No.** 8056-92-6

Synonyms 19-norpregn-4-en-20-yne-3,17-diol, diacetate, (3β,17α)-, mixed with (17α)-3-methoxy-19-norpregna-1,3,5(10)-trien-20-yn-17-ol; Angravid; Bisecurin I; ethynodiol acetate-mestranol mixt; Metnilen; Synchrovet; ethynodiol diacetate mixed with mestranol

RTECS No. RC 8964200

Uses Combined oral contraceptive.

Genotoxicity

Ovulen given orally to mice 14 or 28 μg mg^{-1} day^{-1} for 2 days increased the incidence of polychromatic erythrocytes with micronuclei in bone marrow smears (1).
In vitro human lymphocyte cells (24 hr) 0.1-0.6 μg ml^{-1} induced no mutagenic effects (1).

Other effects

Other adverse effects (human)
A woman who used ovulen as an oral contraceptive for 4 yr developed a hepatocellular carcinoma and died one month after presentation with disseminated metastases (2).

References

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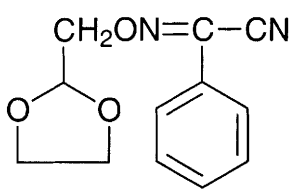
042 oxabetrinil



$C_{12}H_{12}N_2O_3$ **Mol. Wt.** 232.24 **CAS Registry No.** 74782-23-3

Synonyms α-[(1,3-dioxolan-2-ylmethoxy)imino]benzeneacetonitrile; CGA 92194; (Z)-1,3-dioxolan-2-ylmethoxyimino(phenyl)acetonitrile; Concep II

RTECS No. CY 1709000

Uses Herbicide safener. Applied as seed treatment to protect sorghum from metolachlor injury.

Physical properties

M. Pt. 77.7°C **Specific gravity** 1.33 at 20°C **Partition coefficient** log P_{ow} 2.76 (1)
Volatility v.p. 4.0×10^{-6} mmHg at 20°C
Solubility Water: 20 mg l^{-1} at 20°C. Organic solvents: acetone, cyclohexanone, dichloromethane, toluene, xylene

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >5000 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat ~1.5 mg l^{-1} air (1).
LC_{50} dermal rat >5000 mg kg^{-1} (1).

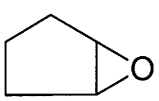
Legislation

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).
WHO Toxicity Class Table 5 (4).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, 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. 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

043 6-oxabicyclo[3.1.0]hexane



C_5H_8O **Mol. Wt.** 84.12 **CAS Registry No.** 285-67-6
Synonyms cyclopentene oxide; cyclopentene epoxide; cyclopentene oxide; 1,2-epoxycyclopentane
EINECS No. 206-005-6 **RTECS No.** RN 8935000

Physical properties

B. Pt. 102°C **Flash point** 10°C **Specific gravity** 0.964

Genotoxicity

Escherichia coli PQ37 SOS Chromotest with and without metabolic activation negative (1).
In vitro Chinese hamster V79 cells (metabolic activation unspecified) induced sister chromatid exchanges (2).

References

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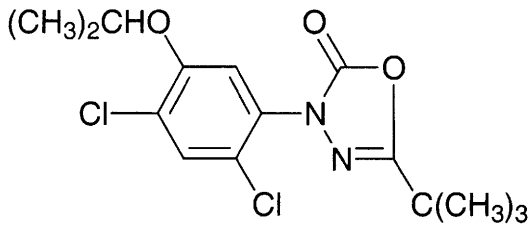
044 oxadiazon



$C_{15}H_{18}Cl_2N_2O_3$ **Mol. Wt.** 345.22 **CAS Registry No.** 19666-30-9

Synonyms 3-[2,4-dichloro-5-(1-methylethoxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3*H*)-one; 2-*tert*-butyl-4-(2,4-dichloro-5-isopropoxyphenyl)Δ^2-1,3,4-oxadiazolin-5-one; G 315; Ronstar; RP 17623; Foresite

EINECS No. 243-215-7 **RTECS No.** RO 0874000

Uses Herbicide.

Physical properties

M. Pt. 88-90°C **Partition coefficient** log P_{ow} 4.80 (1) **Volatility** v.p. $<1 \times 10^{-6}$ at 20°C
Solubility Water: 0.7 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, ethanol, 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) carp 9-15.4 mg l^{-1} (1).
LC_{50} (96 hr) rainbow trout, bluegill sunfish, catfish 1.2, 1.2 and >15.4 mg l^{-1}, respectively (2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* 0.5-8.0 mg l^{-1} (2).
LD_{50} >400 μg bee^{-1} (2).

Bioaccumulation
Average bioconcentration in willow shiner 1226 after 7-14 days exposure. Excretion rate constant from whole body of fish was 0.30 day^{-1} (3).
The biological concentration (dry weight) in *Spirodela polyrhiza* in Lake Kojima, Japan was several hundred times higher with respect to lake water concentration (4).
Oxadiazon uptake, depuration rates and bioconcentration factors (BCF) were measured for the bivalve *Corbicula leana* and the river snail *Cipangopludina chinensis* under field conditions (Kokai river, Japan) during 1992/1993. Field values *Corbicula leana* 1992 [1993]: uptake rate constant 126 [24.2] ml g^{-1} day^{-1}, depuration rate constants 0.18 [0.11] day^{-1}, BCF 700 [220]. Field values 1992 *Cipangopludina chinensis* BCF 210 ±120 (5).

Environmental fate

Degradation studies
Completely degraded by bacteria alone and partially degraded by bacteria with fungi (6).

Persisted in sandy loam soil 60 days after treatment at 1.0 kg ha^{-1} (7).
Degraded in a test method by non-acclimated microbes in activated sludge in field soil and river sediment with added glucose and peptone under aerobic and anaerobic conditions; biodegradation rate constants (K_B) 0.26 and 0.15, respectively (8).

Adsorption and retention
Strongly adsorbed by soil colloids and humus with very little migration or leaching. Soil $t_{1/2}$ ~3-6 months (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck, bobwhite quail >1000, 6000 mg kg^{-1}, respectively (1).
LD_{50} oral rat, mouse >8000 mg kg^{-1} (1).
LC_{50} (duration unspecified) inhalation rat >200 mg l^{-1} (1).
LD_{50} dermal rat >8000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials, rats and dogs recieving 100 mg kg^{-1} diet showed no ill-effects (1).

Metabolism and toxicokinetics
In mammals, following oral administration, 93% is eliminated within 72 hr, predominantly in the faeces (10).

Legislation

WHO Class Table 5 (11).
EPA Toxicity Class IV (2).
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).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (14)

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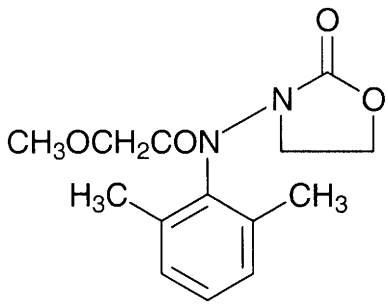
13. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
14. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK

045 oxadixyl



$C_{14}H_{18}N_2O_4$ **Mol. Wt.** 278.31 **CAS Registry No.** 77732-09-3

Synonyms *N*-(2,6-dimethylphenyl)-2-methoxy-*N*-(2-oxo-3-oxazolidinyl)acetamide; 2-methoxy-*N*-(2-oxo-1,3-oxazolidin-3-yl)acet-2′,6′-xylidide; Sandofan; SAN 371F

RTECS No. AB 8131400

Uses Systemic fungicide used for control of Peronosporales.

Physical properties

M. Pt. 104-105°C **Partition coefficient** log P_{ow} 0.643-0.799 at 22-24°C (1) **Volatility** v.p. 3.3×10^{-9} mmHg at 20°C

Solubility Water: 3.4 g kg^{-1} at 25°C. Organic solvents: acetone, diethyl ether, dimethyl sulfoxide, ethanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) carp, rainbow trout, bluegill sunfish >300-360 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia* sp. 530 mg l^{-1} (1).

Environmental fate

Degradation studies

Degradation in soil very slow, $t_{1/2}$ ~300 days in laboratory; degradation products are mainly polar (1).

Adsorption and retention

A significant proportion of polar metabolites bind to soil matrix. Adsorption increases with increasing organic matter content in soil (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >2510 mg kg^{-1} (1).

LD_{50} oral ♀ rat, ♂ mouse, ♀ mouse, ♂ rat 1860-3480 mg kg^{-1} (1).

LC_{50} (6 hr) inhalation rat >6 mg l^{-1} (1).

LD_{50} dermal rat, rabbit >2000 mg kg^{-1} (1).

LD_{50} intraperitoneal ♂, ♀ rat 490-550 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Eight day oral LC_{50} for mallard duck, Japanese quail >5620 mg kg^{-1} diet (1).

In feeding trials, no-effect level for rats (90 day) and for dogs (6 month) was 250 mg kg^{-1} (1).

Teratogenicity and reproductive effects
No teratogenic or reproductive effects were seen in rats at up to 1000 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics
Absorption in rats following oral administration was rapid and almost complete, 81-92% being eliminated in faeces and urine in 144 hr. Metabolised by hydrolysis at various points on the methoxyacetamide moiety and oxidation of methyl group on phenyl ring to alcohol (1).

Legislation

WHO Toxicity Class III (2).
EPA Toxicity Class III (formulation) (3).
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).

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O46 oxalic acid

$$HO_2CCO_2H$$

$C_2H_2O_4$ **Mol. Wt.** 90.04 **CAS Registry No.** 144-62-7

Synonyms ethanedioic acid; Aktisal; Aquisal

EINECS No. 205-634-3 **RTECS No.** RO 2450000

Uses Analytical reagent. In calico bleaching and dyeing. Bleaching straw and leather. Reducing agent. Stain/colour remover. Oxalates manufacture. In blue ink. Dye intermediate.
Occurrence In sorrel, spinach, broccoli, rhubarb leaves and other plants. Product of metabolism of many moulds.

Physical properties

M. Pt. 189.5°C (sublimes) **B. Pt.** 150°C **Specific gravity** 1.90 at 17°C with respect to water at 4°C
Partition coefficient log P_{ow} –0.81-0.43 (1) **Volatility** v.p. 3.06×10^{-3} mmHg at 33°C
Solubility Water: 95 g l^{-1} at 15°C. Organic solvents: diethyl ether, ethanol, glycerol

Occupational exposure

FR-VME 1 mg m^{-3}
SE-LEVL 1 mg m^{-3} **SE-STEL** 2 mg m^{-3}
UK-LTEL 1 mg m^{-3} **UK-STEL** 2 mg m^{-3}
US-TWA 1 mg m^{-3} **US-STEL** 2 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 skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) mosquito fish, bluegill sunfish 1350, 4000, respectively, static bioassay (2).
Goldfish survived for 0.4-0.5 hr at 1000 ppm, pH 2.6 and 4 days at 200 ppm, pH 5.3 (3).

Invertebrate toxicity

LOEC *Microcystis aeruginosa* 80 mg l^{-1} (4).
Toxicity threshold (cell multiplication inhibition test) *Pseudomonas putida*, *Scenedesmus quadricauda* and *Entosiphon sulcatum* 1550, 790, 222 mg l^{-1}, respectively (5).
Gammarus pulex, *Tubifex tubifex*, *Luminae ovate*, *Sialis flavilatera* perturbation level 25, 80, 60, 1000 mg l^{-1}, respectively (6).

Toxicity to other species

LD_{Lo} subcutaneous frog 757 mg kg^{-1} (7).

Environmental fate

Degradation studies

100 ppm treated by activated sludge process at 20°C for 120 hr degraded by 20-30% (8).
Oxalic acid reacts with a number of cations to form soluble as well as insoluble salts (9).
BOD_{20} 0.115 mg O_2 l^{-1} (6).
COD 0.126 mg O_2 l^{-1}; ThOD 0.125 mg O_2 l^{-1} (10).
Wastewater treatment, activated sludge, 4.5% of ThOD after 6 hr, 0.4% of ThOD after 12 hr, toxic after 24 hr (11).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 7500 mg kg^{-1} (12).
LD_{Lo} subcutaneous cat 112 mg kg^{-1} (7).

Sub-acute and sub-chronic data

Long-Evans rats administered diets containing 2.5-5% oxalic acid for 70 days had decreased body weights and growth rates. Organ weights were reduced at 5%, but organ weight/body weight ratios increased (13).
200 g administered to a horse over 3 days was not lethal (14).

Teratogenicity and reproductive effects

Disrupted oestrus cycles were seen in rats maintained on diets containing 2.5% or 5% oxalic acid (duration unspecified) (13).
Mice administered 8400 mg kg^{-1} for 7 days prior to mating and through day 21 of gestation in ♀ showed decreased fertility in ♂ and embryo toxicity and foetotoxicity in ♀ (15).

Metabolism and toxicokinetics

Absorbed primarily in the small intestine and excreted unchanged in the urine. No evidence is available for utilisation or metabolism in human tissue (16,17).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation (18).
250 µg instilled into rabbit eye (24 hr) caused severe irritation (18).
May cause corrosion of the skin (19).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (20).
Escherichia coli WP2s(λ) microscreen assay without metabolic activation positive (21).

Other effects

Other adverse effects (human)

Ingestion of large doses causes severe corrosive action on the alimentary tract mucosa (22).

Symptoms of acute poisoning in humans can include severe gastro-intestinal pain and distress, cardiovascular collapse, bleaching of mucous membranes, neuromuscular symptoms and kidney damage (22).

A 53-year-old man suffered vomiting, diarrhoea and loss of consciousness after ingesting soup containing about 500 g of sorrel. He had metabolic acidosis, hypocalcaemia, liver cell necrosis and raised blood urea and serum creatinine levels. He died following a deep coma, respiratory depression, kidney and liver failure, and disturbances in cardiac rhythm (23).

Splashes of oxalic acid have produced burns of the human epithelium with subsequent recovery (24).

Inhalation of spray carrying oxalic acid when cleaning car radiators caused nosebleed, headaches, vomiting, backache and loss of weight (25).

Pain, cyanosis, gangrenous changes and arteritis in the fingers was reported after chronic skin exposure (26,27).

Railroad workers exposed to high concentrations of oxalic acid solutions reported an increased incidence of kidney stones and a prevalence of urolithiasis at 53.3% as opposed to 11.9% in unexposed workers (28).

Any other adverse effects

Some sheep are able to adapt to up to 12% oxalic acid in diet without showing symptoms of toxicity, possibly due to bacterial degradation of oxalic acid in their rumen (29).

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047 oxamyl

$$(CH_3)_2NCOC(SCH_3)=NOCONHCH_3$$

$C_7H_{13}N_3O_3S$ **Mol. Wt.** 219.26 **CAS Registry No.** 23135-22-0

Synonyms ethanimidothioic acid, 2-(dimethylamino)-*N*-[[(methylamino)carbonyl]oxy]-2-oxo-, methyl ester; oxamimidic acid, (*N*',N')-dimethyl-*N*-[methylcarbamoyl)oxy]-1-thio-, methyl ester; DPX 1410; DuPont 1410; thioxamyl; Vydate; Blade

EINECS No. 245-445-3 **RTECS No.** RP 2300000

Uses Insecticide. Nematicide. Acaricide.

Physical properties

M. Pt. 100-102°C; changes to a dimorphic form m. pt. 108-110°C **B. Pt.** decomp. on distillation
Specific gravity 0.97 at 25°C **Partition coefficient** log P_{ow} –0.446 at pH 5 (1)
Volatility v.p. 31×10^{-6} mmHg at 25°C
Solubility Water: 280 g l^{-1} at 25°C. Organic solvents: acetone, ethanol, isopropanol, methanol, toluene

Occupational exposure

UN No. 2757
Supply classification very toxic
Risk phrases Very toxic by inhalation and if swallowed – Harmful in contact with skin (R26/28, R21)
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) rainbow trout, bluegill sunfish, goldfish 4.2, 5.6 and 27.5 mg l^{-1}, respectively (1).

Invertebrate toxicity
LD_{50} (oral) 0.078-0.11 μg bee^{-1}; (contact) 0.27-0.36 μg bee^{-1} (1).

Environmental fate

Degradation studies
Rapidly degraded in soil, $t_{1/2}$ 7 days (1).

Abiotic removal
Rapidly and extensively degraded in solvents (methanol and hexane) and solid state under a 300 nm light $t_{1/2}$ 7 hr and 2 hr, respectively (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral quail 4.2 mg kg^{-1} (3).
LD_{50} oral mouse, rat 2.3-2.5 mg kg^{-1} (4).
LC_{50} (1 hr) inhalation rat 170 mg m^{-3} (3).
LD_{50} dermal rabbit 740 mg kg^{-1} (5).

Carcinogenicity and chronic effects
In 2-yr feeding trials, no-effect level for rats was 50 mg kg^{-1} in diet and dogs 100 mg kg^{-1} diet (1).
Rats fed 500 ppm in diet showed clinical signs of cholinesterase activity inhibition and weight loss after 2 days. Feeding 100 or 150 ppm for 90 days or 2 yr showed depressed body weight gains (6).

Mice fed 50 or 75 ppm in diet for 2 yr showed reduced body weight compared with controls, but no other adverse effects (6).

Teratogenicity and reproductive effects

Litter sizes of rats fed 100 or 150 ppm in diet were reduced in one- and three-generation studies. Pup body weight were reduced, but no teratogenic response was seen (6).

No teratogenic response was seen in rabbits fed dose levels where maternal toxicity was encountered (6).

Metabolism and toxicokinetics

Metabolised in rats by hydrolysis to methyl *N'*-hydroxy-*N'*,N'-dimethyl-1- thiooxamimidate or converted enzymically via *N,N*-dimethyl-1-cyanoform amide into *N,N*-dimethyloxamic acid; 70% of metabolites excreted in urine and faeces were conjugates of the oximino compound, the acid and their monomethyl derivative (7).

Legislation

WHO Toxicity Class 1b (8).

EPA Toxicity Class 1 (1).

ADI 0.03 mg kg^{-1} body weight (1).

Other comments

Swabs from the hands of workers handling plants sprayed with 0.2% solution showed the plants could be handled safely after 4 days (9).

Metabolised in fall armyworm (*Spodoptera frugipeda*), velvet bean caterpillar (*Anticarsia gematalis*), cabbage looper (*Tricoplusia ni*) and corn earworm (*Heliothis zea*) by *S*-dimethylase enzyme (10).

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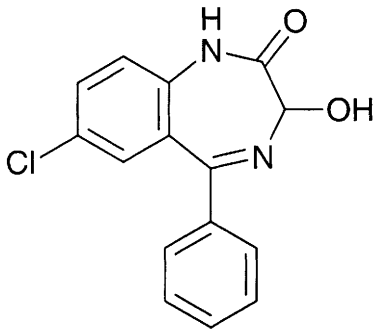
O48 oxazepam



$C_{15}H_{11}ClN_2O_2$ **Mol. Wt.** 286.72 **CAS Registry No.** 604-75-1

Synonyms 7-chloro-1,3-dihydro-3-hydroxy-5-phenyl-2*H*-1,4-benzodiazepin-2-one; Anxiolit retard; Bonare; Lumbial; Nesontil; Propax

EINECS No. 210-076-9 **RTECS No.** DF 1400000

Uses Anxiolytic. Skeletal muscle relaxant.

Physical properties

M. Pt. 205-206°C

Solubility Water: 30 mg l^{-1}. Organic solvents: chloroform, dioxane, ethanol

Environmental fate

Degradation studies

Degraded by *Bifidobacterium* sp. (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling >100-178, 100 mg kg^{-1}, respectively (2).

LD_{50} intraperitoneal mouse, rat 767, 1535 mg kg^{-1}, respectively (3,4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).

♂, ♀ Swiss-Webster mice (aged 3 months) received 0.05 or 0.15% in diet 12 months, and then a control diet for a further 2 months, before being sacrificed. Liver cell adenomas were reported in 3/12 ♂ receiving 0.05% and 8/13 ♂ and 5/8 ♀ receiving 0.15%. No liver tumours were seen in controls (6).

Teratogenicity and reproductive effects

Mice treated orally on days 12-16 of pregnancy with 15 mg kg^{-1} 2× daily showed a transient retardation of postnatal body growth and neurobehavioural development; a reduction of hyperactivity response to amphetamine in open-field tests on day 14-16 postnatal; selective impairment of adult active avoidance in 4 go - no-go discrimination tasks. Several negative results were also observed, viz no changes in homing performance on postnatal day 10; an intact hyperactivity response to scopolamine on postnatal days 21-23; a lack of effect on adult activity; a normal passive-performance in the go-no go tasks (7).

A significant association was found between the intake of benzodiazepines including oxazepam by human mothers during the first trimester of pregnancy and oral clefts in infants (8).

Metabolism and toxicokinetics

Following oral administration in miniature swine and humans, metabolised to 6-chloro-4-phenyl-2(1*H*)-quinazolinone, 5-*p*-hydroxyoxazepam; 2-amino-5-chlorobenzophenone; 2'-benzoyl-4'-chloro-2,2-dihydroxyacetanilide; and 2'-benzoyl-4'-chloro-2-hydroxy-2-ureidoacetanilide (9).

Six healthy volunteers received oxazepam 15 mg intravenously and orally at intervals of at least 1 wk. Elimination $t_{1/2}$ was 6.7 hr; plasma $t_{1/2}$ was 5.8 hr. After oral dose, peak plasma level was reached in 1.7-2.8 hr. Absorption was almost complete, with bioavailability 98%. Urinary recovery was 80% after intravenous and 71.4% after oral dose. Oxazepam was extensively bound to plasma with a free fraction of 4.5% (10).

Crosses the placenta and is detected in breast milk (11).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (12).

Aspergillus nidulans without metabolic activation, no non-disjunction and crossing-over reported (13).

Other effects

Other adverse effects (human)

Inhibited cholinesterase activity in human foetal and adult brain *in vitro* (14).

Any other adverse effects

In rats, prolonged oral administration resulted in changes in behaviour and development of tolerance. This did not occur with prolonged intraperitoneal administration (15).

Other comments

May be habit forming.

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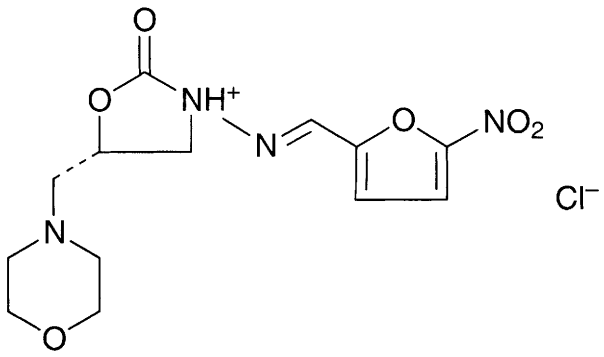
049 oxazolidinone hydrochloride



$C_{13}H_{17}ClN_4O_6$ **Mol. Wt.** 360.75 **CAS Registry No.** 3031-51-4

Synonyms L-furaltadone hydrochloride; furmethonol; 1,5-(morpholinomethyl)-3-[(5-nitrofurfurylidene)amino]-2-oxazolidinone hydrochloride; 5-(morpholinomethyl)-3-[(5-nitrofurfurylidine)amino]-2-oxazolidnone, monohydrochloride; 5-(4-morpholinylmethyl)-3-[[(5-nitro-2-furanyl)methylene]amino]-(*S*)-2-oxazolidine, monohydrochloride

RTECS No. RQ 3640000

Uses Antibacterial, antiprotozoal agent.

Physical properties

M. Pt. 223-228°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 600 mg kg^{-1} (1).

LD_{50} intravenous mouse 400 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).

Weanling ♀ Sprague-Dawley rats administered 1000 ppm in diet for 46 wk followed by a control diet for 20 wk, 31/32 rats surviving >10 wk developed 41 tumours, including 6 benign and 25 malignant mammary tumours, 7 lymphoblastic lymphomas and 2 transitional-cell carcinomas of the renal pelvis (3).

Metabolism and toxicokinetics

Detected in milk of cows and dogs up to 4 hr after administration of 20 mg kg^{-1} (route unspecified) and in the bile of chickens and dogs. Detected in cerebrospinal fluid of dogs 0.5-4 hr after oral or intravenous administration (dose unspecified) (4).

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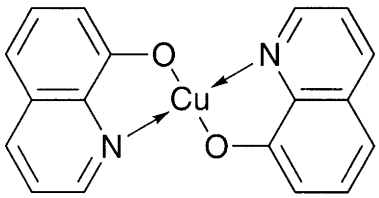
O50 oxine-copper



$C_{18}H_{12}CuN_2O_2$ **Mol. Wt.** 351.85 **CAS Registry No.** 10380-28-6

Synonyms copper 8-hydroxyquinolate; cupric 8-quinolinoxide; bis(8-quinolinolato-*N'*,O_8)copper; bis(quinolin-8-olato)copper; copper oxinate; copper oxine; Arbochanchre; Cancror; Dokirin; Fruitdo; Nytek

EINECS No. 233-841-9 **RTECS No.** VC 5250000

Uses Fungicide. Used in textiles, paint, paper and in agriculture.

Physical properties

M. Pt. Decomposes above 270°C **Specific gravity** 1.63 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.46 at 25°C
Solubility Water: 0.07 mg l^{-1} at pH 7 and 25°C. Organic solvents: pyridine, quinoline

Occupational exposure

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

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) brown trout, rainbow trout 0.2-0.3 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 4700, 9000 mg kg^{-1}, respectively (2).
LC_{50} (duration unspecified) inhalation rat 820 mg m^{-3} (3).
LD_{50} dermal rabbit >2 g kg^{-1} (3).
LD_{50} intraperitoneal rat, mouse 22, 67 mg kg^{-1}, respectively (3,4).

Carcinogenicity and chronic effects
No adequate data for evaluation of carcinogenicity in humans, inadequate evidence for evaluation of carcinogenicity in animals, IARC classification group 3 (5).
Gavage mice (7 days old) 1000 mg kg^{-1} single dose and then the same absolute amount daily up to 4 wk old, followed by 2800 mg kg^{-1} in diet. Tumour incidences were not increased compared with controls (6).
Two groups of mice (strains unspecified) of both sexes were given a single subcutaneous injection of 1000 mg kg^{-1} at 28 days of age. At 78 wk, 6/17 ♂ and 1/18 ♀ of one strain, and 3/18 ♀ mice of the second strain had generalised reticulum-cell sarcomas, compared with 8/141, 1/154 and 5/157 in controls, respectively (7).

Irritancy
Non-irritating to skin. Slightly irritating to rabbit eye (2).

Genotoxicity

Salmonella typhimurium TA98, TA1535, TA1537, TA1538 with metabolic activation negative, TA100 with metabolic activation positive (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Copper: guide level 100 μg l^{-1} at outlets of pumping and/or treatment works and their substations and 3000 μg l^{-1} after the water has been standing for 12 hr in the piping and at the point where the water is made available to the consumer. Fungicide: maximum admissible concentration 0.1 μg l^{-1} (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).
WHO Toxicity Class Table 5 (11).
EPA Toxicity Class (formulation) I (water-base), II, III (petroleum solvent-base) (2).
ADI 0.02 mg kg^{-1} (2).

Other comments

Reviews on experimental toxicology and human health effects listed (12).
Ampullarium canaliculatus is controlled by 8-hydroxyquinoline copper (13).

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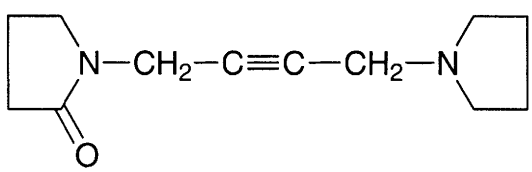
O51 oxotremorin



$C_{12}H_{18}N_2O$ **Mol. Wt.** 206.29 **CAS Registry No.** 70-22-4

Synonyms 1-[4-(1-pyrrolidinyl)-2-butynyl]-2-pyrrolidinone; oxotremorine; oxytremorine

EINECS No. 200-728-0 **RTECS No.** UY 5950100

Uses Pharmacological agent. Cholinergic agonist.

Physical properties

B. Pt. 150-155°C at 0.6 mmHg

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 11.3 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse, rat 3-4.4 mg kg^{-1} (2,3).

LD_{50} intravenous mouse 1400 μg kg^{-1} (4).

ED_{50} intraperitoneal rat for producing lachrymation, salivation, tremor, convulsions and death was 2.5, 1.3, 1.6, 3.2 and 8.3 mg kg^{-1}, respectively (5).

Teratogenicity and reproductive effects

Ventricular injections of 0, 0.5, 1.0, 2.0 μg delayed initiation of sexual behaviour in experienced ♂ rats and slowed its rate. Injections into the preoptic area through cannulae angled to miss all ventricles only decreased the number of intromissions preceding ejaculation (6).

Metabolism and toxicokinetics

Pharmacokinetic parameters were measured following oral and intravenous administration to rats using *ex vivo* [^{3}H]oxotremorine-M binding to the brain. Oxytremorine had a long duration of action (7).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

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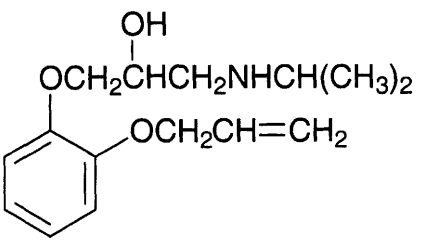
052 oxprenolol



$C_{15}H_{23}NO_3$ **Mol. Wt.** 265.35 **CAS Registry No.** 6452-71-7

Synonyms 1-[(1-methylethyl)amino]-3-[2-(2-propenyloxy)phenoxy]-2-propanol; 1-[*o*-(allyloxy)phenoxy]-3-(isopropylamino)-2-propanol; Coretal

EINECS No. 229-257-9 **RTECS No.** UA 5270000

Uses Antihypertensive. Antianginal. Antiarrhythmic. Beta blocker.

Physical properties

M. Pt. 78-80°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 730 mg kg^{-1} (1).
LD_{90} oral cat 200 mg kg^{-1} (1).
LD_{50} subcutaneous mouse, rat 245, 940 mg kg^{-1}, respectively (1).
LD_{50} intravenous mouse, rat 20, 33 mg kg^{-1}, respectively (2,1).
LD_{50} intraperitoneal mouse 170 mg kg^{-1} (3).

Metabolism and toxicokinetics

Introduced into the stomach of humans dissolved in a meal containing [^{14}C]polyethylene glycol. Oxprenolol was not absorbed in the stomach, but 80% of the drug emptied in the stomach was absorbed in the duodenum and 80% of that released from the duodenum was absorbed in a 30 cm segment of the jejunum (4).
Elimination $t_{1/2}$ 1-3 hr. Metabolised in the liver and almost entirely excreted in urine. Diffuses across the placenta and is present in breast milk. Crosses the blood brain barrier (5).

Genotoxicity

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

Other effects

Other adverse effects (human)

A 16-yr-old ♀ who ingested 8 g oxprenolol was in a coma, with shallow respiration and in shock with unrecordable blood pressure, cool extremeties and scarcely palpable radical and carotid pulses after 2 hr and had grand mal epileptic seizures after 4 hr. The patient recovered after normal blood pressure was restored (7).
Retroperitoneal fibrosis in one patient was associated with the use of oxprenolol (8).

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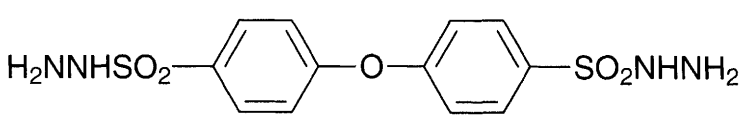
053 4,4′-oxybis(benzenesulfonyl hydrazide)



$C_{12}H_{14}N_4O_5S_2$ **Mol. Wt.** 358.40 **CAS Registry No.** 80-51-3

Synonyms 4,4′-oxydibenzenesulfonyl hydrazide; dihydrazinebenzenesulfonic acid; diphenyl oxide 4,4′-sulfohydrazide

EINECS No. 201-286-1 **RTECS No.** DB 7321000

Uses Blowing agent for polyurethanes, plastics and rubbers. Insect repellant. Catalyst for polymerisation of thick films.

Physical properties

M. Pt. 160-161°C (decomp.)

Genotoxicity

In vitro rat, mouse hepatocytes DNA repair test positive (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (2).

Other comments

Reviews on human health effects, experimental toxicology and environmental effects listed (3).

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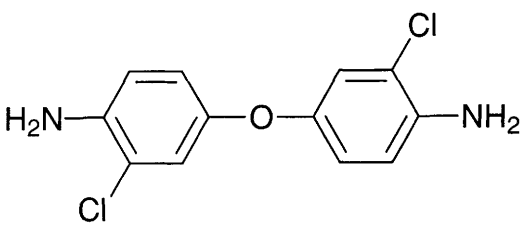
O54 4,4′-oxybis(2-chloroaniline)



$C_{12}H_{10}Cl_2N_2O$ **Mol. Wt.** 269.13 **CAS Registry No.** 28434-86-8

Synonyms 3,3′-dichloro-4,4′-diaminodiphenyl ether; 4,4′-oxybis(2-chlorobenzenamine); bis(4-amino-3-chlorophenyl) ether

RTECS No. KM 9625000

Uses Hardener for epoxy resins.

Physical properties

M. Pt. 128-129°C

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rat >10 g kg^{-1} (1).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).

Subcutaneous rat, 250-1000 mg kg^{-1} once wkly for 27 wk. Within a median induction time of 300 days, 37/40 rats had a total of 65 malignant and 2 benign tumours; 51 were ear-duct carcinomas and 16 occurred at other unspecified sites. No tumours were found in controls (1).
Subcutaneous rat (13 month) 400 mg kg^{-1} wk^{-1}. Between 200 and 340 days, the animals were sacrificed serially and sections of the ear duct showed multiple circumscribed areas with a high alkaline phosphatase activity. After 390 days the 4 remaining rats had papillomas, papillary carcinomas, squamous-cell carcinomas and carcinomas and adenomas of the Zymbal gland. No such tumours were found in controls (3).

Genotoxicity

In vitro primary rat hepatocytes DNA repair test positive (4).

Other comments

Properties, production, carcinogenicity and toxicity of 3,3′-dichloro-4,4′-diaminophenyl ether reviewed (5).

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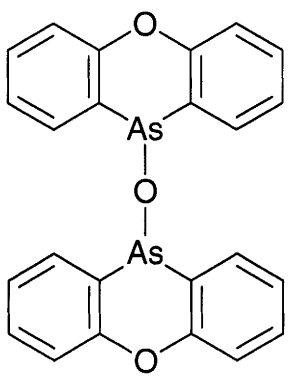
O55 10,10′-oxybisphenoxarsine



$C_{24}H_{16}As_2O_3$ **Mol. Wt.** 502.23 **CAS Registry No.** 58-36-6

Synonyms 10,10′-oxydiphenoxarsine; DID47; Vinadine; Vinyzene; 10,10′-oxybis-10*H*-phenoxarsine; bis(phenoxarsin-10-yl) ether; 10,10′-bis(phenoxarsinyl)oxide

EINECS No. 200-377-3 **RTECS No.** SP 6800000

Uses Used in fungicidal and bactericidal protection of plastics.

Physical properties

M. Pt. 184-185°C

Solubility Water: 5 ppm at 20°C. Organic solvents: chloroform, ethanol, methylene chloride

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 24 mg kg^{-1} (1).

LD_{50} oral guinea pig, rat 24, 40 mg kg^{-1}, respectively (2).

LC_{Lo} (2 hr) inhalation guinea pig 141 mg m^{-3} (2).

Irritancy

Dermal guinea pig 250 mg (5 day) caused severe irritation (2).

Legislation

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

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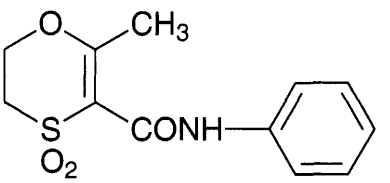
O56 oxycarboxin



$C_{12}H_{13}NO_4S$ **Mol. Wt.** 267.31 **CAS Registry No.** 5259-88-1

Synonyms 5,6-dihydro-2-methyl-*N*-phenyl-1,4-oxathiin-3-carboxamide, 4,4-dioxide; carboxin sulfone; F-461; Plantvax; Vitavax sulfone

EINECS No. 226-066-2 **RTECS No.** RP 4900000

Uses Systemic fungicide.

Physical properties

M. Pt. 119.5-121.5°C **Flash point** 219°C **Specific gravity** 1.41 **Partition coefficient** log P_{ow} 0.772

Volatility v.p. $<1 \times 10^{-6}$ at 20°C

Solubility Water: 1.09 g l^{-1} at 25°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol, 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} (96 hr) rainbow trout, bluegill sunfish 19.9, 28.1 mg l^{-1}, respectively (1).

Invertebrate toxicity

LC_{50} (96 hr) *Daphnia* sp. 69 mg l^{-1} (2).

LD_{50} contact bee >181 μg bee^{-1} (2).

Environmental fate

Degradation studies

It is oxidised to its sulfoxide in soil (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2000 mg kg^{-1} (4).

LD_{50} dermal rabbit >16,000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

8-day dietary LC_{50} mallard duck, bobwhite quail >4640, >10,000 mg kg^{-1} diet, respectively (1).

Carcinogenicity and chronic effects

In 2-yr feeding trials, rats and dogs receiving 3000 mg kg^{-1} diet showed no ill-effects (1).

Genotoxicity

Saccharomyces cerevisiae with and without metabolic activation negative (5).

Aspergillus nidulans 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) of Staturtory Instrument No. 472, 1991 (7).

WHO Toxicity Class Table 5 (8).

EPA Toxicity Class IV (formulation) (2).

ADI 0.15 mg kg^{-1} (2).

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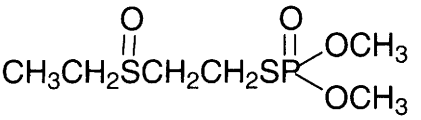
057 oxydemeton-methyl



$C_6H_{15}O_4PS_2$ **Mol. Wt.** 246.29 **CAS Registry No.** 301-12-2

Synonyms *S*-[2-(ethylsulfinyl)ethyl] *O,O*-dimethyl phosphorothioate; BAY 21097; R 2170; phosphorothioic acid, *S*-[2-(ethylsulfinyl)ethyl] *O,O*-dimethyl ester; Aimcosystox; Anthonox; Mesodrin; Metasystemox R; Metox; Metasystox R

EINECS No. 206-110-7 **RTECS No.** TG 1420000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. –20°C **B. Pt.** 106°C at 0.01 mmHg **Specific gravity** 1.289 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} –0.745 **Volatility** v.p. 2.86×10^{-5} mmHg at 20°C
Solubility Water: miscible. Organic solvents: acetone, dichloromethane, diethyl ether, ethanol, propan-2-ol

Occupational exposure

UN No. 3018
Supply classification toxic, dangerous for the environment
Risk phrases Toxic in contact with skin and if swallowed – Very toxic to aquatic organisms (R24/25, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – 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, S23, S36/37, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) rainbow trout, bluegill sunfish 10 mg l^{-1} (1).
LC_{50} (96 hr) channel catfish, largemouth bass, 18, 31 mg l^{-1}, respectively (2).

Invertebrate toxicity
LC_{50} (96 hr) *Gammarus lacustris* 0.19 mg l^{-1} (3).
LC_{50} (96 hr) *Gammarus fasciatus* 1000 µg l^{-1} (4).
LC_{50} (96 hr) *Pteronarcys californica* 0.035 mg l^{-1} (5).
Toxic to bees (1).

Environmental fate

Abiotic removal
Degraded by oxidation of sulfoxide to a sulfone group and oxidative and hydrolytic cleavage of the side-chain, with formation of dimethylphosphoric acid and phosphoric acid (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, pigeon 15-75 mg kg^{-1} (1,6-8).
LC_{50} (1 hr) inhalation rat 1500 mg m^{-3} (1).
LD_{50} dermal rat 100-250 mg kg^{-1} (1,9).

LD_{50} intraperitoneal rat, mouse 8, 20 mg kg^{-1}, respectively (10,11).
LD_{50} intravenous rat 47 mg kg^{-1} (12).

Sub-acute and sub-chronic data

Oral rat (75 day) 5 mg kg^{-1} diet produced no pathological symptoms, 10 mg kg^{-1} diet caused fatalities from day-6 of administration (1).

Teratogenicity and reproductive effects

Oral rat single dose of 0, 0.5, 1.5 on 4.5 mg kg^{-1} on days 6-15 of gestation produced a dose-related reduction in maternal cholinesterase activity in plasma (30-72%), red blood cell (18-56%) and brain (21-68%). The high dose reduced food consumption, suppressed body weight gain and produced tremors in 98% of the dams. No embryotoxic, foetotoxic or teratogenic effects were observed (13).
♀ Rats dosed with 2.5 mg kg^{-1} day^{-1} suffered an increase in numbers showing no corpora lutea. This dose level also caused increased epididymal vacuolation and testes weight decreases in ♂s and severe brain, plasma, and red blood cell cholinesterase inhibition in both sexes. At this dose level neurotransmitters may have caused disruption at the pituitary level (14).

Genotoxicity

Salmonella typhimurium TA 100, TA 1535 with metabolic activation positive (15).
Saccharomyces cerevisiae strain D4 mitotic gene conversion at the trp 5 locus positive (16).
♂ *Drosophila melanogaster* Hikone R (resistant) strain fed oxydemeton-methyl at up to 3.0 mM showed a slightly higher than normal incidence of recessive lethal mutations. No mutations were seen in Berlin wild ♂s fed the non-toxic dose of 0.043 mM for 3 days (17).
Mice injected intraperitoneally twice (24 hr interval) with 1-3 mg kg^{-1} oxydemeton-methyl suffered an average 7-10.33 micronucleated cells per 1000 polychromatic erythrocytes compared with 2.66 for controls (18).
Human lymphocytes incubated *in vitro* (37°C, 50 hr) with oxydemeton-methyl showed chromosome aberrations (mainly chromatid and isochromatid breaks). Chromosome damage increased with increasing oxydemeton-methyl concentration (18).

Other effects

Other adverse effects (human)

35 workers became ill after entering a cauliflower field contaminated with insecticide residues including oxydemeton-methyl. One was pregnant with a 4-wk-old foetus. At birth, the ♀ infant had multiple cardiac defects, eye defects, cerebral and cerebellar atrophy and facial anomalies. There was no history of birth defects or maternal risk factor and oxydemeton-methyl was the only chemical to have reported reproductive 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).
WHO Toxicity Class Ib (22).
EPA Toxicity Class I (formulation) (23).
ADI 0.3 μg kg^{-1} for total of oxydemeton-methyl, demeton-*S*-methyl and demeton-*S*-methyl sulfone (23).
EEC maximum residue limits, carrots no detectable residue, other vegetables and fruit 0.4 ppm (1).

Other comments

Residues have been isolated from crops. Metabolite of demeton-*S*-methyl (24,1).
Considered an endocrine disruptor in the female (25).

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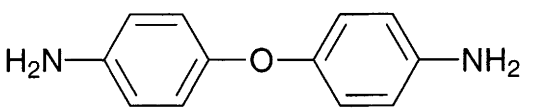
O58 4,4′-oxydianiline



$C_{12}H_{12}N_2O$ **Mol. Wt.** 200.24 **CAS Registry No.** 101-80-4

Synonyms 4,4′-diaminodiphenyl ether; diaminodiphenyl ether; 4,4′-oxybis(benzenediamine); 4,4′-oxybisbenzenamine; bis(*p*-aminophenyl) ether; *p,p*′-diaminophenyl ether; 4,4′-oxybis(aniline)

EINECS No. 202-977-0 **RTECS No.** BY 7900000

Uses Antioxidant, epoxy resin hardener, manufacture of high temperature resistant polyimide resins.

Physical properties

M. Pt. 186-187°C **B. Pt.** >300°C **Partition coefficient** log P_{ow} 2.1571 (1)
Solubility Organic solvents: acetone

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 3.2 ppm (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, mouse 685-725 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse, rat 300, 365 mg kg^{-1}, respectively (3).

Sub-acute and sub-chronic data

Oral rat (15 days) 72.5 mg kg^{-1} daily was reported to decrease blood haemoglobin and increase splenic and adrenal weight. Inhalation rat (4 month) 4.2-4.8 mg m^{-3} for 4 hr day^{-1} produced a decrease in blood haemoglobin, but no change in the weight or histological appearance of individual organs (3).

Oral rat, mouse (90 days) 0-2000 mg kg^{-1} diet. Concentration-dependent retardations in body weight gain were observed in rats and mice fed ≥600 mg kg^{-1}. Fatality occurred in rats given 1000 or 2000 mg kg^{-1}, but not in mice. Diffuse parenchymatous goitre, pituitary hyperplasia, seminiferous tubular degeneration and atrophy of the prostate and seminal vesicles occurred in rats fed 600 mg kg^{-1} and mice fed 1000 mg kg^{-1} and above. Bone marrow hypoplasia and renal microlithiasis were also observed in rats, but the latter lesion was not concentration-dependent (4,5).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (6).

Oral mouse (103 wk) 150, 300 or 800 mg kg^{-1}. There was a treatment-related incidence of adenomas of the Harderian gland, hepatocellular adenomas or carcinomas, and follicular cell adenomas of the thyroid. Oral rat (103 wk) 200, 400 or 500 mg kg^{-1}. There was a significant increase in the occurrence of hepatocellular carcinomas, neoplastic nodules of the liver and follicular cell adenomas of the thyroid (4).

Oral rat (up to 826 days), total dose 4.12 g per animal. 1 kidney carcinoma, 3 reticulum cell sarcomas, 1 liver fibrosarcoma, 1 neurogenic sarcoma, 2 seminomas and 1 mammary gland fibroadenoma had developed in the 7 surviving animals from 48 treated. Subcutaneous mouse (271 days) 5 mg per animal wkly. Of 9/33 surviving animals, 3 developed 3 tumours (2 lymphomas and 1 adenoma). The incidence of lymphomas was 6% in controls. Subcutaneous rat (529 days) 25 mg per animal wkly. Among 39/62 surviving animals, 7 developed 7 *tumours* (2 lymphomas, 1 reticulum cell sarcoma, 1 liver fibrosarcoma, 1 carcinoma of the kidney and 2 mammary gland fibroadenomas) (7).

Subcutaneous rat (up to 670 days) 100-300 mg kg^{-1} wkly. Of 40 treated rats, 10 developed malignant liver tumours and 12 benign liver tumours. 0/50 controls had liver tumours (8).

Gavage rat (9 month), 10 doses of 40 mg, the maximum tolerated dose, were given at 3 day intervals. No mammary tumours but 1 squamous metaplasia of the uterus was observed. Among 132 controls 3 mammary carcinomas were observed (9).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (10).

Elicited DNA repair in rat primary hepatocytes *in vitro* (11).

Mutagenic in the L-5178Y tk+/tk– mouse lymphoma cell forward mutation assay (12).

Other comments

Physical properties, use, analysis, carcinogenicity, mammalian toxicity and mutagenicity reviewed (13).

Reported to inhibit the growth of spontaneous mammary tumours and transplanted tumours in mice (14).

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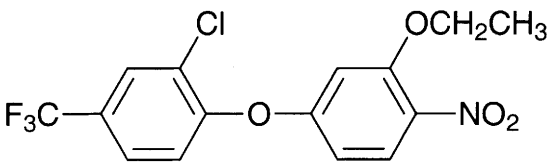
O59 oxyfluorfen



$C_{15}H_{11}ClF_3NO_4$ **Mol. Wt.** 361.70 **CAS Registry No.** 42874-03-3

Synonyms 2-chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl) benzene; Goal; RH 2915; RH 2915D

EINECS No. 255-983-0 **RTECS No.** KN 6900000

Uses Herbicide

Physical properties

M. Pt. 85-90°C **B. Pt.** 358.2°C (decomp.) **Specific gravity** 1.35 at 73°C **Partition coefficient** log P_{ow} 4.468 (1)
Volatility v.p. 2.01×10^{-7} mmHg at 25°C
Solubility Water: 0.116 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, cyclohexanone, dimethylformamide

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, trout, channel catfish 0.2-0.41 mg l^{-1} (1).

Invertebrate toxicity
Not toxic to honey bees at 0.025 mg bee^{-1} (1).

Environmental fate

Degradation studies
In a study using sterile and non-sterile samples of water and sediment taken directly from the field, degradation was greater in the presence of non-sterile sediment than in the presence of sterile sediment. $t_{1/2}$, >2 wk in non-sterile sediment (2).

Abiotic removal
No significant hydrolysis occurred in 28 days at pH 5-9 and 25°C. UV light decomposes aqueous suspension (1).

Adsorption and retention
Strongly adsorbed in soil, not readily desorbed and negligible leaching. $t_{1/2}$, ~56 day (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail >5000 mg kg^{-1} (1).
LD_{50} oral mallard >4000 mg kg^{-1} (1).
LD_{50} oral ♂ rat, dog >5000 mg kg^{-1} (1,4).
LD_{50} dermal rabbit >10,000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

NOEC (90 day) oral rat 1000 mg kg^{-1} in diet (1).
NOEC (90 day) oral dog 40 mg kg^{-1} in diet (1).

Metabolism and toxicokinetics

Following oral administration with a ^{14}C-labelled compound for 7 consecutive days, 2-4% of radioactivity was recovered in tissues and urine. 95% of the label was recovered in the faeces. Unchanged compound accounted for ~ 75% of faecal radioactivity. Faecal metabolites included: *N*-[4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-ethoxyphenyl]acetamide; 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrophenol;4-[2-chloro-4- (trifluoromethyl)phenoxy]-2-ethoxybenzenamine; and *N*-[4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-hydroxyphenyl]acetamide (5).

Irritancy

Non-irritating to rabbit skin (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).
Log P_{ow} exceeds European Union recommended limit of 3.0 (8).
WHO Toxicity Class Table 5 (9).
EPA Toxicity Class IV (formulation) (2).
ADI 0.003 mg kg^{-1} (2).

Other comments

In a study of mycorrhizal fungi, *Paxillus involutus* was especially sensitive, whilst mycelial growth of *Hebeloma crustiliniforme* was only inhibited at the highest levels. Spore germination of *Glomus mosseae* was sensitive to higher concentrations. Concentration range tested was 0.1-1000 ppm (10).
At application rate of 0.144 kg ha^{-1} exerted a significant detrimental effect on soil microflora (11).

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O60 oxygen

O_2

O_2 **Mol. Wt.** 32.00 **CAS Registry No.** 7782-44-7

Synonyms dioxygen; molecular oxygen

EINECS No. 231-956-9 **RTECS No.** RS 2060000

Uses Medical gas. In oxyacetylene flame welding. Used by divers for submarine work. Rocket propellant.
Occurrence Occurs naturally as diatomic gas. The most abundant element on earth; makes up 46.6% of earth's crust; 20.95% of dry air.

Physical properties

M. Pt. –218.4°C **B. Pt.** –182.96°C **Specific gravity** 1.429 g l^{-1} at 0°C and 760mmHg; 1.14 g ml^{-1} at –183°C
Solubility Water: 1 vol. dissolves in 32 vol. water at 20°C. Organic solvents: ethanol, organic liquids (usually to a greater extent than in water)

Occupational exposure

UN No. 1072 (compressed)

UN No. 1073 (refrigerated liquid) **HAZCHEM Code** 2S (compressed) **HAZCHEM Code** 2PE (refrigerated liquid) **Conveyance classification** non-flammable non-toxic gas, fire intensifying hazard
Supply classification oxidising
Risk phrases Contact with combustible material may cause fire (R8)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from combustible material (S2, S17)

Ecotoxicity

Fish toxicity
At 27.5°C the optimum dissolved oxygen concentration for growth of common carp was 3.5-4.0 µg l^{-1}. At 2.0-3.0 µg l^{-1} growth rates decreased markedly, fish did not accept feed and moved towards oxygen inflow (1).

Environmental fate

Nitrification inhibition
Denitrifying activity in freshwater sediment decreased with increasing oxygen concentrations of ≥7.9 µg ml^{-1} but increased at 7.9-11.1 µg ml^{-1} (2).

Carbonaceous inhibition
Several methanogenic bacteria die when exposed to low concentrations of oxygen, possibly due to a series of biochemical oxidation reactions (3,4).

Degradation studies
Paracoccus denitrificans and *Pseudomonas aeruginosa* convert 87% NO_3^- into N_2 and N_2O under both aerobic and anaerobic conditions. Production of N_2O by *P. denitrificans* increased and N_2 decreased in the presence of O_2 while concentrations of both N_2 and N_2O increased with *P. aeruginosa* (5).

Mammalian & avian toxicity

Acute data
Poisoning occurs in humans inhaling pure oxygen at atmospheric pressure in 5 hr, at 1500 mmHg in 3 hr and at 3750 mmHg in a few minutes (6).

At ≤2 atm oxygen, pulmonary toxicity appears below central nervous system toxicity; at >2 atm the reverse applies. Symptoms of pulmonary toxicity include decreased vital capacity, cough and substernal distress. CNS toxicity symptoms include nausea, mood changes, vertigo, twitching, convulsions and loss of consciousness (7).

Carcinogenicity and chronic effects

Exposure of strain A mice for 48 hr to 100% oxygen immediately or 2 days after administration of the carcinogen dibenz[*a*,*h*]anthracene enhanced tumour development (8).

Teratogenicity and reproductive effects

Growth rates of mouse pronuclear embryos exposed to atmospheric oxygen concentrations for 1 hr were significantly lower (to the blastocyte stage) than embryos in a low oxygen (5%) cultures (9).

Irritancy

Liquid oxygen in contact with the skin produces cold burns (7).

Genotoxicity

Using the comet alkaline assay, DNA damage is seen in leucocytes from patients treated with hyperbaric oxygen. However, strand breaks induced by hyperbaric oxygen are rapidly repaired and do not result in detectable chromosome damage (10).

Human lymphocytes incubated 3-7 days with 20, 40, 50, 60% oxygen increased chromosomal aberrations at 40-60% compared with 20% (normotoxic), especially at longer incubation times (11).

Chinese hamster V79-379A lung fibroblasts exposed to 40-95% oxygen at atmospheric pressure for 6-96 hr. Growth rate and survival inhibited by 50% by 24 hr exposure to 95% O_2. Mutations to azaguanine resistance observed after exposure to 60-95% for 24-48 hr. Many abnormalities reported – binucleate and multinucleate cells, micronuclei, and chromosomal damage (chromatid gaps and breaks); damage increased in a dose-dependent way reaching 100% of nuclei after 72 hr exposure to 95% O_2 (12).

Other effects

Other adverse effects (human)

In 1940s and 1950s an epidemic of retinopathy of prematurity affected 10,000 babies, probably by excessive administration of oxygen to neonates. Use of O_2 was curtailed and incidence reduced (13).

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O61 oxygen difluoride

OF_2

F_2O **Mol. Wt.** 54.00 **CAS Registry No.** 7783-41-7

Synonyms oxygen fluoride (OF_2); difluorine monoxide; difluorine oxide; fluorine monoxide; fluorine oxide; oxydifluoride

EINECS No. 231-996-7 **RTECS No.** RS 2100000

Physical properties

M. Pt. –223.8°C **B. Pt.** –145.3°C **Specific gravity** 1.90 at –224°C
Solubility Water: 6.8 ml gas 100 ml^{-1} at 0°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
SE-LEVL 2 mg m^{-3} (as F)
US-STEL ceiling limit 0.05 ppm (0.11 mg m^{-3})

UN No. 2190 **Conveyance classification** toxic gas, fire intensifying hazard, corrosive

Mammalian & avian toxicity

Acute data
LC_{50} (1 hr) inhalation monkey, mouse, dog, rat 26, 62, 128, 136 ppm, respectively (1,2).

Legislation

Air containment standards and permissible exposure limits in the workplace set by the US Occupational Safety and Health Administration (3).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluoride: maximum admissible concentration 1500 and 700 µg l^{-1}, respectively, at 8-12 and 25-30°C average temperature (4).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
WHO guideline for drinking water quality 1.5 mg fluoride l^{-1} (6).

Other comments

Reviews on experimental toxicology, human health effects and workplace experience listed (7).

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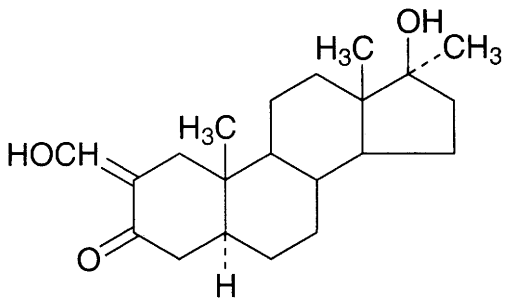
O62 oxymetholone



$C_{21}H_{32}O_3$ **Mol. Wt.** 332.48 **CAS Registry No.** 434-07-1

Synonyms 17-hydroxy-2-(hydroxymethylene)-17-β-methyl-5α-androstan-3-one; Adroyd; Anadrol; anasterone; C.I. 406; oxymethenolone; Raboral

EINECS No. 207-098-6 **RTECS No.** BV 8060000

Uses Androgen, anabolic steroid.

Physical properties

M. Pt. 178-180°C

Solubility Organic solvents: chloroform, ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, no adequate data for evaluation of carcinogenicity to animals, IARC classification group 2A (1).

May reasonably be anticipated to be a carcinogen (2).

Benign hepatoma, primary hepatocellular carcinoma, hepatic cholangiocarcinoma and peliosis hepatis have been recorded in humans (3-8).

The National Toxicology Program tested rats and mice via gavage. Equivocal evidence of carcinogenicity in ♂ rats, clear evidence of carcinogenicity in ♀ rats (9).

Cases of leukaemia reported in patients taking the steroid (10,11).

Metabolism and toxicokinetics

No unmetabolised compound was detected in excreta in a study of bodybuilders (12).

This synthetic androgen is readily absorbed from the gastro-intestinal tract, metabolised in the liver and eliminated in bile following oral administration. Peak concentrations were found in plasma 1-2 hr following dosing. Unique analytical problems continue to plague the investigations of the rate and metabolism of oxymetholone. It is very poorly recovered from blood or plasma and binds tightly to the stationery phase of any chromatographic system that has been used to purify or quantify the parent compound (9).

Other effects

Other adverse effects (human)

Male bodybuilders using anabolic steroids showed higher levels of transaminase and a higher systolic blood pressure than controls. Cholesterol associated with lipoprotein ratios were disturbed. Premature atherogenesis and hepatotoxicity may be long-term risks (13).

The use of anabolic steroids by bodybuilders inhibits the excretion of normal urinary steroids (12).

Hyperglucagonaemia and peliosis hepatis reported (14-16).

Any other adverse effects

Pretreatment had no effect on phalloidin-induced peliosis hepatitis-like lesion in mice (17).

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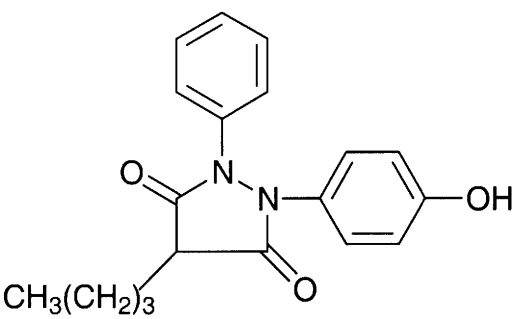
O63 oxyphenbutazone



$C_{19}H_{20}N_2O_3$ **Mol. Wt.** 324.38 **CAS Registry No.** 129-20-4

Synonyms 4-butyl-1-(4-hydroxyphenyl)-2-phenyl-3,5-pyrazolidinedione; *p*-hydroxyphenylbutazone; Butapirone; Floghene; Metabolite I; Oxalid; Tanderil

EINECS No. 204-936-2 **RTECS No.** UQ 8400000

Uses Has been used clinically for its analgesic, antipyretic and anti-inflammatory properties.

Physical properties

M. Pt. 95°C (monohydrate crystals), 124-125°C (anhydrous crystals from diethyl ether and petroleum ether)
Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 350 mg kg^{-1} (1,2).
LD_{50} oral hamster, guinea pig 1180, 2720 mg kg^{-1}, respectively (3).
LD_{50} intravenous mouse, rat, rabbit, dog 52-178 mg kg^{-1} (4-7).
LD_{50} intraperitoneal mouse 100 mg kg^{-1} (8).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (9).

Other effects

Other adverse effects (human)

Effects on the blood include fatal agranulocytosis and aplastic anaemia (10-12).

Any other adverse effects

Shown to be porphyrinogenic in animals and in *in vitro* systems (13).
Parenteral albino rat 100 mg kg^{-1} caused gastric ulcers. The protective effect of the stomach mucous was weakened by disrupted levels of hexosamine, fucose and sialic acid (14).

Other comments

Transfer across the human placenta studied (15).
Properties, absorption and metabolism reviewed (16).
Metabolism of phenylbutazone reviewed (17).

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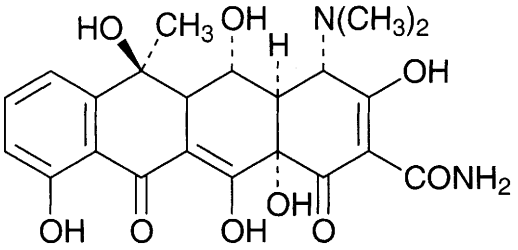
O64 oxytetracycline



$C_{22}H_{24}N_2O_9$ **Mol. Wt.** 460.44 **CAS Registry No.** 79-57-2

Synonyms 2-naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-, [4*S*-(4α,4aα,5α,5aα,6β,12aα)]-; Adamycin; 5-hydroxytetracycline; Liquamycin; Oxymycin; Oxytetracid; terrafungine

EINECS No. 201-212-8 **RTECS No.** QI 7875000

Uses Antibiotic. Treatment for lethal yellowing in palm trees. Superseded in its use against some plant pathogens.
Occurrence From fungus *Streptomyces rimosus*.

Physical properties

M. Pt. 121-122°C (dihydrate)
Solubility Water: solubility dependent on pH. Organic solvents: absolute ethanol, ethanol

Environmental fate

Nitrification inhibition
No inhibition of sewage treatment works (recirculating system) at 50 mg l^{-1} over 26 days (1).

Degradation studies
Microbial pretreatment of pharmaceutical waste water by a mixed culture of bacteria and the yeast *Trichosporon* in semi-aerobic conditions followed by anaerobic incubation reduced the initial concentration 0.60 to ~0.35 g l^{-1} after 40 hr (2).
96% degradation of organic matter in pharmaceutical waste water was achieved in continuous cultivation and adapted activated sludge in the temporary presence of mixed microbial culture (3).
Found in fish-farm bottom deposits at levels capable of causing antimicrobial effects ≤12 wk after application. Estimated $t_{1/2}$, ~10 wk (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 2240, 4800 mg kg^{-1}, respectively (5,6).
LD_{50} intravenous mouse, rat 140, 260 mg kg^{-1}, respectively (5,6).
LD_{Lo} intravenous dog 220 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 5706 mg kg^{-1} (8).
LD_{Lo} intraperitoneal guinea pig 2250 mg kg^{-1} (8).

Carcinogenicity and chronic effects
Oral (2 yr) F344/N rat, B6C3F1 mouse 24,000 or 50,000 ppm and 6300 or 12,500 ppm, respectively (as hydrochloride). Dose-related increased survival was observed for ♂ rats and decreased body weight gain in mice. Focal cellular change and fatty metamorphosis occurred in ♂ rat livers. The incidence of proliferative changes (adenoma, hyperplasia and adenocarcinoma) was not affected by exposure. Non-carcinogenic with possible protective effects against some spontaneous neoplastic and non-neoplastic changes (9).

Metabolism and toxicokinetics

Following a single intravenous dose of 7.5 mg kg^{-1} to sheep and lambs the plasma $t_{1/2}$ in the β-elimination phase were, respectively, 20.32 and 8.91 hr. In sheep, body clearance was 75 ml hr^{-1} kg^{-1} and in lambs, 118 ml hr^{-1} kg^{-1} (10).

Absorption from human gastro-intestinal tract: ~3 hr (11).

Sensitisation

Hypersensitivity reactions including rashes, exfoliative dermatitis, asthma, angiodema, urticaria, epidermal necrolysis and drug fever (12).

Genotoxicity

In vitro mouse lymphoma L5178Y tk^+/tk^- without metabolic activation positive (13).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchange and chromosomal aberrations negative (as hydrochloride) (14).

Pisum sativum germination reduction positive (15).

Other effects

Other adverse effects (human)

Reported side-effects include vomiting, nausea, diarrhoea and increased intracranial pressure with visual disturbance, headache and papilloedema. A bulging fontanelle may occur in infants. Renal disease patients may show further renal impairment. Severe and occasionally fatal hepatotoxicity involving fatty changes in the liver and pancreatitis has been reported. Abnormal pigmentation of the skin and eye, myopia, haemolytic anaemia, thrombocytopenia, hypoprothrombinaemia and reduced serum-vitamin B concentrations occasionally occur (12).

Any other adverse effects

Occlusive effects were observed following instillation into the fallopian tubes and spermatic ducts of rats (16). Depresses enzyme activity in rabbit skeletal muscles. Oral administration caused a greater effect than parenteral administration. Lactate dehydrogenase, glycerolphosphate dehydrogenase and NADH diaphorase activities were reduced more than that of NADPH diaphorase in the triceps brachi. All these activities were more depressed than that of succinate dehydrogenase in the quadriceps femoris. Enzyme activity decrease was greater in larger diameter fibre than small ones (17).

Other comments

Bioavailability in man studied (18).

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O65 ozone

O_3

O_3 **Mol. Wt.** 48.00 **CAS Registry No.** 10028-15-6

Synonyms triatomic oxygen

EINECS No. 233-069-2 **RTECS No.** RS 8225000

Uses Air and water disinfectant. Bleaching textiles, waxes and oils. In organic synthesis.

Occurrence In atmosphere (about 0.05 ppm at sea level).

Physical properties

M. Pt. -193°C **B. Pt.** -111.9°C **Specific gravity** 2.144 g l^{-1} at 0°C and 760mmHg; 1.614 g ml^{-1} at -195.4°C

Solubility *Water:* 49 cm^3 100 cm^{-3} at 0°C. *Organic solvents:* oils (unspecified)

Occupational exposure

FR-VME 0.1 ppm (0.2 mg m^{-3}) **FR-VLE** 0.2 ppm (0.4 mg m^{-3})

JP-OEL 0.1 ppm (0.20 mg m^{-3})

SE-LEVL 0.1 ppm (0.2 mg m^{-3}) **SE-CEIL** 0.3 ppm (0.6 mg m^{-3})

UK-STEL 0.2 ppm (0.40 mg m^{-3})

US-TWA 0.05 ppm (heavy work); 0.08 ppm (moderate work); 0.1 ppm (light work)

Risk phrases Very toxic by inhalation (R26)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 9.3 μg l^{-1} (1).

LC_{50} (24 hr) bluegill sunfish 0.06 mg l^{-1} (2).

LC_{50} (24 hr) yellow perch embryo 0.21 mg l^{-1} (3).

LC_{50} rainbow trout embryo 0.19-0.31 mg l^{-1} (3).

Invertebrate toxicity

Mycobacterium kansasii, Escherichia coli and *Tetrahymena pyriformis* were subjected to 0.5-2 min aeration with 1 mg O_3 l^{-1}. Specific changes in phospholipid content occurred only at 30 sec ozonisation. Longer periods of ozonisation did not cause further changes in phospholipid content. Superoxide dismutase had a protective role (4).

On exposure *Euglena gracilis* suffered damage to the plasma membrane. Disruption to vitamin B_{12} and acetate uptake was seen within 15 min of treatment. Leakage of potassium was detected after 30 min of treatment. Recovery times were within 5 hr for vitamin B_{12} and potassium uptake and 20 hr for acetate uptake (5).

Inactivation of the cytosolic enzymes of *Saccharomyces cerevisiae* occurred following treatment in suspension. Of those enzymes studied, glyceraldehyde-3-phosphate dehydrogenase exhibited the greatest inactivation. Often affected to lesser extents were: NAD-glutamate dehydrogenase, 6-phosphofructokinase, NAD-alcohol dehydrogenase, and pyruvate decarboxylase activities. Levels of nucleoside triphosphates including ATP, were reduced to ~50% of the pre-treatment amounts. ATP lost from the cells appeared in the medium along with NAD and protein, suggesting that the cells had been permeabilised (6).

Toxicity to other species

Birch saplings (*Betula pendula*) exposed to high drought stress under controlled chamber conditions were more resistant to 130 ppb ozone than well and moderately watered plants. Under field conditions, however, low drought stress increased the negative effects of slightly elevated ozone levels (7).

Ivy plants exposed to chronic (60 ppb, 30 days, 5 hr day^{-1}) and acute (200 ppb, 5 hr) ozone levels suffered a decrease in photosynthetic pigments and an alteration in the fatty acid composition of the cuticle. Glyoxalase I and II activity increased significantly following acute treatment. An increase in diffusion resistance and a reduction of CO_2 assimilatory activity was observed in both old and recently expanded leaves (8).

Two-year-old Norway spruce [*Picea abies* L. Karst.] exposed to 1.5 × ambient ozone in open-top chambers for 1 yr suffered statistically significant ozone-induced changes in ultrastructure only in the chloroplasts. The stroma were granulated and granules were about 1.5 × the size of the chloroplast ribosomes (9).

Young cloned Norway spruce (*Picea abies*) trees exposed to 25 and 50 ppb ozone in open-top chambers for 3 months suffered a dose-dependent increase in chromosomal aberrations in root tip meristems which were still present after one year (10).

Damage caused by ozone to native plant species in the sub-Alpine region of southern Switzerland was investigated during 1993-1996. Black cherry was very sensitive to ozone at higher elevation plots and suffered adaxial foliar stipple and leaf reddening. Of the species tested so far, *Viburnum lantana*, *Morus nigra*, *Betula pendula*, *Rumex acetosa*, and *Prunus serotina* appear to be the most sensitive to ozone damage (11).

Dry weight of rice plants exposed to 0.10 ppm was reduced by 50% at 5 and 6 wk (administered from vegetative to early heading stages). Root/shoot ratio and nitrogen uptake rate were modified under long-term exposure (12).

Wild plants were exposed to levels in a daily pattern mimicking atmospheric occurrence in southwest Germany. Yield was generally reduced, particularly in the roots. No resistance was seen in plants selected from sites of higher burden (13).

Mammalian & avian toxicity

Acute data

LC_{50} (3 hr) inhalation rabbit 36 ppm (14).

LC_{50} (4 hr) inhalation rat 4800 ppm (15).

LC_{50} (3 hr) inhalation mouse, guinea pig, cat 12,600-34,500 ppb (14,16,17).

LC_{50} (4 hr) inhalation hamster 10,500 ppb (15).

TC_{Lo} (3 hr) human 0.2 ppm (18).

Intrapleural or intra-arterial (135 min) rat 0.12, 0.25, 0.50 or 1.00 ppm caused increased frequency of breathing and tidal volume decrease as a function of both concentration and exposure duration. Cardiopulmonary measures and breathing mechanics were only marginally affected (19).

Inhalation (3 hr) rat 1 ppm caused heart rate and mean arterial blood pressure to decrease. Effects were more marked in 11-wk-old rats than those aged 4 or 8 wk. There were no sex-related differences in the responses (20).

Rat exposed to 0.4 ppm (3, 6 or 12 hr) showed ~15% decrease in Fc-receptor-mediated phagocytosis by alveolar macrophages. Recovery above control levels occurred within 12 hr of exposure. In mice alveolar macrophage function change was not seen until 12 hr of exposure (21).

Sub-acute and sub-chronic data

Rats exposed to 0.4 ppm 12 hr day^{-1} for 3 or 7 days did not show altered alveolar functions, with the exception of reduced superoxide production at 3 days of exposure. Mice given repeat treatments did not exhibit any further decrease in phagocytosis over the single dose, however superoxide production by alveolar macrophages was inhibited by ~50%.

In both rats and mice alveolar macrophage number increased (21).

Inhalation (1, 3, 13, 52 or 78 wk) rat at 0.06-0.25 ppm to mimic exposure patterns in high-pollution summer environments for 5 day wk^{-1}. Natural killer cell activity of spleen cells, T-cell mitogen responses of spleen cells and histopathology of spleen, femur, thymus and mandibular, mediastinal and peribronchial lymph nodes were unaffected (22).

BALB/c mice (1, 3, 7 or 14 day) continuously exposed to 0.8 ppm exhibited delayed hypersensitivity reaction to sheep red blood cells. Lymphocyte numbers were reduced in both thymus and blood. The percentage of T- and B-lymphocytes in blood was the same as in the controls (23).

Carcinogenicity and chronic effects

The National Toxicology Program tested rats and mice via inhalation. No evidence of carcinogenicity in ♂ and ♀ rats and ♂ mice, some evidence of carcinogenicity in ♀ mice (24).

Teratogenicity and reproductive effects

Inhalation ♀ mouse (days 7-17 of pregnancy) 0-1.2 ppm. No increase in stillbirths or neonatal mortality were observed, however postnatal bodyweight was significantly depressed in the 1.2 ppm offspring (25).

Metabolism and toxicokinetics

Predicted lower respiratory tract uptake during exercise in human ranges from 87 to 93% compared with 84-88% for quiet breathing. The total quantity absorbed per minute increases with age. The largest tissue dose was predicted to occur in the centriacinar region, where often studies have shown maximal morphological damage (26).

Sensitisation

May have a role in causing asthmatic attacks rather than enhancing allergic sensitisation in guinea pigs sensitised with ovalbumin (27).

Increased ambient air concentration significantly raised the frequency of asthma attacks amongst city dwellers (28).

Genotoxicity

Salmonella typhimurium TA100, TA102, TA104 with and without metabolic activation negative (in non-toxic dose range) (29).

Escherichia coli B DNA single- and double-strand breaks in wild type and the mutant MQ1844 (*ozr*B). Another type of DNA damage repaired only by the *ozr*B gene product may be responsible for the killing effect (30).

Guinea pigs exposed for 2 h to 0, 0.4, or 1 ppm ozone showed a concentration-dependent increase in DNA single-strand breaks in lung cells, which was reflected by an increased DNA length after single-cell gel electrophoresis.

In human subjects exposed without exercise to 0.4 ppm ozone for 1-2 hr, the bronchoalveolar lavage and bronchial epithelial cells showed no change in DNA single-strand breaks compared with controls. When the subjects exercised, there was an increase in single-strand breaks in epithelial cells from those receiving a placebo pretreatment (rather than steroids) compared with the non-exercising results (31).

Other effects

Other adverse effects (human)

Lung function was impaired in young adults following exposure (2 hr) to 0.15 ppm with intermittent light exercise. Smokers were affected more than non-smokers (32).

Exercising men suffered mild subjective respiratory irritation at 0.12-0.14 ppm. 0.20-0.30 ppm had no adverse effects on patients with chronic heart or lung disease (33).

In vitro (24 hr) human alveolar macrophage 0.1-1.0 ppm. There was a minimal effect on protein expression or synthesis, but responses to particulate immune complexes and to bacterial lipopolysaccharide were impaired. PGE_2 and arachidonic acid were released, suggesting the cell membrane was damaged. Susceptibility to infections agents may be increased in the longer term (34).

Any other adverse effects

1.0-2.0 ppm decreased survival time of influenza-infected rats and mice and suppressed the capacity of lung macrophages to destroy *Listeria* (33).

Erythrocytes (species unspecified) exposed showed lesions in the proteins of the plasma membrane. Secondary oxidants were as damaging as ozone. Toxic effect consists of oxidative inactivation of membrane-bound enzymes and membrane-structure disturbance (35).

Airway hyper-responsiveness in guinea pigs was closely related to dose (36).

A single exposure to ozone (3ppm, 3hr) inhibited the increase in airway responsiveness but increased the bronchoconstrictor response induced by trimellitic anhydride (TMA) in TMA-sensitised guinea pigs. The inflammatory airway response to TMA was unchanged by pre-exposure to ozone (37).

Legislation

Swedish threshold limit value in working environment, 0.1 ppm (29).

Other comments

Ozone is probably the most important regional air pollutant affecting forest trees at the present time. It is, however, difficult to extrapolate results from experiments on seedlings, exposed to controlled concentrations of ozone, to large forest trees. These issues of scaling tree size and age responses to ozone are reviewed (38).

Mouse lung carcinogenesis reviewed (39).
Contamination of aircraft cabins and toxicity reviewed (33).
Health effects including carcinogenesis reviewed (40-44).
Reviews on experimental toxicology, epidemiology, human health effects, ecotoxicology (limited), environmental effects and workplace experience listed (45).

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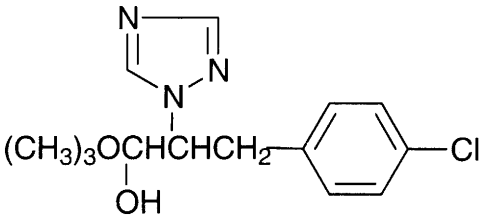
P1 paclobutrazol



$C_{15}H_{20}ClN_3O$ **Mol. Wt.** 293.80 **CAS Registry No.** 76738-62-0

Synonyms (*R**,*R**)-(±)-β-[(4-chlorophenyl)methyl]-α-(1,1-dimethylethyl)- 1*H*-1,2,4-triazole-1-ethanol; ICI-PP 333; PP 333

RTECS No. XZ 4803300

Uses Plant growth regulator with fungicidal activity.

Physical properties

M. Pt. 165-166°C **Specific gravity** 1.22 **Partition coefficient** log P_{ow} 3.201 (1)
Volatility v.p. 7.52×10^{-9} mmHg at 20°C
Solubility Water: 26 mg l^{-1} at 20°C. Organic solvents: acetone, cyclohexanone, *n*-hexane, methanol, methylene dichloride, propylene glycol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 27.8 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* sp. 33.2 mg l^{-1} (1).
NOEL oral honeybee >0.002 mg bee^{-1} (1).
NOEL contact honeybee >0.040 mg bee^{-1} (1).

Environmental fate

Degradation studies
Soil $t_{1/2}$ 0.5-1.0 yr. $t_{1/2}$ in calcareous clay loam, pH 8.8, 14% organic matter <42 days. $t_{1/2}$ in coarse sandy loam, pH 6.8, 4% organic matter >140 days (1).

Abiotic removal
At pH 4, 7 and 9 stable to hydrolysis. Not degraded in 10 days at pH 7 by UV light (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard >7900 mg kg^{-1} (1).
LD_{50} oral ♀, ♂ rat 1300, 2000 mg kg^{-1}, respectively (1).
LD_{50} oral ♂, ♀ mouse 490, 1200 mg kg^{-1}, respectively (1).
LD_{50} oral ♂, ♀ rabbit 840, 940 mg kg^{-1}, respectively (1).
LD_{50} o ral guinea pig 400, 600 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation ♀, ♂ rat 3.13, 4.79 mg l^{-1} air, respectively (1).
LD_{50} dermal rat, rabbit >1000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
NOEL (1 yr) oral dog 75 mg kg^{-1} day^{-1} in die t (1).

Carcinogenicity and chronic effects
NOEL (2 yr) oral rat 250 mg kg^{-1} day^{-1} in diet (1).

Irritancy
Dermal rabbit, the wettable powder formulation is a mild irritant and moderate irritant to 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).
EPA Toxicity Class IV (formulation) (1).
FAO/WHO meeting on Pesticide Residues: ADI 0.1 mg kg^{-1} body weight (1).

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P2 palladium chloride

$$PdCl_2$$

Cl_2Pd **Mol. Wt.** 177.33 **CAS Registry No.** 7647-10-1

Synonyms dichloropalladium; palladium dichloride; palladium(II) chloride; palladous chloride

EINECS No. 231-596-2 **RTECS No.** RT 3500000

Uses In photography. Toning solutions. In manufacture of indelible ink. Electroplating clocks. In detection of carbon monoxide gas leaks. Reagent in organic syntheses.

Physical properties

M. Pt. 678-680°C (decomp.) **Specific gravity** 4.00 at 18°C
Solubility Water: soluble. Organic solvents: acetone, (dihydrate) ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2700 mg kg^{-1} (1).
LD_{50} intratracheal rat 6 mg kg^{-1} (2).
LD_{50} intravenous rat 3 mg kg^{-1} (2).
LD_{Lo} intravenous rabbit 18.6 mg kg^{-1} (3).
LD_{50} intraperitoneal rat, mouse 70, 174 mg kg^{-1} respectively (2,3).

Metabolism and toxicokinetics
Following intravenous injection to rabbit, palladium was found in the bone marrow, lungs, spleen, kidneys and muscle (4).
Following oral administration of $^{103}PdCl_2$ to rats, it was excreted almost entirely in faeces. Whole-body retention was <0.5%. Following intravenous administration excretion was via urine and faeces. At 24 hr, kidneys and liver

contained just detectable levels of ^{103}Pd following oral administration, but ^{103}Pd was detected in all tissues examined when given by intravenous route. After 104 days ^{103}Pd was still detectable in all tissues examined in the intravenously dosed animals, with highest levels in the kidney, spleen, liver, lung and bone. In intratracheally administered animals, levels were highest in the lung followed by kidney, spleen, bone and liver (2,5).
Does not readily cross the placental barrier (5).

Irritancy
In patch testing of 95 subjects, 15 showed irritant reaction with either erythema or erythema and oedema (6).

Other effects

Any other adverse effects
ID_{50} (72 hr) mouse 3T3-L1 fibroblast-like cells 103 mg l^{-1} (7).
Intravenous injection to rabbit at 0.6 mg kg^{-1} was lethal, with damage to the heart. Albuminuria and haemolysis were induced. Tissue damage occurred in the liver, kidneys and bone marrow (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides: guide level 25 mg l^{-1} (8).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

Reviews on experimental toxicology, epidemiology and human health effects listed (10).

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P3 papain

CAS Registry No. 9001-73-4

Synonyms Arbuz; C 400; E.C. 3.4.4.10; E.C. 3.4.22.2; papainase; Papayotin; Summetrin; Velardon; vegetable pepsin

EINECS No. 232-627-2 **RTECS No.** RU 4950000

Uses Tenderiser of meat. For bating skins. For clearing beverages. Proteolytic enzyme. Digestive aid. Debriding agent. Anthelmintic. For the removal of protein deposits from soft contact lenses.
Occurrence Proteolytic enzyme in latex of *Carica papaya*.

Physical properties

Solubility Water: incompletely soluble in water. Organic solvents: glycerol

Occupational exposure

Supply classification harmful

Risk phrases Irritating to eyes, respiratory system and skin – May cause sensitisation by inhalation (R36/37/38, R42)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – Avoid contact with the skin – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing and gloves (S2, S22, S24, S26, S36/37)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 12500 mg kg^{-1} (1).

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

Sensitisation

Hypersensitivity reactions have occurred in humans (3).

Genotoxicity

Bacillus DNA repair test (metabolic activation unspecified) negative (4).

Other effects

Other adverse effects (human)

Destruction, with perforation of the oesophageal wall occurred in a woman given 1.2 g over 12 hr to treat an obstruction caused by impacted meat. Days later she died from haemorrhage when descending thoracic aorta ruptured (5).

Ocular and periorbital angioedema occurred within 4 hr following use of papain-containing contact lens cleansing solution (6).

Other comments

Toxicity reviewed (7).

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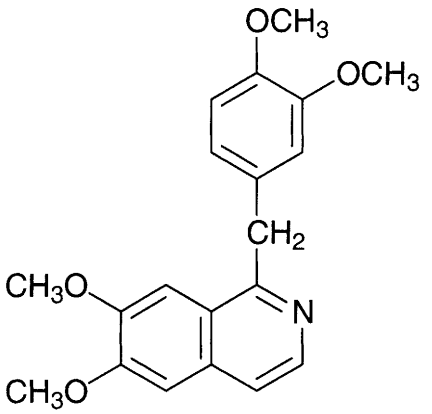
P4 papaverine



$C_{20}H_{21}NO_4$ **Mol. Wt.** 339.39 **CAS Registry No.** 58-74-2

Synonyms 1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxyisoquinoline; 6,7-dimethoxy-1-veratrylisoquinoline; papaverin

EINECS No. 200-397-2 **RTECS No.** NW 8450000

Uses Smooth muscle relaxant. Cerebral vasodilator.
Occurrence An alkaloid present in opium (0.8-1.0%).

Physical properties

M. Pt. 147°C **B. Pt.** 135-140°C at 11 mmHg (decomp., sublimes) pressure and 2 mm distance.
Specific gravity 1.337 at 20°C with respect to water at 4°C
Solubility Organic solvents: hot benzene, glacial acetic acid, acetone, carbon tetrachloride, chloroform, petroleum ether

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

Toxicity to other species
LD_{Lo} subcutaneous frog 140 mg kg^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} subcutaneous pigeon 150 mg kg^{-1} (2).
LD_{50} oral mouse, rat 230, 325 mg kg^{-1}, respectively (3,4).
LD_{Lo} oral rabbit 190 mg kg^{-1} (1).
LD_{50} intravenous rat, mouse, rabbit 18, 25, 25 mg kg^{-1}, respectively (4,5).
LD_{50} subcutaneous rat, mouse 151, 280 mg kg^{-1}, respectively (4).
LD_{Lo} subcutaneous dog, cat, 120 mg kg^{-1} (1,2).
LD_{50} intraperitoneal rat, mouse 64, 117 mg kg^{-1}, respectively (6,7).
LD_{50} intramuscular mouse 175 mg kg^{-1} (8).
LD_{50} intradermal mouse 150 mg kg^{-1} (5).

Teratogenicity and reproductive effects

In vitro neurulating embryos (species unspecified) exhibited altered neural tube development (9).

Metabolism and toxicokinetics

Following intravenous administration of 80 mg to humans the calculated $t_{1/2}$ ranged from 1.2 to 6.6 hr (mean 3.0 hr). Bioavailability was highly variable, but reproducible within the same individual. Mean total plasma clearance was 836 ml min^{-1}. Oral administration (80 mg) showed unacceptable interindividual variation in bioavailability (10).

Biological $t_{1/2}$ when given by mouth to human is between 1 and 2 hr. It is bound (~90%) to plasma proteins. Metabolism takes place in the liver and excretion, as glucuronide-conjugated phenolic metabolites, is via the urine (11).

Other effects

Any other adverse effects

Increased the total and regional coronary blood flow in dogs with cardiac catheterisation. Adverse side-effects were changes in ECG, contractility, creatine phosphate tissue levels and lactate serum levels (12).

Other comments

Usually administered as the hydrochloride (11).

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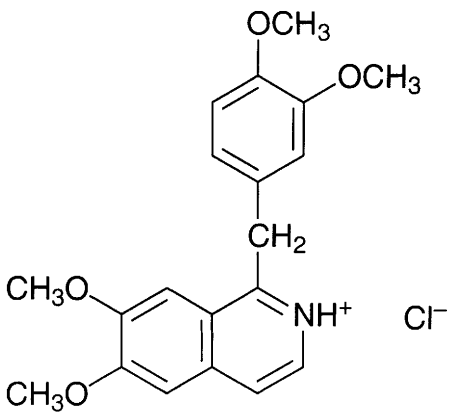
P5 papaverine hydrochloride



$C_{20}H_{22}ClNO_4$ **Mol. Wt.** 375.85 **CAS Registry No.** 61-25-6

Synonyms 1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxyisoquinoline hydrochloride; 6,7-dimethoxy-1-veratrylisoquinoline hydrochloride; papaverine chlorhydrate; Cardiospan; Cerespan; Myobid; Papavorsan; Paperon; Ro-Papav; Vasal

EINECS No. 200-502-1 **RTECS No.** NW 8575000

Uses Smooth muscle relaxant. Cerebral vasodilator.

Physical properties

M. Pt. 220-225°C

Solubility Water: 25 g l^{-1}. Organic solvents: chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 130, 360 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal rat 64 mg kg^{-1} (3).
LD_{50} intraduodenal rat 71 mg kg^{-1} (4).
LD_{50} intravenous rat, mouse 20, 27.5 mg kg^{-1}, respectively (5).
LD_{50} subcutaneous mouse, rat 150, 370 mg kg^{-1}, respectively (5).
LD_{50} intraperitoneal mouse 108 mg kg^{-1} (6).

Metabolism and toxicokinetics

Absolute bioavailability by peroral, rectal, vaginal, dermal and buccal administration was 57.2, 25.2, 53.2, 3.2 and 7.5%, respectively, in beagles (7).

Sensitisation

In humans, eosinophilia, altered liver function and jaundice sometimes occur due to hypersensitivity (8).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation negative; TA100 with metabolic activation weakly positive, without negative (9).

Other effects

Other adverse effects (human)

When taken by mouth side effects include malaise, headache, skin rash, sweating, gastro-intestinal disturbance and dizziness. High doses administered parenterally may cause cardiac arrhythmias (8).

When administered intravenously, in the treatment of impotence, dizziness, syncope and abnormal liver function test results occasionally occurred (10,11).

Priapism is the worst acute adverse effect (10-12).

Any other adverse effects

When administered to *in vitro* liver cells (species unspecified), leakage of lactate dehydrogenase increased in a concentration- and time-dependent manner with significant effects occurring after the 8-hr exposure period. GSH also decreased. Lipid peroxidation was not seen. The study concluded that hepatotoxicity may be related to disruption of energy homeostasis and to alterations in the glutathione balance of the cells (13).

Other comments

Physical properties and pharmacokinetics reviewed (14).

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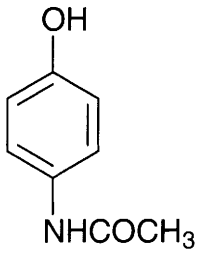
P6 paracetamol



$C_8H_9NO_2$ **Mol. Wt.** 151.16 **CAS Registry No.** 103-90-2

Synonyms *N*-(4-hydroxyphenyl)acetamide; *p*-acetamidophenol; *N*-acetyl-*p*-aminophenol; 4-hydroxyacetanilide; acetaminophen

EINECS No. 203-157-5 **RTECS No.** AE 4200000

Uses Analgesic and antipyretic. In the manufacture of azodyestuffs and photographic chemicals.

Physical properties

M. Pt. 167-169°C

Solubility Organic solvents: acetone, ethanol, ethyl acetate, methanol

Occupational exposure

UK-LTEL 10 mg m^{-3} (total inhalable dust)

Ecotoxicity

Invertebrate toxicity

IC_{50} *Saccharomyces cerevisiae* 92 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2400 mg kg^{-1} (1,2).

LD_{50} oral mouse 338 mg kg^{-1} (1).

LD_{Lo} (unspecified exposure) oral human 150-800 mg kg^{-1} central nervous system, gastro-intestinal tract, and liver effects (3-5).

A single oral dose was administered to fasted adult ♂ mice, which were subsequently sacrificed 30 min to 48 hr after treatment. Damage to liver, kidney, necrosis of bronchiolar epithelium, lymphoid necrosis and testicular changes were observed. Spermatid degeneration with early development of spermatid multinucleated giant cells was a characteristic feature (6).

Sub-acute and sub-chronic data

Single or multiple intraperitoneal doses of 300-1000 mg kg^{-1} with pretreatment (cytochrome P-448 inducer) in C57BL/6 and DBA/2 mice and 500-1500 mg kg^{-1} with pretreatment (cytochrome P-450 inducer) in New Zealand white and chinchilla rabbits showed that susceptibility to acetaminophen cataractogenesis can be genetically predetermined and may involve enzymic bioactivation, possibly independent of hepatic biotransformation and toxicity (7).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, IARC classification group 3 (8).

National Toxicology Program tested mice and rats via dosed-feed. No evidence of carcinogenicity was found for ♂ and ♀ mice and ♂ rats. Equivocal evidence of carcinogenicity was found with ♀ rats (9).

Target organs of carcinogenicity: rat urinary bladder/urethra (10).
Promoted kidney tumour development in rats (11).
Acetaminophen, 1000 or 5000 ppm for 40 wk, produced transient chronic hepatic hyperplasia without evidence of carcinogenicity in B6C3F1 (6 wk old) mice (12).
Did not reveal tumour initiating potential in rats with preexisting fatty liver induced by a choline-deficient diet (13).
Administration of 1.1% or 1.25%, respectively, to B6C3F1 and NIH mice for 41 wk caused severe liver injury characterised by centrilobular necrosis. The results are discussed in terms of their importance to the interpretation of carcinogenicity studies (14).

Teratogenicity and reproductive effects

Low birth-rate, foetal hepatoxicity and neonatal death occurred when ♀ mice (16-19 days pregnant) were administered 42-84 mg kg^{-1} acetaminophen simultaneously with a fatty diet (15).
Acetaminophen administered orally at 14 mg kg^{-1} to near term rats resulted in constriction of the foetal ductum (16).
Addition of acetaminophen to rat embryos in culture produced an increased incidence of morphologically abnormal anterior neuropores. The data suggest that the visceral yolk sac plays a vital role in the metabolic transformation of acetaminophen to catechol and quinone-imine reactive metabolites (17).
Acetaminophen inhibited Na^+, K^+ and Mg^{2+}-ATPase activities *in vitro* in human foetal cerebrum and cerebellum in a dose-dependent manner (18).
Assigned a negative developmental toxicity potential using a toxicity assessment software package (TOPKAT) (19).

Metabolism and toxicokinetics

Metabolised in the liver via two routes, one pathway leads to the formation of *N*-acetyl-*p*-benzoquinone imine (NAPQI) mediated by cytochrome P-450, the other detoxification pathway leads to the formation of glucuronide, sulfate and glutathione conjugates which are excreted in the urine, $t_{1/2}$ 1-4 hr (20,21).
The toxic pathway metabolites predominate in the bile, whereas non-toxic metabolites are excreted in the urine (22).
Passes rapidly into the breast milk of nursing mothers. Acetaminophen and its glucuronide, sulfate, cysteine and mercapturate conjugates were found in the urine of neonates (23).
Following a single intravenous dose of 50 mg kg^{-1} to pregnant guinea pigs (60-65 days gestation), the major detoxification metabolites in the plasma and urine of dams were in the form of gluconurides; the sulfate metabolites predominated in the foetal and neonatal animals (24).
Acetaminophen clearance in healthy human female volunteers was unaffected by chronic conjugated oestrogen treatment (25).
The analgesic effect of acetaminophen was directly related to the circulating level of the compound (26).

Irritancy

Skin rashes have been reported (27).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA102, TA1535, TA1537 with pyrazole-induced metabolic activation negative, TA1535, TA1537 with ethanol-induced metabolic activation negative (28).
In vivo-in vitro replicative DNA synthesis test using rat hepatocytes positive (29).
In vitro testing, acetaminophen was cytotoxic to Chinese hamster ovary V79 cells, inhibited DNA synthesis and increased sister chromatid exchanges (30,31).
Effects on hydroxyurea-resistant mouse mammary tumour cell line (TA3H2) showed that acetaminophen reduced DNA synthesis by inhibiting ribonucleotide reductase activity. In wild-type cells acetaminophen produced a concentration-dependent induction of chromosomal aberrations and sister chromatid exchanges (32).
In *in vivo* testing in the mouse micronucleus test, an increased occurrence of micronuclei in polychromatic bone marrow erythrocytes was seen (33).
In human volunteers, following the oral administration of acetaminophen (1000 mg × 3 doses during 8 hr), blood and buccal mucosal cell samples were taken at time 0, 24, 72 and 168 hr after the first dose. Treatment reduced the level of unscheduled DNA synthesis in 1-methyl-3-nitro-1-nitrosoguanidine-treated lymphocytes and increased the frequency of micronucleated cells in the buccal mucosa at 72 hr (34).
In ouabain-resistant mouse embryo cells (3H10T1/2 clone 8), acetaminophen produced negative mutation, positive induction of non-neoplastic cells and morphological transformation (35).

Other effects

Any other adverse effects

Side-effects of acetaminophen include skin rashes, pancreatitis, thrombocytopenia, leucopenia, pancytopenia, neutropenia and agranulocytosis. Symptoms of overdosage in the first 24 hr are pallor, nausea, vomiting, anorexia and abdominal pain; liver damage may become apparent after 12-48 hr. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death (species unspecified) (20).

Other comments

The pharmacokinetics, toxicity and clinical side-effects, including allergic and skin reactions, of acetaminophen have been extensively reviewed (36-43).

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P7 paraffin wax

CAS Registry No. 8002-74-2

Synonyms hydrocarbon wax; Ceratak; Gatch; hard paraffin; Slopvox

EINECS No. 232-315-6 **RTECS No.** RB 0350000

Uses Stiffening ingredient in ointment bases. In paraffin-wax baths for the relief of pain.
Occurrence Distilled from petroleum or from shale oil.

Physical properties

M. Pt. 50-57°C **Flash point** 199°C **Specific gravity** 0.90
Solubility Organic solvents: benzene, carbon disulfide, chloroform, diethyl ether, oils; miscible when melted with spermaceti and fats

Occupational exposure

FR-VME 2 mg m^{-3} (fume)
UK-LTEL 2 mg m^{-3} (fume) **UK-STEL** 6 mg m^{-3} (fume)
US-TWA 2 mg m^{-3} (fume)

Mammalian & avian toxicity

Irritancy
As fumes, a mild human eye, nose and throat irritant (1).

Other effects

Other adverse effects (human)
When injected may produce granulomatous reactions (2).

Other comments

Reviews on experimental toxicology, human health effects and workplace experience listed (3).

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P8 paraformaldehyde

$(HCHO)_n$

$(CH_2O)_n$

CAS Registry No. 30525-89-4

Synonyms Aldacide; Flo-Mor; Paraform

RTECS No. RV 0540000

Uses Disinfectant, fumigant, antiseptic. In treatment of minor throat infections. Active ingredient of contraceptive creams. In dentistry. In the manufacture of synthetic horn, ivory and resins. Drilling fluid additive.

Physical properties

M. Pt. 163-165°C (decomp.) **Flash point** 71°C (closed cup)

Occupational exposure

UN No. 2213 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid

Ecotoxicity

Invertebrate toxicity

LC_{50} (96 hr) *Mysidopsis bahia* 31 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

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

LD_{Lo} dermal rabbit 1 g kg^{-1} (3).

Carcinogenicity and chronic effects

Carcinogenicity in inhalation rat under investigation by Chemical Industry Institute of Toxicology, Research Triangle Park, NC (4).

Irritancy

Dermal rabbit (24 hr) 500 mg and 100 mg instilled into rabbit eye caused severe irritation (3).

Vapour is irritant to human eyes, nose and upper respiratory tract and may cause oedema of the larynx, coughing and dysphagia (5).

Sensitisation

Allergic and other reactions reported when used as a root canal sealant in dentistry (5).

Type I allergic response occurred in a man given a root canal paste containing the compound. The subject had a history of atopy and a previous allergic response to topical formaldehyde (6).

Genotoxicity

In vitro human lymphocyte sister chromatid exchange induction low below 5 μg ml^{-1} (7).

Other effects

Other adverse effects (human)

When included in endodontic filling material has been associated with nerve damage (8,9).

Ingestion may cause vomiting, vertigo, convulsions, bloody diarrhoea, convulsions, loss of consciousness, circulatory failure and death. Vapour can cause pneumonia, bronchitis and pulmonary oedema (5).

Other comments

Laboratory activated sludge and septic tank treatment units withstood loading to 25% of the recommended dose without loss of efficiency. Higher doses caused a temporary reduction in COD removal (10).
Autoignition temperature, 300°C

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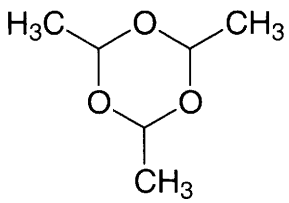
P9 paraldehyde



$C_6H_{12}O_3$ **Mol. Wt.** 132.16 **CAS Registry No.** 123-63-7

Synonyms 2,4,6-trimethyl-1,3,5-trioxane; 2,4,6-trimethyl-*s*-trioxane; elaldehyde; paraacetaldehyde; paracetaldehyde; Paral; PCHO

EINECS No. 204-639-8 **RTECS No.** YK 0525000

Uses Sedative and hypnotic drug. In the manufacture of organic compounds. Solvent.

Physical properties

M. Pt. 12°C **B. Pt.** ~124°C **Flash point** 17°C (closed cup) **Specific gravity** 0.994 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 0.59/0.95 (calc.) (1) **Volatility** v.p. 25.3 mmHg at 20°C ; v.den. 4.5 **Solubility** Water: 1 in 8 at 25°C. Organic solvents: chloroform, diethyl ether, miscible with ethanol

Occupational exposure

UN No. 1264 **HAZCHEM Code** 2[redacted] **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 empty into drains – Take precautionary measures against static discharges (S2, S9, S16, S29, S33)

Ecotoxicity

Bioaccumulation

Confirmed to be non-accumulative or low accumulative (2).

Environmental fate

Abiotic removal

There was a 73.9% reduction following wastewater treatment. Activated carbon adsorbability 0.148 g g^{-1} C (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >100 mg kg^{-1} (4).
LD_{50} oral rat 1.65 g kg^{-1} (5).
LD_{50} oral rabbit 3304 mg kg^{-1} (6).
LD_{Lo} oral cat 3300 mg kg^{-1} (7).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (8).
LD_{50} dermal rabbit 14 g kg^{-1} (8).
LD_{Lo} intraperitoneal rat 2100 mg kg^{-1} (9).
LD_{Lo} subcutaneous rat 1650 mg kg^{-1} (10).

Carcinogenicity and chronic effects

Negative in mouse tumour-initiation bioassay (11).

Metabolism and toxicokinetics

Readily absorbed in man, particularly when administered by oral and intramuscular routes. $t_{1/2}$, 4-10 hr. Widely distributed. Metabolism, probably to acetaldehyde, in the liver accounts for 80% of the dose. Aldehyde dehydrogenase oxidises the acetaldehyde to acetic acid. Unmetabolised drug is excreted through the lungs; little appears in the urine. Passes the placental barrier (12).

Irritancy

Dermal rabbit (duration unspecified) open to atmosphere 500 mg caused well defined erythema and slight oedema and 5 mg instilled into rabbit eye (duration unspecified) caused severe irritation (8).
May cause skin rashes (12).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (13).

Other effects

Other adverse effects (human)

LD_{Lo} (route unspecified) 1462 mg kg^{-1} (14).
Oral and rectal administration may cause gastric or rectal irritation. Intramuscular administration is painful and nerve damage, sterile abscesses and tissue necrosis may occur. Intravenous administration may cause pulmonary oedema and haemorrhage, cardiac dilatation, hypotension and circulatory collapse. Overdose leads to hepatic, renal and lung damage, respiratory depression and coma. Prolonged use may lead to dependence (12).
Analgesic, sedative and hypnotic effects and possible hallucination and headache are induced by low doses (15).
Chronic effects include muscular weakness, fatigue and digestive disturbances (16).

Legislation

A controlled substance (depressant) listed in the US Code of Federal Regulations (17).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Pollutant of drinking water in areas irrigated with sewage water (19).

Decomposes on storage and deaths from corrosive poisoning have occurred following the use of old stock (12).
Hazards reviewed (20).
Reviews on experimental toxicology, human health effects and physico-chemical properties listed (21).
May be habit forming.
Autoignition temperature, 235/238°C

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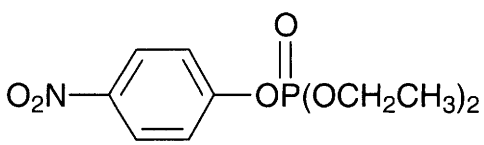
P10 paraoxon



$C_{10}H_{14}NO_6P$ **Mol. Wt.** 275.20 **CAS Registry No.** 311-45-5

Synonyms diethyl *p*-nitrophenyl phosphate; phosphoric acid, diethyl 4-nitrophenyl ester; E600 (pesticide); phosphacol; miotisal; *p*-nitrophenyl diethyl phosphate

EINECS No. 206-221-0 **RTECS No.** TC 2275000

Uses Insecticide.

Occurrence Environmental pollutant and food contaminant. Active metabolite of parathion in many species, including humans.

Physical properties

B. Pt. 169-170°C at 1 mmHg **Specific gravity** 1.2683 at 25°C with respect to water at 4°C
Solubility Water: 2.4 g l^{-1}. Organic solvents: diethyl ether and other organic solvents

Ecotoxicity

Fish toxicity
Cholinesterases in fish are sensitive to paraoxon inhibition, but less so than in mammals (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 760, 1800 μg kg^{-1}, respectively (2,3).
LD_{50} oral chicken 2 mg kg^{-1} (2).
LD_{50} intravenous rat, mouse 240 and 520 μg kg^{-1}, respectively (4,5).
LD_{Lo} intravenous rabbit 100 μg kg^{-1} (6).
LD_{50} subcutaneous rat, rabbit, mouse 230-270 μg kg^{-1} (7,8).
LD_{50} intraperitoneal mouse, rat 330, 930 μg kg^{-1}, respectively (9,10).
LD_{50} intramuscular rat, mouse 446, 710 μg kg^{-1}, respectively (11,12).
LD_{50} intraperitoneal chicken 0.5-1.5 mg kg^{-1} (13).

Metabolism and toxicokinetics
Paraoxon can be metabolised in mammalian liver. Centrilobular hepatocytes in rat have been found to be rich in paraoxonase and paraoxon acetylase (14).

Other effects

Any other adverse effects
The compound is a potent inhibitor of acetylcholinesterase and cholinesterase (true and pseudo-cholinesterase) activities following single or multiple administration. The central, autonomic and voluntary nervous systems are all affected. Signs of parasympathetic over-activity such as salivation and lachrymation can often be seen along with skeletal muscle fasciculation resulting from motor overactivity. Death at toxic doses usually results from respiratory and cardiovascular malfunction (2,13,15,16).
Hypothermia produced by paraoxon may not be mediated by inhibition of cholinesterases (15).
Paraoxon does not induce neurotoxicity nor inhibit neuropathy target esterase (17).
Inhibitor of deacetylases in human and rat hepatocytes at 10^{-4} M (18).
Mammalian-activated *o*-, *m*-, and *p*-phenylenediamine, benzidine, 2,3-diaminophenazine or 2-aminofluorene as well as plant-activated benzidine or 2-aminofluorene expressed an elevated mutgenic potency when assayed with *Salmonella typhimurium* strain YG1024 in the presence of paraoxon (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 4 (Release into Air) and Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (21).

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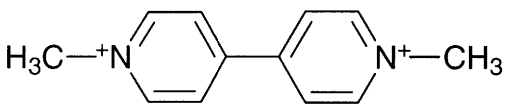
P11 paraquat



$C_{12}H_{14}N_2$ **Mol. Wt.** 186.26 **CAS Registry No.** 4685-14-7

Synonyms 1,1'-dimethyl-4,4'-bipyridinium; dimethyl viologen; methyl viologen(2+); paraquat dication; paraquat ion; Chlorozon; Crisquat; Cyclone; Dinoquat; Efoxon; Forquat; Gałokson; Herboxone

EINECS No. 225-141-7 **RTECS No.** DW 1960000

Uses Herbicide.

Physical properties

M. Pt. >300°C (dichloride) **B. Pt.** 175-180°C **Specific gravity** 1.24 at 20°C with respect to water at 4°C (dichloride) **Partition coefficient** log P_{ow} 2.44 (calc.) (1)
Solubility Water: 700 g l^{-1} at 25°C (dichloride). Organic solvents: ethanol

Occupational exposure

DE-MAK 0.1 mg m^{-3} (total dust) (dichloride)
FR-VME 0.1 mg m^{-3}
US-TWA 0.5 mg m^{-3} (total dust); 0.1 mg m^{-3} (respirable fraction)
Supply classification toxic
Risk phrases Toxic in contact with skin and if swallowed – Irritating to eyes, respiratory system and skin (R24/25, R36/37/38)
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)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) freshwater fish *Cnesterdon decemmaculatus* ♂ 67.40, ♀ 52.48 mg l^{-1} (2).
LC_{50} (48 hr) rainbow trout, brown trout 32, 82 mg (dichloride) l^{-1}, respectively (3-5).
LC_{50} (96 hr) guppy, *Rasbora trilineata* 7, 12 mg l^{-1}, respectively (5).
LC_{50} (duration unspecified) tilapia 31.5 mg l^{-1}. Lipid peroxidation occurred in the gills and liver. 21 mg l^{-1} caused an increase in gill carbonic anhydrase activity (6).

Invertebrate toxicity

LC_{50} (96 hr) *Gammarus lacustris* 11 mg l^{-1} (7).
LC_{50} (48 hr) *Daphnia pulex* 3.7 mg l^{-1} (8).
EC_{50} (96 hr) for growth (μg l^{-1}): *Scenedesmus dimorphus*, 39.8; *Ankistrodesmus falcatus*, 93.3. EC_{50} (96 hr) for dry weight gain (μg l^{-1}): *S. dimorphus*, 73.9; *S. quadricauda*, 132; *A. falcatus*, 114 (9).
A level of 1 mg l^{-1} reduced carbon fixation by phytoplankton by 53% (10).
Paraquat affected the population growth of each of four species of green algae studied – *Scenedesmus quadricauda*, *Scenedesmus acutus*, *Selenastrum capricornutum*, and *Chlorella vulgaris* – in a different way (11).

Bioaccumulation

Not significantly accumulated by earthworms and other soil invertebrates (12).

Environmental fate

Nitrification inhibition

Significantly reduced nitrogen fixed by soybeans inoculated with *Bradyrhizobium japonicum* (13).
Ammonium and nitrite oxidation was completely inhibited in a mixed culture of nitrifying bacteria at 1 μg ml^{-1} (14).

Carbonaceous inhibition

4 wk after application of 9.6 μg active ingredient g^{-1} soil (10 × maximum recommended field application rate) cellulose degradation in upland and flooded soils was 23.5 and 51.2%, respectively. Without pesticide application the figures were 24.9 and 54.5%, respectively (15).

Degradation studies

No significant degradation in sterile and non-sterile soil incubated aerobically and anaerobically for 90 days at 25°C in the dark at soil concentrations of 15-25 mg kg^{-1} (16).
Degraded by an unspecified yeast, *Fusarium* sp. and *Penicillium* sp. isolated from paddy soil. The yeast required nutrient sources to complete elimination, the two fungi did not. Accumulated in *Fusarium* and *Penicillium* cells, some of which was metabolised to monoquat, *N*-methylisonicotinic acid, methylamine, carbon dioxide and monopyridone (in *Fusarium* only) (17).

Abiotic removal

Stable to photolysis in soil with natural sunlight for 24 months (1).
Stable to hydrolysis at 25 and 40°C and pH 5, 7 and 9 for up to 30 days (18).
Absorption capacity of activated carbon 37.2 and 93.2 mg, carbon at concentrations of 0.373 and 37.3 mg l^{-1}, respectively (19).

Adsorption and retention

Strongly absorbed up to the cation exchange capacity of montmorillonite and illite, and 57% of the capacity of kaolinite (20).

Mammalian & avian toxicity

Acute data

LC_{50} oral rat, guinea pig, cat 30-112 mg kg^{-1} (21).
LC_{50} (4 hr) inhalation rat 0.6-1.4 mg m^{-3} (22).
LD_{50} dermal rat, rabbit 60, 90 mg kg^{-1}, respectively (23,24).

Sub-acute and sub-chronic data

LC_{50} (5 day) oral bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck 970-4050 mg kg^{-1} diet (dichloride) (25).

Subcutaneous rabbit (30 day) 1.5 mg kg^{-1} day^{-1} of the dichloride produced no toxic symptoms, no effect on body weight and no alterations in serum enzyme levels, although there were decreases in haemoglobin, leukocytes and red blood cell counts. Depletion of lymphocytes was evident in lymph nodes, spleen follicles and the medulla of the thymus. Slight pulmonary congestion was reported (26).

Caused dose-related lung injury and lung fibrosis at doses of 0.001-1.0 mg kg^{-1} instilled into rat lung (27).

Carcinogenicity and chronic effects

Oral mouse (2 yr) 0, 2, 6, 15 or 18 mg kg^{-1} did not induce a significant increase in tumours. Renal tubular degeneration in ♂ mice, weight loss and decreased food intake in ♀ were reported in the 6 mg kg^{-1} dose group (28).

Found not to be synergistically carcinogenic when administered to rats at 1/250 LD_{50} for 6 months after a tumour-promoting single dose of 3,4-benzopyrene (29).

Oral rat (30 month) 0, 1.25, 3.75 or 7.5 mg kg^{-1} day^{-1} did not cause a significant increase in tumour incidence. A dose-related increase of slight hydrocephalus was noted in ♀ rats that died after wk-52. Also, increased incidences of spinal chord cysts and cystic spaces were noted in ♂ rats that died after wk-52. Eye opacities, cataracts and non-neoplastic lung lesions (alveolar macrophages and epithelialisation, and slight peribronchiolar lymphoid hyperplasia) were observed at 3.75 mg kg^{-1} and above (30).

Teratogenicity and reproductive effects

Oral rat (3 generations) 0, 1.25, 3.75 or 7.5 mg kg^{-1} (technical paraquat dichloride; 32.7% cation w/w) day^{-1}. No adverse reproductive effects were reported. An increased incidence of alveolar histiocytes in the lungs was observed in the 3.75 and 7.5 mg kg^{-1} groups (31).

Gavage mouse 0, 1, 5 or 10 mg paraquat ion kg^{-1} day^{-1} on days 6-15 of gestation caused no teratogenic effects. Partially ossified sternebrae were observed in 26% of the high dose foetuses (32).

Metabolism and toxicokinetics

In vitro studies demonstrated greater paraquat absorption by the small intestine compared with other regions of the gastro-intestinal tract of the rat. The stomach and oesophagus had the lowest rate of absorption (33).

Following oral administration to pigs of ^{14}C-methyl labelled and ^{14}C-ring labelled paraquat dichloride, radioactivity was associated mostly with unchanged paraquat in the lungs, heart, liver and kidney, with trace amounts in the brain, muscle and fat (34,24).

Paraquat was poorly absorbed from the gastro-intestinal tract of pigs and rats and excreted in the faeces mainly unchanged after 2-3 days. Some microbial degradation was identified in the gut of rats. A portion of these degradation products was absorbed and excreted in the urine (35,36).

In vitro human skin permeability was 3×10^{-5} cm hr^{-1} at steady state in solution of 1 mg ml^{-1}. Binding to skin was negligible. Modelling predicted for intact human skin and diluted solutions that systemic toxicity would be unlikely, but the risk increased significantly with damaged skin or concentrated solutions (37).

Irritancy

Dermal rabbit (24 hr) 172 mg caused irritation and 35 mg (0.1 ml of 35% solution) instilled into rabbit eye caused severe irritation (38).

Sensitisation

No allergic or irritant reactions seen in patch-testing of 442 human subjects (39).

Genotoxicity

Human lymphocytes in culture exposed to paraquat with or without metabolic activation. Slight but significant increase in sister chromatid exchanges, no increase in frequency of chromosome aberrations or micronuclei (40).

Increasing frequencies of sister-chromatid exchanges were found in cultured Chinese hamster lung cells exposed to increasing concentrations of paraquat (0.08-20.0 μM). There was no induction of chromosomal aberrations at low paraquat concentrations that stimulated the cell cycle rate, but at the higher concentrations found to inhibit the cell cycle rate an increased number of chromatid gaps and breaks were observed, especially after long incubation periods (41).

Paraquat caused chromosomal aberrations in cultured Chinese hamster ovary cells without metabolic activation. With metabolic activation the induction of aberrations was signigicantly lower (42).
The frequency of chromosomal aberrations increased following the treatment, before emergence, of spring barley at a rate of 1.2-2 kg ha^{-1} paraquat (43).
Induced cytotoxicity and chromosome aberrations in V-79 Chinese hamster cells but did not induce gene mutations at the HPRT locus or increased DNA migration in the Comet assay under the same treatment conditions. The authors suggest that since chromosome aberrations only occur after treatment with high concentrations of paraquat which cause cell death, and are not preceded by an induction of DNA strand breakage in intact cells, their biological signficance is questionable (44).

Other effects

Other adverse effects (human)

In acute poisoning plasma levels had a mean distribution $t_{1/2}$ of 5 hr and mean elimination $t_{1/2}$ of 84 hr. Cardiovascular collapse occurred early during the course of the poisoning and was associated with the distribution phase. Death related to pulmonary fibrosis occurred late and was associated with the elimination phase. Muscle may represent an important reservoir, explaining the long persistence of paraquat in urine and plasma for weeks or months after poisoning (45).
Premalignant skin lesions, including hyperpigmented macules and hyperkeratosis, observed among paraquat factory workers (46).
In 15 cases of single exposure to skin or eyes no systemic effect was seen. Only local lesions were caused to healthy skin (47).
Clinical symptoms of acute poisoning progress through three stages: pulmonary oedema, headache and dyspeptic disturbances; toxic effects caused by damage to liver, kidneys and cardiovascular system; and development of fibrosis of the lungs (48).
Exposure to salts at 0.44-0.66 mg m^{-3} and when present in water at 0.05-0.08 mg did not affect health, blood catalase and peroxidase activities nor morphological composition of peripheral blood (49).
Of 296 workers spraying the compound, 55 had separated nails (49).
Evidence of inflammation, polypous bronchitis, adenomatosis and atelectasis in lungs with dystropic processes and contractual degeneration in cardiac muscle was found in fatal poisoning cases. Death of a child was reported to be caused by a fibroblast reaction which then promoted the development of pulmonary insufficiency (50).
On day-19 after accidentally swallowing the compound (gramoxone) a man suffered fatal acute asphyxia (51).

Any other adverse effects

Significantly stimulated lipid peroxidation in mouse brain microsomes in a dose-dependent manner. Stimulation occurred in only a narrow concentration range in lung microsomes (52).
Experimental Parkinsonism was not induced in mice following intraperitoneal administration (53).
Caused a 6-8 fold increase in malondialdehyde and a 30-55% decrease in reduced glatathione of rabbit lens *in vitro* (54).
The toxicity of paraquat was studied using isolated renal proximal tubular segments from rabbits. The cytotoxic effects were determined using markers of oxidative stress and tubular metabolism. Using 0.5 and 5 mM paraquat the status of glutathione (GSH/GSSG ratio) decreased and formation of malondialdehyde increased, indicating oxidative stress. A reduction in accumulation of *p*-aminohippuric acid and tetraethylammonium and a decrease in basal oxygen consumption indicated inhibition of the Na/K-ATPase. Mitochondrial electron-chain functions appear to have been disrupted, impairing metabolic functions (55).
Nicotinamide inhibits paraquat toxicity in rats by competing for the same active site on NADH/ubiquinone oxireductase (complex 1) (56).
Injection of paraquat (25 nmol 0.5 μl^{-1}) into rat hippocampus caused DNA fragmentation, nuclear chromatin marginalisation and compaction in all hippocampal subsectors (57).

Legislation

EEC maximum residue level for fruit and vegetables 0.05 ppm (3).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ 1^{-1}$ (58).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No 472, 1991 (59).
WHO Toxicity Class II (60).
EPA Toxicity Class II (formulation) (61).
ADI 0.004 mg kg^{-1} body weight (as paraquat ion) (61).
UK advisory value for drinking water 10 $\mu g\ l^{-1}$ (62).

Other comments

Residues have been isolated from crops (1).
Physical properties, environmental fate, metabolism, mammalian toxicity, teratogenicity, carcinogenicity and mutagenicity reviewed (1,63).
Excess zinc protects against paraquat-induced metal-mediated cellular injury in *Escherichia coli* (64).
Poisoning reviewed (65).
Biochemical, cellular and tissue effects, systemic toxicity and organ toxicity tested for by the US National Institute of Diabetes and Digestive and Kidney Diseases. Pharmacokinetics and metabolism studied for the Heart and Vascular Diseases Program of the US National Heart, Lung and Blood Institute (66).
Pharmacokinetics and metabolism reviewed (67).
Paraquat is the active ingredient of the aqueous commercial form of gramoxone (dichloride or bis(methyl sulfate) salt of paraquat) and dipyridyl phosphate herbicides. The respective CAS Registry Numbers for the dichloride and methosulfate are 1910-42-5 and 2074-50-2.
Metabolic pathways reviewed (68).

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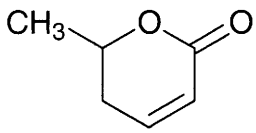
P12 parascorbic acid



$C_6H_8O_2$ **Mol. Wt.** 112.13 **CAS Registry No.** 10048-32-5

Synonyms *S*-5,6-dihydro-6-methyl-2*H*-pyran-2-one; 5-hydroxy-2-hexenoic acid lactone; 2-hexen-5,1-olide; δ-Δα,β-hexenolactone; sorbic oil

RTECS No. UQ 0525000

Occurrence Sole constituent of Vogelbeeröl, an oil distilled from the juice of ripe berries from the mountain ash, *Sorbus aucuparia*.

Physical properties

B. Pt. at 22 mmHg **Specific gravity** 1.079 at 18°C with respect to water at 4°C
Solubility Water: soluble. Organic solvents: alcohol, ether

Mammalian & avian toxicity

Acute data

LD_{50} dermal rabbit 5040 mg kg^{-1} (1).
LD_{50} intravenous mouse 195 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 250 mg kg^{-1} (3).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (4).
Subcutaneous injection to 2 groups of ♂ rats of 2 or 20 mg kg^{-1} in oil twice weekly for 32 weeks resulted in local sarcomas in 4/6 and 4/5 rats within 95-106 weeks; the first tumours appeared 61-63 weeks after the start of treatment (5).

Other comments

Physico-chemical properties, human health effects, exposure levels (environment and workplace), experimental toxicology, workplace experience and epidemiology reviewed (6).

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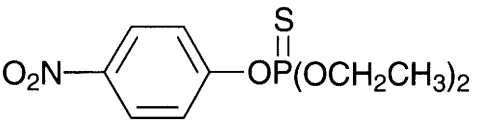
P13 parathion



$C_{10}H_{14}NO_5PS$ **Mol. Wt.** 291.26 **CAS Registry No.** 56-38-2

Synonyms *O,O*-diethyl *O*-4-nitrophenyl phosphorothioate; phosphorothioic acid, *O,O*-diethyl *O*-(*p*-nitrophenyl) ester; Folidol; Paraphos; Rhodiatox; Thiophos

EINECS No. 200-271-7 **RTECS No.** TF 4550000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 6°C **B. Pt.** 150°C at 0.6 mmHg **Specific gravity** 1.265 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.83 (1) **Volatility** v.p. 3.78×10^{-5} mmHg at 20°C
Solubility Water: 24 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, diethyl ether, ethanol, petroleum oils

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.1 mg m^{-3}
JP-OEL 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 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) golden orfe, fathead minnow, largemouth bass, rainbow trout 0.19-1.5 mg l^{-1} (2-4).

Invertebrate toxicity
EC_{50} (5 min) *Photobacterium phosphoreum* 8.4-68 ppm Microtox test (5).
LC_{50} (96 hr) *Gammarus fasciatus* 3.5 µg l^{-1} (6).
EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) >25mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) >25 mg l^{-1} (7).
LC_{50} (48 hr) *Daphnia magna* 0.37 µg l^{-1} (8).
Growth of *Prorocentrum micans* was inhibited at 1 ppm, whereas *Chlorella vulgaris* and *Chlorella emersonii* needed tens of ppm. Osmiophilic vesicles in the chloroplasts was an effect common to all the algae tested. *Prorocentrum micans*, *Crypthecodinium cohnii* and *Chlorella emersonii* yielded aminoparathion as the primary degradation product. *Woloszynskia coronata*, *Chlorella vulgaris* and *Dunaliella marina* had no biodegradable effect (9).

Bioaccumulation
Bioconcentration factor in mussels and mummichog fish 50-80 (10).

Environmental fate

Degradation studies

Reported to be degraded by *Pseudomonas diminuta* (11).
Concentrations of 1-5 ppm, 95% degradation within 10 day by the marine dinoflagellate *Prorocentrum micans*.
Major metabolite aminoparathion (12).
Degradation in estuarine water, 30°C, $t_{1/2}$ 48 day (13).
At 80 days after application of 1000 ppm to silty clay acid and sandy clay neutral soils 91.5 and 90.0 ppm remained, respectively (14).

Abiotic removal

Undergoes hydrolysis at the ester linkage yielding diethylphosphorothioic acid and *p*-nitrophenol (15).
In the environment the sulfur bound to the phosphorus is substituted by oxygen to yield paraoxon. This substitution is enhanced under UV light. Paraoxon is hydrolysed to yield diethylphosphoric acid (15,16).
Photodegradation rate in water by natural sunlight: aqueous acetone (20 ml l^{-1}) >sea water >river water >distilled water. ~ $t_{1/2}$ in distilled and river water, 35 and 7 days, respectively, under sunlight (17).

Adsorption and retention

Freundlich coefficient at 10°C was 0.17 for a saline soil, 0.27 for rendzina, 28.8 for bentonite, and 3×10^7 for biogerol. Organic matter was the primary factor controlling adsorption (18).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3.6-13 mg kg^{-1} (19,20).
LD_{50} oral quail 4.2 mg kg^{-1} (21).
LC_{50} (4 hr) inhalation ♂ rat 84 mg m^{-3} (22).
LD_{50} oral redwing blackbird, starling, 2.37 and 5.62 mg kg^{-1}, respectively (21).
LD_{50} dermal rat 7-21 mg kg^{-1} (20).
LD_{50} intraperitoneal rat, mouse 3, 10 mg kg^{-1}, respectively (22,23).
LD_{50} intravenous rat, cat, dog 3-20 mg kg^{-1} (22,24).

Sub-acute and sub-chronic data

LD_{50} (8 day) oral Japanese, bobwhite quail 195 mg kg^{-1} diet (25).
Oral human (122 day) the maximum dietary concentration of parathion that had no effect on red blood cell cholinesterase activity was 50 μg kg^{-1} day^{-1} (26).
Intragastric rat total dose 6.5 or 13 mg kg^{-1} over 6 days under light:dark cycles of 14:10 with light off at 2100 hr. Pineal *N*-acetyltransferase activity was increased at 0100 hr. Hydroxyindole-*O*-methyltransferase activity was unaffected. The high dose increased pineal and serum melatonin levels at 2300 and 0100 hr. This effect was only seen at 0100 hr with the lower dose. At both doses 5-hydroxytryptophan was decreased at 2000 hr. The lower dose increased levels at 2300 hr. 5-HT was significantly decreased at 2300 hr and 5-hydroxyindoleacetic acid was lower, but only significantly so for the high dose at 2000 hr (27).

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (28).
National Toxicology Program tested rats and mice via feed. Negative results were reported for ♂ and ♀ mice, equivocal results were reported for ♂ and ♀ rats (29).
Oral rat (100 wk) 20-80 mg kg^{-1} diet for up to 67 wk. Although a dose-related increase in the incidence of adrenal cortical adenomas was observed, the significance of these lesions is not well understood (30,31).

Teratogenicity and reproductive effects

Chicken and pheasant eggs, injection of 0.05-0.10 mg caused dose-related teratogenic effects and embryo mortality (32).
Intraperitoneal mouse, 4-12 kg kg^{-1} on day 12-14 gestation caused resorption and a significant reduction in foetal weight (33).

Oral rat, 0.01-1.0 mg kg^{-1} on day 2-15 of gestation. A reduction in plasma pseudocholinesterase activity and plasma renin activity was reduced in ♀ neonates and electrocardiographic patterns altered in 24-day-old ♂, ♀ progeny (34).

Metabolism and toxicokinetics

Following oral administration to rats, 4-nitrophenol and paraoxon were the principal urinary metabolites (35).
In humans parathion is absorbed from the skin, cornea, conjunctiva and the respiratory mucosa (36,37).
Within 48 hr of oral administration of 2 mg to human volunteers, 30-40% of parathion metabolites were eliminated in the urine. *p*-Nitrophenol and diethyl thiophosphate were excreted more rapidly and very little of these metabolites appeared in the urine 8 hr after dosing. Urinary excretion of diethyl phosphate persisted for up to 24 hr (38,39).

Genotoxicity

Salmonella typhimurium microsomal mutagenicity assay (500 μg $plate^{-1}$ positive (40).
Human fibroblasts, unscheduled DNA synthesis positive (10 μmol l^{-1}) (41).

Other effects

Other adverse effects (human)

Volunteers who consumed 0.05 mg kg^{-1} body weight showed no illness, no depression of red-blood cell or plasma cholinesterase activities. Lower doses induced an increase in the plasma cholinesterase activity (42,43).

Any other adverse effects

The acute toxicity of parathion is due to inhibition of acetyl cholinesterase activity at nerve endings. The effects are manifested by muscarinic, nicotinic and central nervous system symptoms, i.e. sweating, salivation, diarrhoea, bronchorrhoea, bradycardia, bronchoconstriction, muscle fasciculation and coma. The cause of death is primarily respiratory failure (16).
Its metabolite paraoxon contributes to toxicity of parathion (44).
Intragastric ♂ rat, single doses of 50-200 μg kg^{-1}, 6, 12 or 24 hr before examination. Parathion caused a dose- and time-dependent increase in the activities of β-glucuronidase, α-glucosidase and acid phosphatase, and a decrease in the activity of alkaline phosphatase activity in the testes, epididymis, prostate and seminal vesicles (45).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (46).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (47).
EEC Maximum residue limit for fruit and vegetables 0.5 ppm (2).
WHO Toxicity Class Ia (48).
EPA Toxicity Class I (formulation) (49).
ADI 0.004 mg kg^{-1} body weight (49).

Other comments

Attributed endocrine disruption effects in wildlife. Avian reproduction impaired, reduced egg production, reduced adult body weight; fish reproduction impaired, vertebral anomalies; mysid growth reduced (50).
Residues have been isolated from water, sediments, soil, and crops and fishes (30,51).
Human exposure toxicity reviewed (52).
Physical properties, uses, occurrence, analysis, carcinogenicity, mammalian toxicity, mutagenicity and metabolism of parathion reviewed (30,53).
Environmental fate of parathion reviewed (51).

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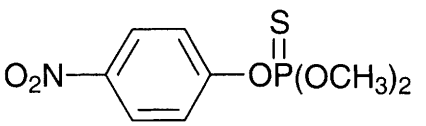
P14 parathion-methyl



$C_8H_{10}NO_5PS$ **Mol. Wt.** 263.21 **CAS Registry No.** 298-00-0

Synonyms *O,O*-dimethyl *O*-(4-nitrophenyl) phosphorothioate; dimethyl parathion; demethylfenitrothion; metaphos; methylthiophos; Folidol M; Metacide; Metron; Nitrox; Penncap

EINECS No. 206-050-1 **RTECS No.** TG 0175000

Uses Insecticide.

Physical properties

M. Pt. 35-38°C **B. Pt.** 154°C at 1 mmHg **Specific gravity** 1.358 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.11 (calc.) (1) **Volatility** v.p. 9.7×10^{-6} mmHg at 20°C
Solubility Water: 50 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, carbon tetrachloride, chloroform, dichloromethane, diethyl ether, ethanol, methanol, mineral oils

Occupational exposure

FR-VME 0.2 mg m^{-3}
UK-LTEL 0.2 mg m^{-3} **UK-STEL** 0.6 mg m^{-3}
US-TWA 0.2 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) – 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) golden orfe, rainbow trout, fathead minnow, large-mouth bass 2.7-8.9 mg l^{-1} (2,3).

Invertebrate toxicity
LC_{50} (96 hr) sand shrimp, grass shrimp, hermit crab 2-7 μg l^{-1} static bioassay (3).
EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) 20 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) >67 mg l^{-1} (4).

Environmental fate

Degradation studies

Degraded to carbon dioxide and water by a *Bacillus* sp. isolated from soil. A mixed bacterial culture from the soil, including a *Pseudomonas* sp. could not utilise methyl parathion as a sole carbon source (5).
In anaerobic sediments, aminomethyl parathion was identified as the reduction product. In heat-sterilised sediments the rate of reduction was halved (6).

Abiotic removal

Undergoes photodegradation to methyl paraoxon (7).
Undergoes hydrolysis in flooded soils. Hydrolysis products include *p*-nitrophenol (8).
At concentrations up to 0.6 mg l^{-1} in water, reduction to < 0.1 µg l^{-1} was achieved with ozone concentrations of 1.5-2.3 mg l^{-1} for pH 8.0-8.5 in 8-12 min. Chlorination produced the same degree of oxidation at concentrations of 35-67 mg l^{-1} for 37-70 hr (9).
Under laboratory conditions, granular activated carbon removed >99% methyl parathion from water (1).
Reacts with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ ~87 hr (10).

Adsorption and retention

Organic matter was the most important single factor affecting adsorption. Cation exchange capacity was also significant. In soil materials where organic matter was <1%, oxalate-extractable manganese and calcium were associated with adsorption (11).
Between October 1985 and June 1986, 0.15-0.19% was transported to a depth of 100 cm by rainfall leaching in a series of Greek soils (12).

Mammalian & avian toxicity

Acute data

LD_{50} oral starling, redwing blackbird 7.5, 10 mg kg^{-1}, respectively (13).
LD_{50} oral rat, mouse 14, 200 mg kg^{-1}, respectively (14,15).
LC_{50} (4 hr) inhalation rat 34 mg m^{-3} (16).
LD_{50} dermal mouse 1200 mg kg^{-1} (17).
LD_{50} subcutaneous rat, mouse 6, 18 mg kg^{-1}, respectively (18,19).
LD_{50} intraperitoneal rat, mouse 2.8, 5.4 mg kg^{-1}, respectively (20,21).
LD_{50} intravenous rat, mouse 9.0, 9.8 mg kg^{-1}, respectively (22).

Sub-acute and sub-chronic data

Oral bobwhite quail (8 day) 0, 14, 20, 28, or 40 ppm diet caused a dose-related reduction in body weight, egg production, egg weight, shell strength and shell thickness (23).
Oral mouse (4 wk) 0.1, 0.7 or 3.0 mg kg^{-1} day^{-1}. Immunosuppression was reported. Increased mortality after intraperitoneal injection of active *Salmonella typhimurium* was associated with an increase in the number of viable bacteria in blood, decreased total γ-globulins and specific immunoglobulins in serum, and reduced splenic blast transformation in response to mitogens (24).

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (25).
National Toxicology Program tested rats and mice via feed. Negative results were reported in rats and mice (26).
Oral mouse (2 yr) 62.5 or 125 mg kg^{-1} diet, reduced to 20 or 50 mg kg^{-1} diet at wk-37 up to wk-102. Rats were fed 20 or 40 mg kg^{-1} diet for 105 wk. No statistically significant difference in tumour incidence was observed. No sign of cholinergic toxicity was reported in this study (27).

Teratogenicity and reproductive effects

Oral rat 0.1, or 3.0 mg kg^{-1} on 6 alternative days between days 6-15 of gestation, or 3.0 mg kg^{-1} on 8 alternative days between days 5-19 of gestation. In the 3.0 mg kg^{-1} groups increased resorptions and decreased foetal body weight were reported (28,29).

Intraperitoneal mouse, 20 or 60 mg kg^{-1} on day-10 of gestation. The high dose caused foetal death, body weight reduction, cleft palate and an increased incidence of cervical ribs. Teratogenic effects in the low-dose group were not significantly different from those in controls (30).
Intraperitoneal rat, 5, 10 or 15 mg kg^{-1} on day-12 of gestation caused signs of toxicity and body weight reduction in dams in all treated groups. Mean foetal weight was reduced in the high-dose group, but no teratogenic effects were observed in any group (30).
Intraperitoneal rat, 4 or 6 mg kg on day-9 or day-15 of gestation did not cause any teratogenic or other foetal effect (31).
Oral rat(3-generation study), 0, 10 or 30 mg kg^{-1} diet. The high dose reduced reproductive performance of parents and survival and body weight of weanling rats (32).
Pregnant rats received daily doses from day-6 through to day-15 of gestation at doses of 0.5 and 1.5 mg kg^{-1} body weight. Dams were sacrificed on day-20 of gestation and foetuses were examined for external and visceral anomalies. Significant decrease in dam weight gain during pregnancy and increase in resorption rate were observed in rats receiving 1.5 mg kg^{-1}. No increases were seen in skeletal or visceral anomalies, but an increased incidence of haemorrhagic spots in brain and upper body were seen in pups (33).

Metabolism and toxicokinetics

Metabolised to methyl paraoxon in perfused rat liver *in situ* (34).
Following intraperitoneal administration to rats and mice methyl parathion was found to be covalently bound to DNA, RNA and proteins of various organs (35).
After an oral dose of ^{32}P-methyl parathion to mice, 75% of the radioactivity appeared rapidly as metabolites in the urine, most of this within 18 hr, and up to 10% was excreted in the faeces (36).
Methyl parathion and methyl paraoxon may be metabolised in rodent liver to dimethyl phosphorothioic acid (or dimethyl phosphoric acid) plus *p*-nitrophenol, and to *O*-methyl *O*-(*p*-nitrophenyl) phosphorothioate or *O*-methyl *O*-(*p*-nitrophenyl) phosphate (37).

Irritancy

Dermal rabbit (4 hr) 0.5 ml caused mild irritation, and 0.1 ml instilled into rabbit eye caused conjunctival irritation in washed and non-washed eyes (38,39).

Sensitisation

No significant reaction was observed in patch tests on agricultural workers (40).
In patch tests on 294 human subjects there was 1 case of allergic reaction (41).

Genotoxicity

Drosophila melanogaster sex-linked recessive lethal and total and partial sex-chromosome losses negative. A small increase in the frequency of non-dysjunction was detected after larval treatment (42).
Human peripheral lymphocytes chromosomal aberrations negative, sister chromatid exchanges positive (43).
Rat bone marrow cells micronuclei induction assay positive (44).

Other effects

Any other adverse effects

Subcutaneous rat, single dose of 7.8 mg kg^{-1} in neonates, and 18 mg kg^{-1} in adults, caused ~80% inhibition of brain cholinesterase (45).
Parathion-methyl increases the ordering in fluid membrane bilayers. The effects are most prevalent in low cholesterol membranes such as those of mitochondria and sarcoplasmic reticulum. The effects of parathion-methyl are reduced in membranes with a higher level of ordering, i.e. higher cholesterol levels (46).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (47).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (48).
The log P_{ow} value exceeds the European Community recommended level 3.0 (49).

WHO Toxicity Class Ia (50).
EPA Toxicity Class I (formulation) (51).
EEC maximum residue level for fruit and vegetables 0.2 ppm (2).
ADI 0.003 mg kg^{-1} body weight (51).

Other comments

Residues have been isolated from water, sediments, soil, crops and in fish tissues (28-52).
Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity, teratogenicity, metabolism and mutagenicity of methyl parathion reviewed (9).
Environmental fate of methyl parathion reviewed (52).

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P15 Paris Green

$C_4H_6As_6Cu_4O_{16}$ **Mol. Wt.** 1013.80 **CAS Registry No.** 12002-03-8

Synonyms cupric acetoarsenite; C.I. Pigment Green 21; Basle Green; C.I. 77410; Imperial Green; Mountain Green; New Green; Swedish Green; Vienna Green

RTECS No. GL 6475000

Uses Pigment, particularly for ships. Insecticide. Wood preservative.

Physical properties

Specific gravity >1.1 at 20°C (calculated)

Occupational exposure

SE-LEVL 0.03 mg m^{-3} (as As)
UK-LTEL MEL 0.1 mg m^{-3} (as As)

Environmental fate

Degradation studies
Degraded by *Pseudomonas aeruginosa* and *Bacillus megaterium*. Addition of a carbon source to the medium enhanced growth rate (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, 22-100 mg kg^{-1} (2,3).

Genotoxicity

Salmonella typhimurium 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).

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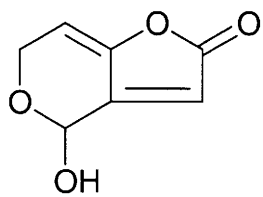
P16 patulin



$C_7H_6O_4$ **Mol. Wt.** 154.12 **CAS Registry No.** 149-29-1

Synonyms 4-hydroxy-4*H*-furo[3,2-*c*]pyran-2(6*H*)-one; clavacin; claviformin; expansin; mycoin; penicidin; Terinin

EINECS No. 205-735-2 **RTECS No.** LV 2625000

Uses Antibiotic.
Occurrence Metabolite derived from a number of fungi e.g. *Aspergillus* and *Penicillium* species.

Physical properties

M. Pt. 111°C
Solubility Organic solvents: acetone, amyl acetate, benzene, diethyl ether, ethanol, ethyl acetate

Occupational exposure

UN No. 2811

Ecotoxicity

Fish toxicity
5 ppm killed trout, bluegill sunfish and goldfish in 0, 0 and 24 hr, respectively. Test conditions: pH, 7.0; dissolved oxygen, 7.5 ppm; total hardness (soap method), 300 ppm; methyl orange alkalinity, 310 ppm; phenolphthalein alkalinity, 0; free carbon dioxide, 5 ppm; temperature, 12.8°C (1).

Invertebrate toxicity
Minimal detectable concentration swarming inhibition *Azospirillum brasilense* and *Proteus mirabilis* 1.0 and 0.1 mg ml^{-1}, respectively (at low concentration stimulates motility) (2).
Minimal detectable concentration growth inhibition *Bacillus thuringiensis* 0.1 mg ml^{-1} (2).

LC_{50} (duration unspecified) brine shrimp 10 ppm (2).
EC_{20} (duration unspecified) *Photobacterium phosphoreum* 0.9 ppm (2).
EC_{50} (15 min) *Photobacterium phosphoreum* 1.34-2.68 ppm Microtox test (3).
ID_{50} (24 hr) growth *Tetrahymena pyriformis* 0.32 μg ml^{-1} (4).
ED_{50} *Tetrahymena pyriformis* 3.2 μg ml^{-1} (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 17, 28 mg kg^{-1}, respectively (6,7).
LD_{50} intravenous mouse, rat 5, 9 mg kg^{-1} respectively (6,8).
LD_{50} intraperitoneal rat, mouse 5 mg kg^{-1} (7,9).
LD_{50} subcutaneous mouse 10-15 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Oral Wistar rat (4 wk) 24, 84 or 295 mg l^{-1} in drinking water. The medium and high doses decreased food and liquid intake and the high doses decreased body weight. Creatinine clearance was decreased. Fundic ulcers appeared in the stomach and enlargement and activation of the pancreatic-duodenal lymph nodes occurred in the high-dose group. Villous hyperaemia in the duodenum affected the two higher dose groups (11).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (12).

Genotoxicity

Salmonella typhimurium TA102 with and without metabolic activation negative (13).
Salmonella typhimurium (strains unspecified) with and without metabolic activation negative (14).
Escherichia coli SOS chromotest with and without metabolic activation negative (14).
Tetrahymena pyriformis (6 hr) 3.2 μg ml^{-1} reduced formation rate of RNA, DNA and proteins. DNA polymerase activity was not affected at ED_{50} concentration. Reversion frequencies of the amber mutant of bacteriophage M13 to the wild type in *Escherichia coli* increased. The study suggests that DNA was the prime site of damage (5).
In vitro rat and mouse hepatocyte primary culture/DNA repair test negative (15).

Other effects

Any other adverse effects

Significantly reduced delayed type hypersensitivity to *Bordetella pertussis* antigen in BALB/c mouse. Anti-keyhole limpet haemocyanin antibody production was unaffected and splenocyte proliferation was increased. Strongly inhibited *in vitro* lymphocyte proliferation (16).

Other comments

Formation by fungi and mammalian toxicity reviewed (17).

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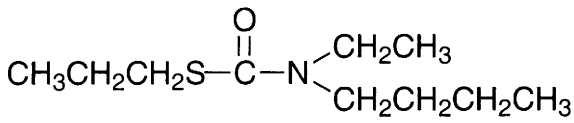
P17 pebulate



$C_{10}H_{21}NOS$ **Mol. Wt.** 203.35 **CAS Registry No.** 1114-71-2

Synonyms butylethylcarbamothioic acid, *S*-propyl ester; butylethylthiocarbamic acid, *S*-propyl ester; PEBC; *S*-propyl butylethylthiocarbamate; R 2061; Tillam

EINECS No. 214-215-4 **RTECS No.** EZ 0400000

Uses Herbicide.

Physical properties

B. Pt. 142°C at 21 mmHg **Flash point** 124°C **Specific gravity** 0.956 at 30°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.840 (1) **Volatility** v.p. 3.5×10^{-2} mmHg at 25°C
Solubility Water: 60 mg l^{-1} at 20°C. Organic solvents: miscible with acetone, benzene, isopropanol, 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) – Do not breathe vapour (S2, S23)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 7.4 mg l^{-1} (2).
LC_{50} (48 hr) silver mullet, killifish 6.25, 7.78 mg l^{-1} (3).

Invertebrate toxicity
LC_{50} (96 hr) *Gammarus fasciatus* 10 mg l^{-1} (4).
LC_{50} (48 hr) *Daphnia magna* 5.9 mg l^{-1} (3).
Not toxic to bees at 0.011 mg bee^{-1} (3).

Environmental fate

Degradation studies
Soil $t_{1/2}$, 2-3 wk disappears mainly by microbial degradation to mercaptan, carbon dioxide and ethylbutylamine (1,3).

Abiotic removal
50% loss occurs in 11 days at pH 4 and 10, and in 12 days at pH 7 at 40°C in water (3).

Adsorption and retention

Log K_{oc}: experimental, 2.80; calculated, 2.89 (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling >100 mg kg^{-1} (6).
LD_{50} oral rat 1.12 g kg^{-1} (7).
LD_{50} oral mouse 1652 mg kg^{-1} (7).
LD_{50} dermal rabbit 4640 mg kg^{-1} (3).

Sub-acute and sub-chronic data

LC_{50} (7 day) oral bobwhite quail 8400 mg kg^{-1} in diet (3).
NOEL (90 day) oral rat 16 mg kg^{-1} day^{-1} (3).
NOEL (90 day) oral dog 20 mg kg^{-1} day^{-1} (3).
NOEL (1 yr) oral dog 5 mg kg^{-1} day^{-1} (3).

Metabolism and toxicokinetics

Rapidly metabolised in animals. In the rat 50% was expired as carbon dioxide in 3 days, about 25% excreted in the urine and 5% in the faeces (3).

Genotoxicity

Salmonella typhimurium TA92, TA98, TA1535, TA1537, TA2637 with and without metabolic activation negative (8).
Escherichia coli and *Saccharomyces cerevisiae* weakly mutagenic, but did not induce point mutations or intragenic mitotic recombination (metabolic activation unspecified) (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 recommended limit of 3.0 (12).
WHO Toxicity Class II (13).
EPA Toxicity Class III (formulation) (1).

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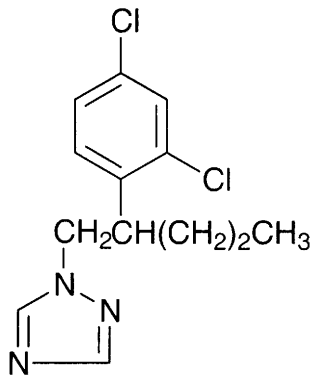
P18 penconazole



$C_{13}H_{15}Cl_2N_3$ **Mol. Wt.** 284.19 **CAS Registry No.** 66246-88-6

Synonyms 1-[2-(2,4-dichlorophenyl)pentyl]-1*H*-1,2,4-triazole; Topaze

EINECS No. 266-275-6 **RTECS No.** XZ 4615000

Uses Fungicide.

Physical properties

M. Pt. 60°C **Specific gravity** 1.3 at 20°C **Partition coefficient** log P_{ow} 3.72 at pH 5.7 and 25°C
Volatility v.p. 1.58×10^{-6} mmHg at 20°C
Solubility Water: 70 mg l^{-1} at 20°C. Organic solvents: acetone, cyclohexanone, dichloromethane, isopropanol, *n*-hexane, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, carp, bluegill sunfish 1.7-4.3, 3.8-4.6, 2.1-2.8 mg l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data
LD_{50} (8 day) oral Japanese quail, mallard duck 2424, >1590 mg kg^{-1}, respectively (1).
LD_{50} oral rat, mouse 2125, 2444 mg kg^{-1}, respectively (1).
LD_{50} dermal rat >3000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral Cr:CD(ICR)BR mouse in diet 1.5-360 mg kg^{-1} bw day^{-1} for 13 wk. Damage occurred only to the liver. No effects were observed on clinical signs, ophthalmoscopy, mortality, food consumption or haematology. Body weight was reduced at the highest dose. At the two highest doses cholesterol levels were lowered. Alanine aminotransferase activity increased in ♂ at the high doses and ♀ showed decreases in albumin and total protein at the top dose. At 75, 150 and 360 mg kg^{-1} relative liver weight was significantly raised. At higher doses centrilobular hypertrophy of the liver occurred. Hepatic degeneration, vacuolisation and coagulative necrosis affected ♂ at high doses. No-observed-adverse-effect level was 45 mg kg^{-1} day^{-1} (2).
Dermal New Zealand white rabbit were given 1000, 1500 or 2000 mg kg^{-1} body weight day^{-1} for 5 day wk^{-1} for 21 days. Food consumption, haematology, body weight, mortality, clinical chemistry and histopathology showed no dose-related changes. No-observed-adverse-effect level was 2000 mg kg^{-1} day^{-1} (2).

Carcinogenicity and chronic effects
Two-year studies on mice and rats (0, 5, 75, 150, 300 ppm in diet) showed no effects on mortality, body weight,

food consumption, haematology, clinical signs, vision, hearing or histopathology. Relative liver weight was increased in high-dose ♂ and ♀ mice and ♀ rats. Tumour incidence was unaffected (2).

Teratogenicity and reproductive effects

Offspring of Charles River rats given 5, 100 or 500 mg kg^{-1} body weight day^{-1} by gavage from days 6 to 15 of gestation showed no teratogenic effects. The number of viable foetuses and foetal weight were decreased at the highest dose. The number of early and late resorption sites and runts was increased at the highest dose. The NOEL for both mother and embryo/foetus was 100 mg kg^{-1} day^{-1} (2).

New Zealand white rabbits were given 10-200 mg kg body $weight^{-1}$ day^{-1} from days 7 to 19 of gestation. At the highest dose the number of early resorptions was slightly increased and number of viable foetuses reduced. At the highest dose, incidence of unossified hyoid body and/or arches and reduced ossification of the skull were slightly raised. Maternal/embryo no-observed-adverse-effect level was 50 mg kg^{-1} day^{-1} (2).

Metabolism and toxicokinetics

Following oral or intravenous administration of ^{14}C-labelled penconazole to Cr:CD(ICR)BR mice most of the radiolabel was excreted in 24 hr. Total recovery of ^{14}C in the urine was 47-66% for ♂ and 63-78% for ♀. Faecal excretion was 19-31% by ♂ and 9-17% by ♀ (2).

In Wistar rats following a single oral dose of 0.5 or 50 mg kg^{-1} body weight (^{14}C phenyl label) detectable tissue residues at the lower dose were only found in liver, femur, kidney and intestinal tract. At the higher dose in ♂ the greatest residual activity was found in the intestinal tract followed by liver, kidney, adrenal glands, skin, carcass, blood and plasma. The residual activity following the higher dose in ♀ was 2 to 9 × lower than in ♂ (2).

Following single oral dose by gavage to Tif:RAIf(SPF) rats, 13 urinary metabolites were identified. Only 0.8% of the dose was unmetabolised. Major metabolic pathways included stepwise oxidation and shortening of the alkyl side chain and cleavage at the nitrogen-carbon bond between the triazole ring and pentyl moiety. Oxidation of the triazole ring moiety, producing the 3- (or 5-) hydroxy derivative, and conjugation, in particular glucuronidation, of the hydroxylated metabolites also occurred (2).

No parent compound was detected in the urine of goats in oral ^{14}C study. In faeces, 17 and 21% of the parent compound were found following administration of, respectively, the phenyl and triazole label. A carboxylic acid was the major metabolite. No free triazole was detected (2).

Irritancy

Dermal rabbit (24 hr) 88.4% purity caused slight erythema. 100 mg inserted into the conjuctival sac of rabbit eye caused slight corneal damage, slight conjunctival redress and chemosis (2).

Sensitisation

No sensitisation was observed in an optimisation test using Firbright white guinea pigs (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (2).

Saccharomyces cerevisiae D7 mitotic gene conversion with and without metabolic activation negative (2).

Mouse embryofibroblasts BALB/3T3 transformation assay negative (2).

In vitro mouse lymphoma L5178Y tk^+/tk^- with and without metabolic activation negative (2).

In vitro human fibroblasts and rat hepatocytes DNA repair test negative (2).

In vitro Chinese hamster bone marrow cells nucleus anomaly and sister chromatid exchange negative (metabolic activation unspecified) (2).

NMRI mouse spermatogonia chromosome aberration negative (metabolic activation unspecified) (2).

♂ NMRI mouse dominant lethal assay negative (2).

Other effects

Any other adverse effects

In a study of drug-metabolising liver enzymes ♂ RAI albino rats and ♂ Mag mice were administered orally 14 doses of 10-320 mg kg^{-1} body weight day^{-1}. At doses ≥80 mg kg^{-1} body weight day^{-1} relative liver weight was increased. Liver DNA content at the highest dose was increased 120 and 125%, respectively, in rats and mice. At doses ≥80 mg kg^{-1} body weight day^{-1} phospholipid contents, microsomal protein and enzyme activities were

significantly increased. Cytochrome P_{450}, epoxide hydrolase and ethoxycoumarin *O*-deethylase were significantly increased in rats at 10 mg kg^{-1} body weight day^{-1}. Smooth endoplasmic reticulum membranes proliferated in both species (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).
Log P_{ow} exceeds European Union recommended limit of 3.0 (5).
WHO Toxicity Class Table 5 (6).
ADI 0.03 mg kg^{-1} body weight (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
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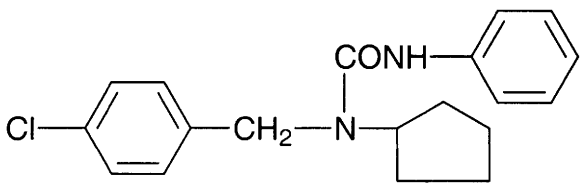
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 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

P19 pencycuron



$C_{19}H_{21}ClN_2O$ **Mol. Wt.** 328.84 **CAS Registry No.** 66063-05-6

Synonyms 1-(4-chlorobenzyl)-1-cyclopentyl-3-phenylurea; *N*-[(4-chlorophenyl)methyl]-*N*-cyclopentyl-*N'*-phenylurea; NTN 19701

EINECS No. 266-096-3 **RTECS No.** YS 6440000

Uses Fungicide

Physical properties

M. Pt. 129.5°C **Partition coefficient** log P_{ow} 4.68 (1) **Volatility** v.p. $<7.25 \times 10^{-6}$ mmHg at 20°C
Solubility Water: 0.3 mg l^{-1} at 20°C. Organic solvents: dichloromethane, *n*-hexane, isopropanol, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) carp 8.8 mg l^{-1} (1).
LC_{50} (96 hr) guppy 5-10 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} (oral and contact) >100 μg bee^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral hen, Japanese quail >2500 mg kg^{-1} (1).
LD_{50} oral canary >1000 mg kg^{-1} (1).
LD_{50} oral dog, mouse, rat >5000 mg kg^{-1} (1).
LD_{50} oral cat >1000 mg kg^{-1} (1).
LC_{50} (1 hr) inhalation rat >0.625 mg l^{-1} (1).
LC_{50} (4 hr) inhalation rat >0.57 mg l^{-1} (1).
LD_{50} (24 hr) dermal mouse, rat >2000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral rat, dog (2 yr), no-adverse-effect level for ♂ rat 50 mg kg^{-1} diet, for ♀ rat 500 kg^{-1} diet, and for dog 1000 mg kg^{-1} diet (1).

Metabolism and toxicokinetics

In rats, following oral administration, up to 74% was eliminated within 3 days in the urine and faeces, either as the unchanged material or as metabolites. Eleven metabolites were identified. The major urinary metabolites were 1-(*p*-chlorobenzyl)-1-cyclopentyl-3-(*p*-hydroxyphenyl)urea (free and glucuronide). Decyclopentylation, hydroxylation at the 3-position of the cyclopentyl moiety, diol formation, thiomethylation at the phenyl ring, and other glucuronides were also observed as metabolites (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (6).
WHO Toxicity Class Table 5 (7).
EPA Toxicity Class IV (formulation) (7).

Other comments

Synthesis, screening, action and degradation reviewed (8).

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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. Ueyama, I. et al *J. Agric. Food Chem.* 1982, **30**, 1061-1067.
4. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, 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. *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.
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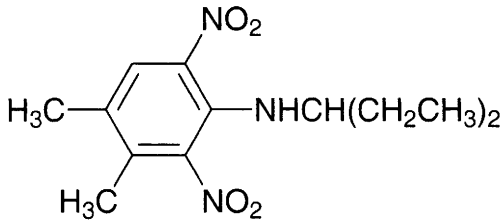
P20 pendimethalin



$C_{13}H_{19}N_3O_4$ **Mol. Wt.** 281.31 **CAS Registry No.** 40487-42-1

Synonyms *N*-(1-ethylpropyl)-2,6-dinitro-3,4-xylidine; *N*-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine; penoxalin; Prowl; Stomp; AC 92553; Herbadox

EINECS No. 254-938-2 **RTECS No.** BX 5470000

Uses Pre-emergence and pre-planting herbicide.

Physical properties

M. Pt. 54-58°C **B. Pt.** decomposes on distillation **Specific gravity** 1.19 at 25°C
Partition coefficient log P_{ow} 5.18 (1) **Volatility** v.p. 3×10^{-5} mmHg at 25°C
Solubility Water: 0.3 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform, corn oil, dichloromethane, heptane, isopropanol, 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) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 0.14, 0.2 mg l^{-1}, respectively (1).

Invertebrate toxicity
LD_{50} (topical) >50 μg bee^{-1} (2).
EC_{50} (48 hr) *Daphnia* 78 μg l^{-1} (adsorbed to algae) (3).

Environmental fate

Degradation studies
Fusarium oxysporum and *Paecilomyces varioti* degraded pendimethalin to *N*-(1-ethylpropyl)-3,4-dimethyl-2-nitrobenzene-1,6-diamine and 3,4-dimethyl-2,6-dinitroaniline; *Rhizoctonia bataticola* degraded pendimethalin, producing only the latter compound (4).

Abiotic removal
Photodegradation products were seen in soil after 15 days. One of the products was identified as *N*-propyl-3,4-dimethyl-2,6-dinitroaniline; two other degradation products were also observed which could not be identified (5).

Mammalian & avian toxicity

Acute data
LC_{50} (8 day) oral bobwhite quail, mallard duck 4187, 10,400 mg kg^{-1}, respectively (1).
LD_{50} oral mouse, rat 1050, 1620 mg kg^{-1}, respectively (1).

LD_{50} oral rabbit, beagle dog >5000 mg kg^{-1} (1).
LD_{50} dermal rabbit >5000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 100 mg kg^{-1} diet (1).

Other effects

Any other adverse effects
Pendimethalin caused central depression in mice and rats, evident from gross observable effects, a marked reduction in spontaneous locomotor activity and potentiation of hypnosis from phenobarbitone, barbitone and diethyl ether (dose and duration unspecified) (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (8).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (9).
EEC MRL wheat 0.5 ppm (1).
WHO Toxicity Class III (10).
EPA Toxicity Class III (formulation) (2).

Other comments

Metabolic pathways reviewed (11).

References

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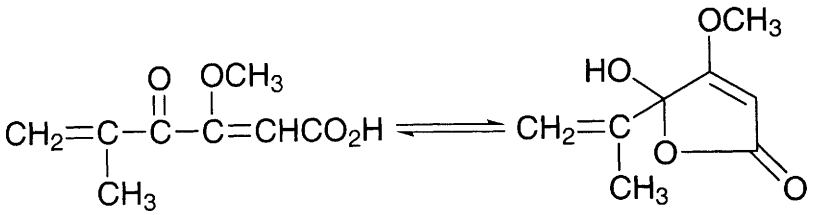
7. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
9. *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.
10. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
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

P21 penicillic acid



$C_8H_{10}O_4$ **Mol. Wt.** 170.16 **CAS Registry No.** 90-65-3

Synonyms 3-methoxy-5-methyl-4-oxo-2,5-hexadienoic acid; γ-keto-β-methoxy-δ-methylene-Δα-hexenoic acid

EINECS No. 202-008-1 **RTECS No.** MM 2625000

Uses Antibiotic

Occurrence Produced by *Penicillium puberlum, P. cyclopium, P. thomii, P. suaveolens, P. baarnense, Aspergillus ochraceus* and *A. melleus* (1).

Physical properties

M. Pt. 83-84°C

Solubility Water: 20 g l^{-1}. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2811

Ecotoxicity

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 1.45-8.73 ppm (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 600 mg kg^{-1} (3).

LD_{50} intravenous mouse 250 mg kg^{-1} (3).

LD_{50} subcutaneous mouse 100 mg kg^{-1} (4).

LD_{50} intraperitoneal rat 90 mg kg^{-1} (5).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (6).

Intratracheal rat 0.3 mg 2 × wk^{-1} for 30 wk. No tumours were detected in any of the animals (1).

Subcutaneous mouse 0.2 mg 2 × wk^{-1} for up to 65 wk. Local tumours developed in 6/19 mice between 38-81 wk (1).

Subcutaneous rat 0.1 or 1 mg in 0.5 ml arachis oil or 2 mg in water 2 × wk^{-1} for 61, 64 or 52 wk, respectively. Local sarcomas or fibrosarcomas developed at 48-67 wk in 4/4 rats receiving 1 mg in oil and at 94-106 wk in 1/4 rats receiving 0.1 mg in oil. Local tumours developed in 4/5 rats receiving 2 mg in water. No tumours occurred in 7 controls (1).

Irritancy

Application to rabbit skin caused severe oedema and necrosis within 2 hr (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).
Induced both single and double strand breaks in DNA of HeLa cells (1).

References

1. *IARC Monograph* 1976, **10**, 211-216.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. *J. Pharmacol. Exp. Ther.* 1946, **88**, 119.
4. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
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P22 penicillin

CAS Registry No. 1406-05-9

EINECS No. 215-794-6 **RTECS No.** RY 4375000

Occurrence An extract of *Penicillium notatum* containing a group of isomeric and closely related penicillins.

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse >2000 mg kg^{-1} (1).
LD_{50} intraperitoneal guinea pig 30 mg kg^{-1} (2).
LD_{50} subcutaneous guinea pig 30 mg kg^{-1} (2).
LD_{Lo} subcutaneous mouse 3200 mg kg^{-1} (3).
LD_{Lo} intravenous mouse 1000 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Intravenous mouse single dose of 0.5, 1.0, 1.5 and 2 g kg^{-1}, then observed for 15 days. Following injection of 0.5 g kg^{-1}, mice became inactive and depressed, followed by a period of increased activity. All mice had watery eyes and yellow biological tissues (possibly due to diffusion of penicillin). At the higher dose levels, the veins of both the ears and the cornea appeared dilated and the body temperature dropped significantly within 30 min of injection. No mice died after injection of 0.5 g kg^{-1}, 6/10 died after injection of 1 g kg^{-1} (4 on day 1, 1 on day 2 and 1 on day 4), 9/10 mice died after injection of 1.5 g kg^{-1} (all on day 1) and 10/10 mice died following injection of 2 g kg^{-1} (all on day 1) (3).
Subcutaneous mice 0.8, 1.6 and 3.2 g kg^{-1} day^{-1} for 5 days then observed for a further 10 days. At 3.2 g kg^{-1} day^{-1} all mice appeared sick and 4/10 died (2 on day 2 and 2 on day 5); these mice showed necrosis at the injection site. The other mice treated with 0.8 and 1.6 g kg^{-1} day^{-1} appeared normal and showed only a slight local reaction at the injection site (3).

Other effects

Other adverse effects (human)

An anaphylactic reaction has been reported which included transient swelling joints and subcutaneous tissues, intestinal purpura and toxic nephritis (4).

Any other adverse effects

Femoral muscle and spinal ganglion removed from 8 or 12 day old chick embryos were cultured in a medium containing penicillin. The compound was cytotoxic to the spinal ganglion (5).

The addition of 20 mg kg^{-1} to the diet of a chicken caused toxicoses in the form of leucopenia, neutropenia or lymphocytosis, which lasted throughout the 270-day experiment (6).

Other comments

Side-effects of penicillin reviewed (7).

Pharmacology, toxicology and clinical use reviewed (8).

Toxicity, methods of detection and inactivation during storage reviewed (9).

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P23 pentaborane(9)

B_5H_9

B_5H_9 **Mol. Wt.** 63.13 **CAS Registry No.** 19624-22-7

Synonyms pentaborane; pentaboron nonahydride

EINECS No. 243-194-4 **RTECS No.** RY 8925000

Physical properties

M. Pt. –46.6°C **B. Pt.** 60°C **Flash point** 30°C **Specific gravity** 0.61

Volatility v.p. 66 mmHg at 0°C ; v.den. 2.2

Occupational exposure

DE-MAK 0.005 ppm (0.013 mg m^{-3})

FR-VME 0.2 mg m^{-3}

US-TWA 0.005 ppm (0.013 mg m^{-3}) **US-STEL** 0.015 ppm (0.039 mg m^{-3})

UN No. 1380 **Conveyance classification** spontaneously combustible substance, toxic

Mammalian & avian toxicity

Acute data

LC_{50} (15 min) inhalation dog 92 mg m^{-3} (1).

LC_{50} (2 min) inhalation monkey 640 mg m^{-3} (1).

LD_{50} intraperitoneal rat 111 mg kg^{-1} (2).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).
Autoignition temp. 35°C.
Spontaneously flammable in contact with air.

References

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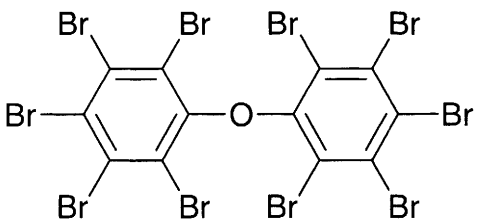
4. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

P24 pentabromophenyl ether



$C_{12}Br_{10}O$ **Mol. Wt.** 959.17 **CAS Registry No.** 1163-19-5

Synonyms decabromodiphenyl oxide; 1,1'-oxybis[2,3,4,5,6-pentabromobenzene]; decabromodiphenyl ether; bis(pentabromophenyl) ether

EINECS No. 214-604-9 **RTECS No.** KN 3525000

Uses Organic synthesis. Flame retardant.

Physical properties

M. Pt. 304°C **Partition coefficient** log P_{ow} 5.236 (1) **Volatility** v.p. 2 mmHg at 278°C
Solubility Water: <1 mg l^{-1}. Organic solvents: cotton seed oil, dimethyl sulfoxide

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 1092 g kg^{-1} (2).

Carcinogenicity and chronic effects
Liver adenomas detected in ♂ and ♀ rats administered pentabromophenyl ether in feed (5%) for 103 wk (3). Carcinogenic in ♂ and ♀ rats. Equivocal results obtained in ♂ mice (4).

Teratogenicity and reproductive effects
Reproductive capacity of rats not affected following 30-day dietary dose of 8 mg day^{-1} (1).

Metabolism and toxicokinetics
After administration of ^{14}C-labelled compound in feed to rats, all activity eliminated in faeces within 2 days (2).

Irritancy
Mild eye irritant in rabbits (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA97, TA1537 with and without metabolic activation negative (3).
Log P_{ow} exceeds European Union recommended limit of 3.0 (6).

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P25 pentachloroacetone

$$CCl_3C(O)CHCl_2$$

C_3HCl_5O **Mol. Wt.** 230.30 **CAS Registry No.** 1768-31-6

Synonyms pentachloropropan-2-one; 1,1,1,3,3-pentachloropropanone; pentachloro-2-propanone; 1,1,1,3,3-pentachloro-2-propanone

EINECS No. 217-188-7 **RTECS No.** UC 3300000

Physical properties

M. Pt. 2.1°C **B. Pt.** 192°C **Specific gravity** 1.69

Environmental fate

Abiotic removal
The degradation of pentachloropropan-2-one depended more on pH and temperature than on light; incubation in sea-water at pH 8 caused immediate disappearance of the compound (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 200 mg kg^{-1} (2).
LC_{50} (2 hr) inhalation mouse 450 mg m^{-3} (2).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA99 without metabolic activation positive; metabolic activation enhanced the effects of TA97 and TA98 but had no effect on the response of TA100. *Salmonella typhimurium* TA1535, TA1537, TA1538 negative. When the responses induced by the compound in solution with dimethyl sulfoxide or acetone

were compared, the effect due to the choice of solvent was minimal, except for the highest doses, at which the acetone solution produced the more toxic effect (3).
Saccharomyces cerevisiae D7 without metabolic activation gene conversion positive (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (5).

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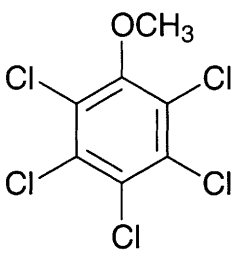
P26 2,3,4,5,6-pentachloroanisole



$C_7H_3Cl_5O$ **Mol. Wt.** 280.36 **CAS Registry No.** 1825-21-4

Synonyms pentachloromethoxybenzene; pentachlorophenyl methyl ether; methyl pentachlorophenate; methyl pentachlorophenyl ether

RTECS No. BZ 8820000

Physical properties

M. Pt. 107-109°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 318 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 281 mg kg^{-1} (1).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via gavage. Some evidence of carcinogenicity (increased incidence of chemically related neoplasms, malignant, benign or combined) in ♂ rats and ♂ mice, equivocal evidence in ♀ rats and no evidence in ♀ mice (2).

Teratogenicity and reproductive effects

♂ and ♀ rats were exposed to dietary levels of 0, 60, 200 or 600 ppm for 181 days through mating and pregnancy; daily intakes were 0, 4, 12 or 41 mg kg^{-1}. A reduction in foetal body weight and in crown-rump lengths of ♂ was

observed at 4 and 41 mg kg^{-1} day^{-1}; ♀ foetuses were unaffected. A significant dose-related decrease in the number of corpora lutea was seen at the highest level of exposure. Dams at the high-dose level showed evidence of toxicity gaining less weight during pregnancy than controls. The compound had no apparent effect on specific skeletal variations and lacked teratogenicity, but was embryolethal (3).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (4).
In vitro mouse lymphoma L5178Y tk^+/tk^- with metabolic activation positive (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (6).

Other comments

A metabolite of pentachlorophenol.

References

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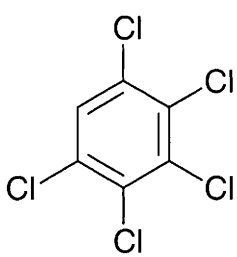
P27 pentachlorobenzene



C_6HCl_5 **Mol. Wt.** 250.34 **CAS Registry No.** 608-93-5

Synonyms QCB

EINECS No. 210-172-0 **RTECS No.** DA 6640000

Uses Formerly used as a pesticide to combat oyster drills. Chemical intermediate.

Physical properties

M. Pt. 84-87°C (98% pure) **B. Pt.** 275-277°C **Specific gravity** 1.609 **Partition coefficient** log P_{ow} 5.03 (1)
Volatility v.p. 3.9×10^{-5} mmHg at 25°C
Solubility Water: 0.2 mg l^{-1} at 22°C. Organic solvents: diethyl ether, hot ethanol

Occupational exposure

Supply classification highly flammable
Supply classification harmful
Supply classification dangerous for the environment
Risk phrases Highly flammable – Harmful if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R11, R22, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – In case of fire and/or explosion do not breathe fumes – If swallowed seek medical advice immediately and show this container or label – Do not mix with oxidising materials – 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, S41, S46, S50, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) sheephead minnow 0.8 mg l^{-1} (2).
LC_{50} (14 day) guppy 0.18 mg l^{-1} (3).
The behaviour of juvenile fathead minnows exposed to 130 μg l^{-1} for 6 days was affected and their lipid content was reduced when compared with controls (4).
NOEL (96 hr) sheepshead minnow 0.3 mg l^{-1} (2).
Mosquito fish (*Gambusia affinis*) exposed for 42 days to sublethal concentrations of pentachlorobenzene as low as 0.010μmol l^{-1} suffered growth rate reduction. EC_{50} and EC_{10} values for four halobenzenes (1,4-dibromobenzene, 1,2,3-trichlorobenzene, 1,2,4-tribromobenzene and pentachlorobenzene) were 0.067-3.4 and 0.00042-0.31 μmol, respectively (within the ranges 5 to 8% and 0.1 to 3.9% of the LC_{50} values) (5).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* 5.3 mg l^{-1} (6).
LC_{50} (21 day) *Daphnia magna* 0.24 mg l^{-1} (7).
EC_{50} (16 day) *Daphnia magna* 0.025 mg l^{-1} (8).
NOEC (16 day) *Daphnia magna* 0.01-0.1 mg l^{-1} (8).
EC_{50} *Selenastrum capricornutum* (96 hr) 6.63 mg l^{-1} (1).
EC_{50} (96 hr) *Skeletonema costatum* 1.98 mg l^{-1} (1).
EC_{50} (96 hr) *Mysidopsis bahia* 0.16 mg l^{-1} (1).

Bioaccumulation
Bioconcentration factor *Siderocapsa treubii* 16,000 (3).
Bioconcentration factor fathead minnow 8400 (4).

Environmental fate

Degradation studies
Usually resistant to microbial degradation (1).

Abiotic removal
May be abiotically degraded by photolysis and oxidative and hydrolytic reactions (1).

Adsorption and retention
Soil sorption coefficient 58,700 (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂, ♀ rat 1080-1125 mg kg^{-1} (9).
LD_{50} oral ♂, ♀ mouse 1175-1370 mg kg^{-1} (9).

Sub-acute and sub-chronic data
Oral rat (28 day) 0, 5, 50 or 500 mg kg $diet^{-1}$. No effect on body weight gain or food consumption. No clinical signs of toxicity or haematological aberrations. Increase in liver weight and mild thyroid changes at 500 mg kg^{-1}. Induction of hepatic enzymes in all treated rats (1).

Rats fed 500 ppm for 2 wk showed significant increases in the weight of the liver, in lipid components in liver and serum, and in levels of cytochrome P_{450} and cytochrome c reductase. Lipid peroxide levels in the liver were elevated and there was an increase in triglyceride and a decrease in vitamin E and glutathione peroxidase levels. Levels of vitamin A in the liver and serum also decreased (10).

Teratogenicity and reproductive effects

Gavage CD-1 mice (8-12 day gestation) treated with a dose predicted to induce a slight degree of maternal toxicity; no effect on viability or weight was observed (11).

Gavage rat (6-15 day gestation) 0, 5, 100 or 200 mg kg^{-1} day^{-1}. Dams showed a non-significant reduction in body weight gain at 200 mg kg^{-1}. There was an increased incidence of extra ribs at doses of ≥50 mg kg^{-1} and sternal defects and decreased foetal weight at 200 mg kg^{-1} (1).

Oral mouse 0, 50 or 100 mg kg^{-1} day^{-1}. There was an increase in the liver weight of dams at 50 and 100 mg kg^{-1} but no embryotoxic, foetotoxic or teratogenic effects (1).

♂ and ♀ rats were administered the compound in their diet from 4-5 wk of age, through mating and during gestation and lactation. Effects included maternal toxicity, tremors in suckling pups, decreases in pre-weaning growth rates and mortality of pups (1).

Metabolism and toxicokinetics

Metabolised primarily to pentachlorophenol by direct oxidation or to 2,3,4,5-tetrachlorophenol via an arene oxide intermediate. Other identified metabolites include 1,2,3,4- and 2,3,5,6-tetrachlorophenol in monkeys and 2,3,4,6-tetrachlorophenol, 2,4,6-trichlorophenol, 1,2,3,4-tetrachlorobenzene and tetrachlorohydroquinone in rats (1). Maximum levels of pentachlorobenzene and its principal metabolite pentachlorophenol were found in rat blood and liver 5-24 hr and 24-48 hr, respectively, after oral administration. The content of pentachlorobenzene was highest in adipose tissue, followed by kidney; spleen content was the lowest. Pentachlorophenol was not detected in adipose tissue and was at its highest level in liver. In blood, pentachlorobenzene was present mainly in red blood cells and pentachlorophenol mainly in plasma (12).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (13).

A CASE study reported that pentachlorobenzene is not mutagenic (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 μg l^{-1} (15).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (16).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (17).

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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

P28 pentachloroethane

CCl_3CHCl_2

C_2HCl_5 **Mol. Wt.** 202.29 **CAS Registry No.** 76-01-7

Synonyms pentalin; ethane pentachloride

EINECS No. 200-925-1 **RTECS No.** KI 6300000

Uses Solvent for oil and grease in metal cleaning. Chemical intermediate in some tetrachloroethylene processes.

Physical properties

M. Pt. -29°C **B. Pt.** 161-162°C **Flash point** 75°C **Specific gravity** 1.67 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.67 (1) **Volatility** v.p. 3.4 mmHg at 20°C ; v.den. 7.2
Solubility Water: 480 mg l^{-1} at 25°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (42 mg m^{-3})

UN No. 1669 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic, dangerous for the environment
Risk phrases Possible risk of irreversible effects – Toxic: danger of serious damage to health by prolonged exposure through inhalation – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R40, R48/23, R51/53)
Safety phrases Restricted to professional users – Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – 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, S23, S36/37, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 7.2 mg l^{-1} (2).
LC_{50} (96 hr) sheepshead minnow 116 mg l^{-1} (3).
LC_{50} (7 day) guppy 15 mg l^{-1} (4).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* 63 mg l^{-1} (5).
EC_{50} (5 min) *Photobacterium phosphoreum* 0.752 ppm Microtox test (6).

Bioaccumulation
Bioconcentration factor bluegill sunfish 67 (14-day exposure) (7).

Environmental fate

Abiotic removal

Photooxidation products may include phosgene and trichloroacetyl chloride (8).
Evaporation of 1 ppm solution from water: 50% after 48 min, 90% after >140 min (9,10).

Adsorption and retention

K_{oc} 117 (11).
K_{oc} 244 (12).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral dog 500 mg kg^{-1} (13).
LC_{Lo} (2 hr) inhalation mouse 35 mg m^{-3} (13).

Sub-acute and sub-chronic data

Exposure of rabbits to 100 mg m^{-3} for 3 hr day^{-1}, 6 × wk^{-1} for 8-10 months resulted in decreased antibody titres (1).
Inhalation cat (23 day) 1 mg l^{-1} 8-9 hr day^{-1}. No signs of toxicity were observed but liver, lung and kidney damage was found on autopsy (14).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (15).
National Toxicology Program tested rats and mice via gavage. Positive results were obtained in ♂ and ♀ mice, equivocal results in ♂ rats and negative results in ♀ rats (16).
Gavage rat (103 wk) 0, 75 or 150 mg kg^{-1} 5 × wk^{-1}. There was a dose-related trend in the incidence of diffuse chronic inflammation and tubular-cell adenomas of the kidneys in ♂ rats (1).
Gavage mice (103 wk) 0, 250 or 500 mg kg^{-1} 5 × wk^{-1}. There was a significant increase in the incidence of hepatocellular carcinomas and adenomas in treated ♀ mice. The incidence of hepatocellular carcinomas in low-dose ♂ was increased compared with controls; early mortality of high-dose ♂ prevented an evaluation of the life-time incidence of hepatocellular carcinomas, but there was in increased incidence compared with controls at wk 44 (1).

Metabolism and toxicokinetics

Following subcutaneous administration of 1.1-1.8 g kg^{-1} to ♀ mice, 12-51% of the dose was expired unchanged, 2-16% as trichloroethylene and 3-9% as tetrachloroethylene; trichloroethanol (16-32% of the dose) and trichloroacetic acid (9-18%) were the major urinary metabolites (1).

Irritancy

Eye and respiratory tract irritant (species unspecified) (14).

Genotoxicity

Salmonella typhimurium TA1535, TA1537, TA98, TA100 with and without metabolic activation negative (17).
In vitro Chinese hamster ovary cells, sister chromatid exchanges with metabolic activation positive, chromosomal aberrations with or without metabolic activation negative (18).
In vitro mouse lymphoma L5178Y tk^+/tk^- without metabolic activation positive (19).
Saccharomyces cerevisiae D7 with metabolic activation positive (14).

Other effects

Any other adverse effects

Oral administration of 525 mg kg^{-1} pentachloroethane to ♂ rats induced hepatic cytochrome P_{450} content and microsomal epoxide hydrolase activities (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (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).

Other comments

An intermediate product in the conversion of trichloroethylene into tetrachloroethylene (1).
Irritant; narcotic (23).
Metabolism reviewed (24).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (25).

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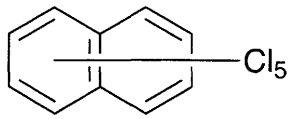
P29 pentachloronaphthalene



$C_{10}H_3Cl_5$ **Mol. Wt.** 300.40 **CAS Registry No.** 1321-64-8

EINECS No. 215-320-8 **RTECS No.** QK 0300000

Uses Used in electric wire insulation. Lubricant additive.

Physical properties

M. Pt. 120°C **B. Pt.** 326-371°C **Volatility** v.p. <1 mHg at 20°C

Solubility Organic solvents: benzene, chloroform

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable dust fraction)

FR-VME 0.5 mg m^{-3}

SE-LEVL 0.2 mg m^{-3} **SE-STEL** 0.6 mg m^{-3}

US-TWA 0.5 mg m^{-3}

Supply classification harmful, dangerous for the environment

Risk phrases Harmful in contact with skin – 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) – This material and its container must be disposed of in a safe way – 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, S35, S60, S61)

Mammalian & avian toxicity

Sub-acute and sub-chronic data

9/10 rats fed a mixture of pentachloronaphthalene and hexachloronaphthalene at a rate of 3 g day^{-1} for 1 month died. All animals lost weight, were sick and showed severe liver injury. When a mixture of tetrachloronaphthalene and pentachloronaphthalene was given to rats at a rate of 0.5 mg day^{-1} for 2 months, some sickness and mortality and liver injury were observed (1).

Rats exposed to 1.16 mg m^{-3} of a mixture of pentachloronaphthalene and hexachloronaphthalene 16 hr day^{-1} for *up to* 4.5 months suffered liver injury; exposure to 8.88 mg m^{-3} resulted in some mortality, poor growth and severe liver injury (1).

Cattle fed 1 mg kg^{-1} of chloronaphthalenes for 7 days showed signs of intoxication 12 days after administration began. These included excessive lachrymation and salivation, nasal discharge, emaciation, diarrhoea and hyperkeratosis of the skin. Lesions of the oesophageal mucosa, cirrhosis of the liver, cystic swelling of the gallbladder mucosa and extrahepatic bile ducts were found at necropsy (1).

Carcinogenicity and chronic effects

Chlorinated naphthalenes are considered to be questionable carcinogens which can cause tumours of the liver (2).

Metabolism and toxicokinetics

Hydroxylation and hydroxylation/dechlorination are common metabolic pathways in rats (1).

Irritancy

Severe irritant by ingestion, inhalation and skin contact (species unspecified) (2).

Other effects

Other adverse effects (human)

Chlorinated naphthalenes have a similar action on the body as chlorinated biphenyls. Chief effects are chloracne of the skin and acute yellow atrophy of the liver (2).

Any other adverse effects

Following ingestion of chloronaphthalenes, chickens developed a thick keratinised layer on the skin of the neck, and the gallbladder, liver, pancreas and kidney were also affected (duration unspecified) (1).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (4).

Other comments

Emits toxic chloride fumes when heated to decomposition (2).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).

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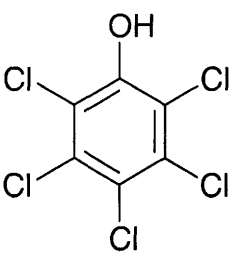
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

P30 pentachlorophenol



C_6HCl_5O **Mol. Wt.** 266.34 **CAS Registry No.** 87-86-5

Synonyms PCP; penchlorol

EINECS No. 201-778-6 **RTECS No.** SM 6300000

Uses Insecticide, fungicide and non-selective contact herbicide. Wood impregnant. Used in synthesis of sodium pentachlorophenate.

Physical properties

M. Pt. 188-191°C **B. Pt.** 309-310°C (decomp.) **Specific gravity** 1.978 at 22°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.32 at pH 7.2 (1) **Volatility** v.p. 1.2×10^{-4} mmHg at 100°C ; v.den. 9.2
Solubility Water: 80 mg l^{-1} at 20°C. Organic solvents: soluble in most organic solvents

Occupational exposure

FR-VME 0.5 mg m^{-3}
JP-OEL 0.5 mg m^{-3}
SE-LEVL 0.5 mg m^{-3} **SE-STEL** 1.5 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. 3155 **HAZCHEM Code** 2X **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, respiratory system and skin – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R26, R36/37/38, R40, 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) – Not recommended for interior use on large surface areas – 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, S52, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (2 day) rainbow trout 0.093 mg l^{-1} (2).
LC_{50} (96 hr) guppy 0.77-0.97 mg l^{-1} (3).
LC_{50} (96 hr) fathead minnow 0.47 mg l^{-1} (4).
LOEC sheepshead minnow 0.088-0.389 mg l^{-1} (5,6).
LC_{50} (6 hr) red abalone 1.6 mg l^{-1}, NOEL 0.8 mg l^{-1} (flowing seawater) (7).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia pulex* 2 mg l^{-1} (8).
LC_{50} (21 day) *Daphnia magna* 0.8 mg l^{-1} (9).
EC_{50} *Daphnia magna* 0.23 mg l^{-1} (9).
NOEC *Daphnia magna* 0.18 mg l^{-1} (10).
EC_{50} rotifer *Brachionus calyciflorus* 1.3 mg l^{-1} (11).
EC_{50} (96 hr) green algae 0.09 mg l^{-1} (12).
EC_{50} (30 min) *Photobacterium phosphoreum* 0.519 ppm Microtox test (13).

Bioaccumulation
Confirmed to be non- or low-accumulative (14).
Bioconcentration factor goldfish 475 (15).
Bioconcentration factor duck mussel 81-461; water temperature and exposure concentration did not affect this value (16).
Bioconcentration factor goldfish, fathead minnow, golden orfe 56, 776, 1047, respectively (17).
Accumulation in golden orfe and zebra fish decreased as pH and water hardness increased (18).

Environmental fate

Degradation studies
Complete decomposition in soil suspensions takes >72 days (19).
Three Gram-negative bacterial strains able to use pentachlorophenol (PCP) as a sole carbon and energy source

were isolated from Alfisol columns under permanent pasture polluted by repeated additions of PCP (7 mg l^{-1}) to levels of 102 and 510 mg kg^{-1} to simulate a dynamic diffuse pollution. In liquid degradation tests on these bacteria *Acinetobacter* C2 and C3 degraded 60% of PCP within 26 days, whereas *Pseudomonas* Si degraded only 25% (20).

Abiotic removal

Photolysis $t_{1/2}$ 3.5 hr at pH 7.3 and ~100 hr at pH 3.3, indicating an increase in rate of photodecomposition with an increase in pH (1).

The photocatalytic degradation of pentachlorophenol in the presence of an aqueous suspension of TiO_2 irradiated with near-UV light was studied. The toxicity of the transient species was compared with that observed for the parent compound by monitoring the inhibitory effect on bacterial respiration (*Escherichia coli*). 2,3,5,6-Tetrachloro-1,4-hydroquinone, 2,3,5,6-tetrachlorophenol and 2,3,5,6-tetrachloro-1,4-benzoquinone were found to be more toxic than the parent compound (21).

Photolysis (1 kW UV reactor) in dilute aqueous solution (0.15 mM) $k_1 = 0.015$ min^{-1}. The toxicity of the solution, as measured by bacterial and 96 hr fathead minnow toxicity tests, decreased as the concentration of pentachlorophenol or the total organic chlorine fell, indicating that UV treatment of pentachlorophenol under the conditions used in this study either does not generate significant levels of acutely toxic intermediates, or that any toxic intermediates are rapidly degraded (22).

Mammalian & avian toxicity

Acute data

LD_{50} oral duck 380 mg kg^{-1} (23).
LD_{50} oral rat 210 mg kg^{-1} (24).
LD_{50} oral rat 50 mg kg^{-1} (23).
LD_{Lo} oral human 29 mg kg^{-1} (23).
LC_{50} (duration unspecified) inhalation rat 355 mg m^{-3} (25).
LD_{50} dermal rat 105 mg kg^{-1} (23).
LD_{Lo} dermal rabbit 40 mg kg^{-1} (23).

Sub-acute and sub-chronic data

No deaths occurred amongst dogs and rats receiving 3.9-10 mg day^{-1} for 70-190 days (24).

Carcinogenicity and chronic effects

National Toxicity Program tested mice via food. Clear evidence of carcinogenicity (increased incidence of dose-related malignant and benign neoplasms) in ♂ mice, some evidence (increased incidence of chemically related neoplasms, malignant or benign or combined) in ♀ mice (26).

Subcutaneous mouse (74 wk) 46.4 mg kg^{-1} in corn oil. The incidence of hepatomas in ♂ (C57BL/6xC3H/Anf)F1 mice was increased over that in controls; no increase was seen with (C57BL/6xAkr)F1 mice of either sex (27).

In a 24-month dietary study, ♂ and ♀ rats were given 0, 1, 3, 10 or 30 mg kg^{-1} 1 × day^{-1}. The mean body weight of ♂ rats was not significantly altered after receiving the diet, whereas the mean body weight of ♀ rats receiving the highest dose level was significantly less than that of the controls. There was no increase in tumour incidence in males or females, at 30 mg kg^{-1} day^{-1} (27).

Teratogenicity and reproductive effects

Rats given 5-50 mg kg^{-1} of purified or commercial grade pentachlorophenol day^{-1} during days 6-15 of pregnancy showed dose-related increases in signs of embryotoxicity and foetotoxicity such as resorptions, subcutaneous oedema, dilated ureters and anomalies of the skull, ribs, vertebrae and sternebrae (27).

In ♂ and ♀ rats exposed to dietary levels of 0, 60, 200 or 600 ppm for 181 days, through mating and pregnancy, the daily intake was 0, 4, 13 or 43 mg kg^{-1}, respectively. Rats consumed more food during pregnancy than control animals but gained less weight; 43 mg kg^{-1} day^{-1} was embryolethal and foetuses at lower dose levels exhibited dose-related decreases in body weight. A reduction in crown-rump length and an increase in foetal skeletal variations were seen at 13 mg kg^{-1} day^{-1} (28).

♀ Mink fed 1 mg kg^{-1} day^{-1} from before mating until weaning suffered decreased fertility compared with controls (29).

Metabolism and toxicokinetics

In mice, excretion occurs mainly in urine with the rest in faeces (30).

Free pentachloroethane and tetrachlorohydroquinone are the principal urinary metabolites in mice and rats; the glucuronide conjugates of both metabolites have also been found in rats (31).

Tetrachlorohydroquinone was not found in the urine of *Macaca mulatta* monkeys (32).

Metabolites identified in rat urine include: 2,3,4,5-tetrachlorophenol, 2,3,4,6-tetrachlorophenol, 2,3,5,6-tetrachlorophenol, tetrachlorocatechol, tetrachlororesorcinol, tetrachlorohydroquinone, trichlorohydroquinone, trichloro-1,4-benzoquinone, and tetrachloro-1,4-benzoquinone (33).

Irritancy

Irritating to skin, eyes and mucous membranes (species unspecified) (24).

Dermal rabbit (24 hr) 10 mg caused mild irritation (34).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (35).

Drosophila melanogaster sex-linked recessive lethal assay negative (27).

In vitro Chinese hamster ovary cells without metabolic activation some increase in sister chromatid exchange, with metabolic activation chromosomal aberrations positive (36).

The metabolite of pentachlorophenol, *p*-tetrachlorohydroquinone, is more toxic to Chinese hamster ovary cells than pentachlorophenol causing DNA single-strand breaks and/or alkali-labile sites at concentrations of 2-10 μg ml^{-1} (37).

Other effects

Other adverse effects (human)

Nine sawmill workers died following exposure to treated wood (38).

Extended periods of exposure resulted in persistent chloracne and nervous system and liver disorders (39).

Penetration through skin was 16% with aqueous based preparations and 62% with diesel oil preparations. The results for aqueous penetration are much higher than the EPA estimate of 1%, indicating a considerably higher risk of dermal penetration (40).

Pentachlorophenol acts on mitochondrial electron transport, uncoupling oxidative phosphorylation and thus increasing metabolic rate and heat generation. Acute poisoning causes changes in breathing, blood pressure and urinary output, high temperature, weakness, headache, vomiting, nausea and abdominal pain; in severe cases there is a rapidly progressive coma (41).

Hyperthermia, profuse sweating and rapid onset of morbidity and early death are associated with acute pentachlorophenol exposure (1).

Any other adverse effects

Inhibits mitochondrial ATP formation in red abalone (42).

Legislation

Included in Schedule 5 and 6 (Release into Water/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (43).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (44).

WHO Class Toxicity Class Ib (45).

EPA Toxicity Class II (24).

Other comments

Considered to have endocrine disruptive effects (46).

Odour threshold 1.6 mg l^{-1} and olfactory threshold 0.03 mg l^{-1} (both in water) (1).

Toxicity decreases as the hardness of the water increases (47).

Occurrence in the environment reviewed (48).

Production, use, occurrence and analysis reviewed (49).
Toxic effects and fatalities due to occupational and accidental exposure reviewed (50).
Health hazards from exposure to pentachlorophenol and related dioxins reviewed (51).
Reviews on human health effects, experimental toxicology, physico-chemical properties are listed (52).

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P31 1,1,2,2,3-pentachloropropane

$CH_2ClCCl_2CHCl_2$

$C_3H_3Cl_5$ **Mol. Wt.** 216.32 **CAS Registry No.** 16714-68-4
EINECS No. 240-766-5 **RTECS No.** TZ 5550000

Physical properties

B. Pt. 196°C **Specific gravity** 1.6

Mammalian & avian toxicity

Acute data

LD_{50} rabbit, guinea pig, mouse 500-560 mg kg^{-1} (route unspecified) (1).
LD_{50} rat 819 mg kg^{-1} (route unspecified) (1).

Sub-acute and sub-chronic data

Inhalation rats (4 wk) 0, 100, 300, 600 or 900 ppm 6 hr day^{-1}, 5 day wk^{-1}. Deaths occurred at ≥300 ppm and liver, kidney and ovary weights were affected (2).

Teratogenicity and reproductive effects

Inhalation rats (pre-mating, mating or gestation) 0, 5 or 15 ppm 6 hr day^{-1}, 5 day wk^{-1}; no treatment-related effects were seen (2).

Irritancy

Exposure to vapours caused significant irritation of mucosal tissue in rats (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 μg l^{-1} (3).

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P32 1,1,2,3,3-pentachloropropane

$$CHCl_2CHClCHCl_2$$

$C_3H_3Cl_5$ **Mol. Wt.** 216.32 **CAS Registry No.** 15104-61-7

Physical properties

B. Pt. 198-200°C **Specific gravity** 1.6086
Solubility Organic solvents: chloroform, diethyl ether, ethanol

Genotoxicity

Salmonella typhimurium TA100, TA1535 without metabolic activation positive (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (2).

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P33 pentadecylamine

$$CH_3(CH_2)_{14}NH_2$$

$C_{15}H_{33}N$ **Mol. Wt.** 227.43 **CAS Registry No.** 2570-26-5
Synonyms 1-pentadecanamine; 1-aminopentadecane; monopentadecylamine; *n*-pentadecylamine; 1-pentadecylamine
EINECS No. 219-912-7 **RTECS No.** RZ 2120000

Physical properties

M. Pt. 36-39°C **B. Pt.** 299-301°C **Flash point** >110°C (closed cup)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 520, 660 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation rat 900 mg m^{-3} (1).
LC_{50} (2 hr) inhalation mouse 2400 mg m^{-3} (1).

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P34 1,3-pentadiene

$$CH_2=CHCH=CHCH_3$$

C_5H_8 **Mol. Wt.** 68.12 **CAS Registry No.** 504-60-9

Synonyms 1-methylbutadiene

EINECS No. 207-995-2 **RTECS No.** RZ 2464000

Uses Monomer in plastics. Maleic acid intermediate.

Physical properties

M. Pt. –87.5°C **B. Pt.** –34°C **Specific gravity** 0.6760 at 20°C with respect to water at 4°C

Solubility Water: >341 mg l^{-1} at room temperature. Organic solvents: acetone, benzene, diethyl ether, ethanol

Ecotoxicity

Bioaccumulation

Not thought to bioconcentrate in aquatic organisms; based on water solubility and vapour pressure.

Bioconcentration factors of <23 to 18 have been obtained by regression analysis (1).

Detected in clams and oysters at concentrations of 3.2 and 1.4 ppb wet weight, respectively, in a Louisiana lake (2).

Environmental fate

Abiotic removal

The estimated Henry's Law constant (6.89×10^{-2} atm $mmole^{-3}$ at 25°C) and known vapour pressure (380-411 mmHg at 25°C) suggest rapid volatilisation from soil (3,4).

In model river 1 m deep flowing at 1 m sec^{-1} with a wind speed of 3 m sec^{-1} the estimate $t_{1/2}$ for volatilisation is 2.4 hr (1,5).

In distilled water direct photochemical degradation did not occur (6,7).

In the atmosphere expected to undergo a rapid gas-phase reaction with photochemically produced hydroxyl radicals and ozone. $t_{1/2}$ for the former 3.8 hr and for the latter 5.2 hr (5,8,9).

Gas-phase reaction with nitrate radicals may be important in urban areas or in polluted atmospheres as night time degradation (10).

May be removed from the atmosphere by moisture deposition, however it would be expected to be rapidly revolatilised (11).

Adsorption and retention

Expected to be high to moderately mobile in soil based on the estimated soil adsorption coefficients ranging from <177 to 140 (1,12).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 18 mg kg^{-1} (13).

Other comments

Released to the atmosphere by biomass combustion, synthetic rubber manufacture and tobacco smoke (14).

In car exhaust (15).

In waste incinerator emissions (16).

Occupational exposure is likely to be via inhalation. Cigarette smoke or wood fire smoke inhalation may be a route of exposure for the general public (14).

Uses reviewed (17).

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P35 pentaerythritol

$$C(CH_2OH)_4$$

$C_5H_{12}O_4$ **Mol. Wt.** 136.15 **CAS Registry No.** 115-77-5

Synonyms 2,2-bis(hydroxymethyl)-1,3-propanediol; tetrahydroxymethylmethane; tetrakis(hydroxymethyl)methane; tetramethylolmethane; methanetetramethylol; Metab-Auxil; Pentek; Penetek

EINECS No. 204-104-9 **RTECS No.** RZ 2490000

Uses In synthetic resins, drugs, explosives and insecticides, and in paint and varnish industries.

Physical properties

M. Pt. 255-259°C **B. Pt.** 276°C at 30 mmHg **Specific gravity** 1.38 at 25°C with respect to water at 4°C
Volatility v.den. 4.70
Solubility Water: 55.6 g l^{-1} at 15°C. Organic solvents: ethanol, ethylene glycol, formamide, glycerol

Occupational exposure

FR-VME 10 mg m^{-3}
SE-LEVL 5 mg m^{-3}
UK-LTEL 4 mg m^{-3} (respirable dust); 10 mg m^{-3} (total inhalable dust) **UK-STEL** 20 mg m^{-3} (total inhalable dust)
US-TWA 10 mg m^{-3}

Ecotoxicity

Bioaccumulation
Confirmed to be non- or low-accumulative (1).

Environmental fate

Degradation studies

COD 1.23 g O_2 g^{-1}; ThOD 1.3 g O_2 g^{-1} (2).

Trickling filter followed by activated sludge 95-96% BOD removal (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 25,500 mg kg^{-1} (4).

LD_{50} oral guinea pig 11,300 mg kg^{-1} (4).

Lethal doses caused ataxia, tremors and loss of righting reflex in mice and guinea pigs. Necropsies showed no pathological changes attributable to the compound (4).

Rats exposed by inhalation to 11 g m^{-3} for 6 hr showed no effects (4).

Rats survived oral doses up to 16,000 mg kg^{-1}, but >5000 mg kg^{-1} caused diarrhoea for 12-36 hr (4).

Sub-acute and sub-chronic data

Rats fed 0.2, 1.0 and 5.0% in a dry diet for 90 days. At the 5% level severe diarrhoea, enlarged caecums and increased caecum to body weight ratios were observed. No histologic changes in the caecum were detected (4).

Rats exposed to 8 g m^{-3} of pentaerythritol 6 hr day^{-1} for 90 days. No effects were observed (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).

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P36 pentaerythritol tetraacrylate

$$C(CH_2OCOCH{=}CH_2)_4$$

$C_{17}H_{20}O_8$ **Mol. Wt.** 352.34 **CAS Registry No.** 4986-89-4

Synonyms 2-propenoic acid, 2,2-bis[[(1-oxo-2-propenyl)oxy]methyl]-, 1,3-propanediyl ester; tetramethylolmethane tetracrylate; acrylic acid, tetraester with pentaerythritol; acrylic acid, neopentanetetrayl ester

EINECS No. 225-644-1

Physical properties

M. Pt. 15-18°C **Flash point** >110°C **Specific gravity** 1.190

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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear eye/face protection (S2, S26, S39)

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Repeated skin application did not cause tumours in mice (1).

Irritancy
Irritating to the eyes (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3).

References

1. DePass, L. R. et al *J. Toxicol. Environ. Health* 1985, **16**(1), 55-60.
2. *Chemical Safety Data Sheets* 1992, **3**, 179-181.
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

P37 pentaerythrityl tetrabromide

$$(BrCH_2)_4C$$

$C_5H_8Br_4$ **Mol. Wt.** 387.73 **CAS Registry No.** 3229-00-3

Synonyms 1,3-dibromo-2,2-bis(bromomethyl)propane; pentaerythritol tetrabromide; pentaerythrityl bromide; tetra(bromomethyl)methane; tetrabromoneopentane; tetrakis(bromomethyl)methane

EINECS No. 221-764-3

Uses Chemical intermediate.

Physical properties

M. Pt. 163°C **B. Pt.** 305-306°C **Specific gravity** 2.596 at 15°C
Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol, toluene

Ecotoxicity

Bioaccumulation
No or low bioaccumulation (1).

References

1. *JETOC Newsletter No. 5* 1987, Japan Chemical Industry Ecology Toxicology and Information Center, Tokyo, Japan

P38 pentaethylenehexamine

$$H_2N(CH_2CH_2NH)_4CH_2CH_2NH_2$$

$C_{10}H_{28}N_6$ **Mol. Wt.** 232.37 **CAS Registry No.** 4067-16-7

Synonyms 3,6,9,12-tetraazatetradecane-1,14-diamine; PEHA

EINECS No. 223-775-9 **RTECS No.** RZ 2680000

Physical properties

M. Pt. -30°C **B. Pt.** 188-193°C at 0.5 mmHg **Flash point** >110°C **Specific gravity** 0.950
Volatility v.den. 0.950

Occupational exposure

Supply classification corrosive, dangerous for the environment
Risk phrases Causes burns – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R34, R43, R50/53)
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) – 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, S26, S36/37/39, S45, S60, S61)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1600 mg kg^{-1} (1).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3).

References

1. Graysom, M. et al (Eds.) *Kirk-Othmer Encyclopedia of Chemical Technology* 3rd ed., 1978, Wiley, New York, NY, USA.
2. Mortelmans, K. et al *Environ. Mutagen.* 1986, 8(Suppl. 7), 1-119.
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P39 pentane

$$CH_3(CH_2)_3CH_3$$

C_5H_{12} **Mol. Wt.** 72.15 **CAS Registry No.** 109-66-0

Synonyms *n*-pentane; Skellysolve A

EINECS No. 203-692-4 **RTECS No.** RZ 9450000

Uses Solvent. Constituent of motor fuel and an intermediate in chemical synthesis.
Occurrence Constituent of petroleum.

Physical properties

M. Pt. –129.7°C **B. Pt.** 36.1°C **Flash point** –49.44°C (closed cup) **Specific gravity** 0.626 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.39 **Volatility** v.p. 400 mmHg at 18.5°C ; v.den. 2.48
Solubility Water: 37 μg l^{-1}. Organic solvents: miscible diethyl ether, ethanol

Occupational exposure

DE-MAK 1000 ppm (3000 mg m^{-3})
FR-VME 600 ppm (1800 mg m^{-3})
JP-OEL 300 ppm (880 mg m^{-3})
SE-LEVL 600 ppm (1800 mg m^{-3}) **SE-STEL** 750 ppm (2000 mg m^{-3})
US-TWA 600 ppm

UN No. 1265 **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 – Do not empty into drains – Take precautionary measures against static discharges (S2, S9, S16, S29, S33)

Ecotoxicity

Fish toxicity
Coho salmon (96 hr) no mortalities at 100 ppm in synthetic sea water at 8°C (1).

Environmental fate

Degradation studies
Biodegradation 0% after 192 hr at 13°C; initial concentration 0.11 μg l^{-1} (2).

Abiotic removal
31.4% photooxidised to CO_2 by UV light in 24 hr in aqueous medium at 50°C (3).

Mammalian & avian toxicity

Acute data
LC_{50} inhalation mice 128,200 ppm (in air) (4).
LD_{50} intravenous mouse 446 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Rat exposed to 3000 ppm 12 hr day^{-1} 7 days wk^{-1} for 16 weeks showed neither signs of abnormal neurobehavioural effects nor signs of neurotoxicity (6,7).

Metabolism and toxicokinetics
2-Pentanol found to be a major metabolite in rat and rabbit microsomes (8).

Other effects

Other adverse effects (human)

Penetrates skin (9).

Skin defatting agent (10).

Any other adverse effects

It partitions readily into adipose tissue (9).

Legislation

Log P_{ow} exceeds European Union recommended limit of 3.0 (11).

Other comments

Toxicity of pentane reviewed (12).

10 minute exposure human 5000 ppm, no symptoms observed (13).

References

1. Morrow, J. E. EPA-660/3-73-018, Jan 1974.
2. Jamison, V. W. et al *Biodegrad. of High-Octane Gasoline Proc. 3rd Int. Biograd. Symp.* 1976, Appl. Sci. Publ.
3. Knoevenagel, K. et al *Arch. Environ. Contam. Toxicol.* 1976, **4**, 324-333.
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9. Perbellini, L. et al *Br. J. Ind. Med.* 1985, **112**, 162.
10. Kow, L. K. *n-Pentane* in Ethel Browning's *Toxicity and Metabolism of Industrial Solvents* 2nd Ed., 1987, 279-286.
11. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
12. Kirwin, L. J. et al *J. Soc. Cosmet. Chem.* 1980, **31**, 367.
13. Patty, F. A. et al *US Bureau of Mines Report of Investigation* 1929, 1-10

P40 2,3-pentanedione

$$CH_3C(O)C(O)CH_2CH_3$$

$C_5H_8O_2$ **Mol. Wt.** 100.12 **CAS Registry No.** 600-14-6

Synonyms pentane-2,3-dione; acetylpropionyl

EINECS No. 209-984-8 **RTECS No.** SA 1850000

Occurrence In foodstuffs, including crab, crayfish, blackberries, meat aromas, mango aroma. In cigarette smoke.

Physical properties

M. Pt. -52°C **B. Pt.** 110-112°C **Flash point** 18°C **Specific gravity** 0.957

Occupational exposure

UN No. 2310 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3000 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (1).

References

1. *Food Cosmet. Toxicol.* 1979, **17**, 699

P41 1-pentanol

$$CH_3CH_2CH_2CH_2CH_2OH$$

$C_5H_{12}O$ **Mol. Wt.** 88.15 **CAS Registry No.** 71-41-0

Synonyms amyl alcohol; pentyl alcohol; *n*-amyl alcohol; Amylol; Pentasol; *n*-butylcarbinol

EINECS No. 200-752-1 **RTECS No.** SB 9800000

Uses An organic solvent and petroleum additive.

Physical properties

M. Pt. –79°C **B. Pt.** 137.5°C **Flash point** 38°C **Specific gravity** 0.824 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} 1.51 **Volatility** v.p. 2 mmHg at 25°C ; v.den. 3.0
Solubility Water: 2.7 g 100 ml^{-1} at 22°C. Organic solvents: soluble in acetone; miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1105 **HAZCHEM Code** 2[redacted]E (flash point <23°C, initial boiling point ≤35°C) **HAZCHEM Code** 3[redacted] (flash point ≥23°C, ≤61°C, initial boiling point >35°C) **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) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 470 mg l^{-1} (1).
LC_{50} (96 hr) zebra fish 530 mg l^{-1} (2).
LC_{50} (48 hr) ide 479-492 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 440 mg l^{-1} (3).
EC_{50} (5 min, 30 min) *Photobacterium phosphoreum* 394 mg l^{-1} Microtox test (4).
Cell multiplication inhibition test, *Pseudomonas putida* 220 mg l^{-1}, *Microcystis aeruginosa* 17 mg l^{-1} and *Scenedesmus* sp. toxic at 280 mg l^{-1} (5,6).
LC_{50} (96 hr) *Nitocra spinipes* 440 mg l^{-1} (7).
Aerobic heterotrophs, *Nitrosomonas* sp. and methanogens were tested for toxicity to amyl alcohol. LC_{50} *Nitrosomonas* sp. 520 mg l^{-1}, methanogens 4700 mg l^{-1} (1).

Environmental fate

Degradation studies

Desulfovibrio vulgaris Marburg DSM 2119 metabolised 1-pentanol to the corresponding acids in the presence of sulfate (8).

Abiotic removal

Air flotation, 89% removal occurred after chemical addition (9).
Absorbability 0.155 g g^{-1} carbon, 71.8% reduction (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2700-3030 mg kg^{-1} (11,12).
LC_{50} (6 hr) inhalation mouse, rat 14,000 mg m^{-3} (13).
LD_{50} dermal rabbit 3600 mg kg^{-1} (13).
Probable human oral lethal dose 0.5-5 mg kg^{-1} (14).

Teratogenicity and reproductive effects

Inhalation rat (1-19 days gestation) 14,000 mg m^{-3} 7 hr day^{-1} reduced maternal feed intake and weight gain, but there were no decreases in foetal weights and no teratogenic effects (15).

Irritancy

Showed severe irritancy in the *in vitro* bovine corneal opacity-permeability assay. This was in accordance with the result obtained by the Draize eye irritation test (16).

Genotoxicity

Single intragastric administration to rat bone marrow of (0.2 LD_{50}) caused chromosomal aberrations and polyploidy (17).

Other effects

Other adverse effects (human)

Narcotic in humans. Symptomatic effects include headache, nausea, depression, diarrhoea, coughing and irritability (13).

Any other adverse effects

Sedative effects on the central nervous system reported (species unspecified) (18).

Other comments

Decomposition product of 15-hydroperoxyeicosatetranoic acid (14).

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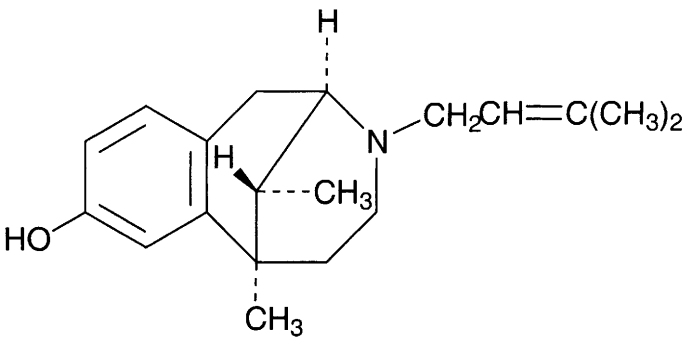
P42 pentazocine



$C_{19}H_{27}NO$ **Mol. Wt.** 285.43 **CAS Registry No.** 359-83-1

Synonyms (2α,6α,11*R**)-1,2,3,4,5,6-hexahydro-6,11-dimethyl-3-(3-methyl-2-butenyl)-2,6-methano-3-benzazocin-8-ol ; 2-(3,3-dimethylallyl)cyclazocine; Fortalgesic; Fortral; Pentagin; Sosigon; Talwin; Win 20228

EINECS No. 206-634-6 **RTECS No.** PB 8750000

Uses Narcotic analgesic.

Physical properties

M. Pt. 145.4-147.2°C

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling >100, 562 mg kg^{-1}, respectively (1).

LD_{50} oral mouse, rat 205, 1110 mg kg^{-1}, respectively (2,3).

LD_{50} intraperitoneal mouse 85 mg kg^{-1} (4).

LD_{50} subcutaneous rat, mouse 61, 80 mg kg^{-1}, respectively (3).

Other effects

Other adverse effects (human)

Effects of use include central nervous system and respiratory depression. cough suppression, and sedation and effects on smooth muscle such as gastro-intestinal motility (5).

Side-effects include nausea and vomiting, light headedness, dizziness, sweating, hallucinations, hypertension and tachycardia (6).

Produces physical dependence, but with less severe withdrawal symptoms than morphine (7).

A man taking 50-75 mg every 4 hr for 8 days suffered toxic epidermal necrolysis attributed to pentazocine (8).

References

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P43 1-pentene

$$CH_3(CH_2)_2CH{=}CH_2$$

C_5H_{10} **Mol. Wt.** 70.13 **CAS Registry No.** 109-67-1

Synonyms α-*n*-amylene; propylethylene

EINECS No. 203-694-5

Occurrence In coal tar.

Physical properties

M. Pt. –165.2°C **B. Pt.** 29.9-30.1°C **Flash point** –51.1°C **Specific gravity** 0.6429 at 20°C with respect to water at 4°C **Volatility** v.p. 400 mmHg at 12.8°C

Solubility Organic solvents: miscible with benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1108 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid

Environmental fate

Degradation studies

Oxidised to the corresponding 1,2-epoxides by methane-oxidising bacteria (H-2 type 1) (1).

Abiotic removal

Photodegraded by hydroxyl radicals in air; hydroxyl radical rate constant K_{OH} 3.19×10^{11} cm^3 $molecule^{-1}$ sec^{-1} (2).

References

1. Imai, T. et al *Appl. Environ. Microbiol.* 1986, **52**(6), 1403-1406.
2. Hodson, J. *Chemosphere* 1988, **17**(12), 2339-2348

P44 3-penten-2-one

$$CH_3CH{=}CHC(O)CH_3$$

C_5H_8O **Mol. Wt.** 84.12 **CAS Registry No.** 625-33-2

Synonyms ethylideneacetone; methyl 1-propenyl ketone

EINECS No. 210-888-3 **RTECS No.** SB 3850000

Physical properties

B. Pt. 122-124°C **Flash point** 21°C **Specific gravity** 0.862

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3730 mg kg^{-1} (1).

LC_{Lo} (4 hr) inhalation rat 250 ppm (2).

LD_{50} dermal rabbit 500 mg kg^{-1} (3).

Irritancy

Dermal rabbit (24 hr) 10 mg had an irritating effect (3).

References

1. *Union Carbide Data Sheet* 20 July 1967, Industrial Medicine and Toxicology Dept., Union Carbide Corporation, 270 Park Avenue, New York, NY, USA.
2. *J. Ind. Hyg. Toxicol.* 1949, **31**, 343.
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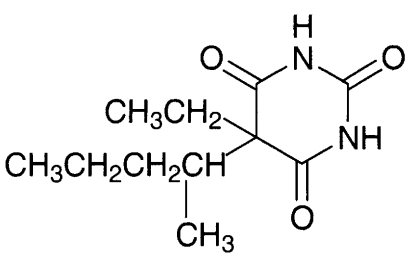
P45 pentobarbitone



$C_{11}H_{18}N_2O_3$ **Mol. Wt.** 226.28 **CAS Registry No.** 76-74-4

Synonyms 5-ethyl-5-(1-methylbutyl)-2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione; 5-ethyl-5-(1-methylbutyl)barbituric acid; pentobarbituric acid; Ethaminal; Neodorm; Rivadorm; Nembutal

EINECS No. 200-983-8 **RTECS No.** CQ 5775000

Uses Hypnotic, sedative. Anaesthetic premedication. Administered parentally as anticonvulsant.

Physical properties

M. Pt. 130°C **Partition coefficient** log P_{ow} 2.10
Solubility Organic solvents: ethanol, carbon tetrachloride, chloroform, diethyl ether

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 170 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 123 mg kg^{-1} (2).
LD_{50} intravenous rabbit, dog, mouse 33-65 mg kg^{-1} (1,3).
♂ Beagle dogs receiving 1 oral dose of 0.3, 1, 3 or 15 mg kg^{-1} and examined 1, 4 and 24 hr after administration showed hyperkinesia, abnormal behaviour, tremor, dose-dependent ataxic effects and a decreased response rate and sedative effect at the highest dose (4).
0.05 ml of a 50 mg ml^{-1} solution of pentobarbital sodium injected directly into the livers of Sprague-Dawley rats, killed 15, 30 or 45 minutes after the injection caused massive haemorrhagic necrosis of the liver and focal necrosis accompanied by inflammatory cell infiltration in rats killed after 30 or 45 min. A significant increase in the bilirubin level was also noted (5).

Teratogenicity and reproductive effects

Ovulation was delayed by 2.5-4 hr in hens given 37 mg kg^{-1} 14-15 hr prior to their 1st or 2nd ovulation in a string of four consecutive ovulations and was blocked when given prior to a 3rd or 4th ovulation. Morphological changes in the follicles paralleled those in egg laying (6).

Metabolism and toxicokinetics

Absorbed from the gastro-intestinal tract in humans following oral or rectal administration. 50% bound to plasma protein; metabolised in the liver by hydroxylation and metabolites excreted in urine. Elimination $t_{1/2}$ 15-50 hr (7).

Other comments

Pharmacological and clinical aspects reviewed (8).

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1. *J. Pharmacol. Exp. Ther.* 1956, **118**, 139.
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P46 2-pentyl acetate

$$CH_3(CH_2)_2CH(O_2CCH_3)CH_3$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 626-38-0
Synonyms 1-methylbutyl acetate; 2-acetoxypentane; 2-pentanol acetate; pent-2-yl ethanoate; *sec*-amyl acetate
EINECS No. 210-946-8 **RTECS No.** AJ 2100000

Physical properties

M. Pt. –100°C **B. Pt.** 131.8-132.0°C at 746 mmHg **Flash point** 32°C **Specific gravity** 0.862-0.866 at 20°C with respect to water at 20°C **Volatility** v.p. 7 mmHg at 20°C
Solubility Water: 0.2 g 100 g^{-1} at 20°C

Occupational exposure

DE-MAK 50 ppm (270 mg m^{-3})
FR-VME 125 ppm (670 mg m^{-3})
SE-LEVL 100 ppm (500 mg m^{-3}) **SE-STEL** 150 ppm (800 mg m^{-3})
UK-STEL 150 ppm (812 mg m^{-3})
US-TWA 125 ppm (665 mg m^{-3})

Mammalian & avian toxicity

Acute data
LC_{Lo} (5 hr) inhalation guinea pig 10,000 ppm (1).

References

1. *Public Health Rep.* 1936, **51**, 811

P47 pentylamine

$$CH_3(CH_2)_4NH_2$$

$C_5H_{13}N$ **Mol. Wt.** 87.16 **CAS Registry No.** 110-58-7

Synonyms 1-pentanamine; 1-aminopentane; *n*-amylamine; monoamylamine; Norleucamine; *n*-pentylamine; 1-pentylamine

EINECS No. 203-780-2 **RTECS No.** SC 0300000

Physical properties

M. Pt. –50°C **B. Pt.** 104°C **Flash point** 4°C **Specific gravity** 0.766 at 19°C
Partition coefficient log P_{ow} 1.49 **Volatility** v.p. 35 mmHg at 26°C
Solubility Organic solvents: ethanol, miscible with diethyl ether

Ecotoxicity

Fish toxicity
LC_{Lo} (24 hr) creek chub 30 mg l^{-1}, LC_{100} (24 hr) 50 mg l^{-1} (1).

Environmental fate

Degradation studies
Confirmed to be biodegradable (2).
200 mg l^{-1} degraded by *Aerobacter* spp. at 30°C; 100% by parent in 25 hr, 100% by mutant in 9 hr (1).

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Inhalation normal mice 97 ppm (duration unspecified) decreased respiratory rate by 50%. Inhalation tracheally cannulated mice 128 ppm caused pulmonary irritation, depressing respiratory rat by 50% (3).

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1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, 200, Van Nostrand Reinhold, New York, NY, USA.
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P48 pentyl ether

$$CH_3(CH_2)_4O(CH_2)_4CH_3$$

$C_{10}H_{22}O$ **Mol. Wt.** 158.28 **CAS Registry No.** 693-65-2

Synonyms 1,1'-oxybispentane; amyl ether; bis(1-pentyl) ether; diamyl ether; dipentyl ether

EINECS No. 211-756-8 **RTECS No.** SC 2900000

Uses Industrial solvent.

Physical properties

M. Pt. –69.43°C **B. Pt.** 187-188°C **Flash point** 57°C (closed cup) **Specific gravity** 0.7833 at 20°C with respect to water at 4°C

Solubility Organic solvents: miscible with diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 3.17 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 164 mg kg^{-1} (2).

References

1. Protic, M. et al *Aquat. Toxicol.* 1989, **14**, 47-64.
2. *J. Pharm. Sci.* 1978, **67**, 566

P49 pentyl propionate

$$CH_3CH_2CO_2(CH_2)_4CH_3$$

$C_8H_{16}O_2$ **Mol. Wt.** 144.21 **CAS Registry No.** 624-54-4

Synonyms amyl propionate; *n*-pentyl propionate; *n*-pentyl propanoate

EINECS No. 210-852-7 **RTECS No.** UA 2533000

Occurrence Found in flavour component of bananas.

Physical properties

M. Pt. –73.1°C **B. Pt.** 168.6°C **Flash point** 41°C (open cup) **Specific gravity** 0.8761 at 20°C with respect to water at 4°C **Volatility** v.den. 5.0
Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

Risk phrases Flammable (R10)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Genotoxicity

Saccharomyces cerevisiae D61.M without activation negative (1).

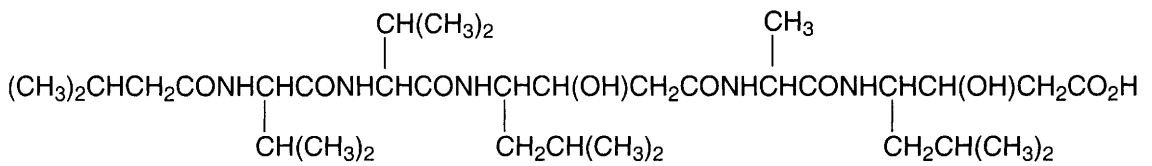
Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (2).
Acute toxicity data presented (3).

References

1. Zimmerman, F. K. et al *Mutat. Res.* 1989, **224**(2), 287-303.
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.
3. Myers, R. C. et al *Acute Toxic. Data* 1992, **1**(3), 197

P50 pepstatin A



$C_{34}H_{63}N_5O_9$ **Mol. Wt.** 685.90 **CAS Registry No.** 26305-03-3

Synonyms Pepsin inhibitor S 735A; Procidin S 735A; *N*-[(3-methyl-1-oxobutyl)-L-valyl-L-valyl-4-amino-3-hydroxy-6-methylheptanoyl-L-alany l]-4-amino-3-hydroxy-6-methylheptanoic acid; *N*-isovaleryl-L-valyl-L-valyl-3-hydroxy-6-methyl-γ-aminoheptanoyl-L-alanyl-3-hy droxy-6-methyl-γ-aminoheptanoic acid

EINECS No. 247-600-0 **RTECS No.** SC 6155000

Uses Enzyme inhibitor (Pepsin).
Occurrence Isolated from culture broth of *Streptomyces testaceus* and other strains.

Physical properties

M. Pt. 228-229°C (decomp.)
Solubility Organic solvents: acetic acid, dimethyl sulfoxide, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal dog, rabbit, rat 450-875 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 1090 mg kg^{-1} (1).

Teratogenicity and reproductive effects

Up to 300 mg l^{-1} had no effect on rat visceral yolk sac lysosomal proteolysis in Sprague-Dawley rat embryos cultured *in vitro* from days 10-12 gestation, hence there was no developmental toxicity (2).

Other comments

Nine cells infected with human immunodeficiency virus incubated with pepstatin A at 0.069 g l^{-1} for 2, 4 or 11 days contained less HIV core antigen than controls (3).

References

1. *J. Antibiot.* 1970, **23**, 259.
2. Daston, G. P. et al *Teratology* 1991, **43**(3), 253-261.
3. Von der Helm, K. et al *FEBS Lett.* 1989, **247**(2), 349-352

P51 peracetic acid

$$CH_3CO_2OH$$

$C_2H_4O_3$ **Mol. Wt.** 76.05 **CAS Registry No.** 79-21-0

Synonyms peroxyacetic acid; ethaneperoxoic acid; acetic peroxide; acetyl hydroperoxide; Desoxon 1; Osbon AC; peroxoacetic acid; Proxitane 4002

EINECS No. 201-186-8 **RTECS No.** SD 8750000

Uses Oxidising agent. Used in photographic film recovery washing processes and electrodeposit photoresist compounds. Water purification.

Physical properties

M. Pt. 0.1°C **B. Pt.** 105°C **Flash point** 40.5°C **Specific gravity** 1.15 at 20°C

Solubility Water: freely soluble in water. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2131

Supply classification oxidising, corrosive

Risk phrases May cause fire – Flammable – Harmful by inhalation, in contact with skin and if swallowed – Causes severe burns (R7, R10, R20/21/22, R35)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed in a cool place – Keep away from oxidisable organic or flammable materials – 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, S3/7, S14, S36/37/39, S45)

Ecotoxicity

Invertebrate toxicity

In vitro Mycobacterium tuberculosis (1 hr) inhibition observed at 0.5% concentration (1).

Environmental fate

Abiotic removal

Reacts with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 445 days (atmospheric concentration 5×10^5 hydroxyl radicals cm^{-3} (2).

Hydrolyses slowly to the parent compound and hydrogen peroxide (3).

Volatilisation from model river (1 m depth; flow 1 m sec^{-1}; wind velocity 3 m sec^{-1}); model pond water (2 m depth) 167 days (4,5).

Adsorption and retention

Estimated K_{oc} 7.5 (non-ionised peracetic acid) predicts high mobility in soil, but, concurrent reactivity with soil materials is likely and this will negate the potential importance of leaching (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1540 mg kg^{-1} (7).

LD_{50} oral mouse 210 mg kg^{-1} (8).

LD_{50} oral guinea pig 10 mg kg^{-1} (8).

LC_{50} (duration unspecified) inhalation rat 450 mg m^{-3} (7).

LD_{50} dermal rabbit 1410 mg kg^{-1} (7).

The probable human oral lethal dose is 50-500 mg kg^{-1} (9).

Sub-acute and sub-chronic data

Bronchopneumonia was observed in mice and guinea pigs following exposure to 186 or 280 mg m^{-3}, 30 min twice daily for 90 day (10,11).

Dermal (1, 7, 14 day) guinea pig 50 µl resulted in a decrease of Langerhans cells, with the largest decrease occurring at 14 days (12).

Carcinogenicity and chronic effects

Inhalation (90 day) mouse, guinea pig, 186 or 280 mg m^{-3}, 30 min twice daily, induced liver granuloma and an increased incidence of lung tumours (10).

Irritancy

Dermal rabbit, open to atmosphere, 500 mg caused severe irritation and 1 mg caused severe irritation to rabbit eyes (7).

It is intensely irritating to human nasal passages (13).

Guinea pigs exposed to 1 or 3% solutions for 3 days showed eye irritation and coughing; histopathological changes of the respiratory tract mucous were noted (14).

A 3% solution caused dermatitis on guinea pig skin (15).

Genotoxicity

Salmonella typhimurium (strain unspecified) with and without metabolic activation negative (16).

Other effects

Any other adverse effects

Rabbits 0.02% caused no toxicity to the blood, liver and kidney functions and had no local irritation to the skin and muscle (17).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Effective disinfectant in farm animal housing foundations to prevent the infection of livestock by *Mycobacterium tuberculosis* (1).

Reviews on human health effects, epidemiology, workplace experience and experimental toxicity listed (19). Explodes violently when heated to 110°C.

References

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2. Atkinson, R. *Int. J. Chem. Kinet.* 1987, **19**, 799-828.
3. *Kirk-Othmer Encyclopedia of Chemical Technology* 3rd ed., 1982, **17**, 60-61, John Wiley & Sons, New York, NY, USA.
4. Lyman, W. J. et al *Handbook of Chemical Property Estimation Methods* 1990, **15**, 15-29, Washington, DC, USA.
5. *USEPA. EXAMS II Computer Simulation* 1987, Washington, DC, USA.
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7. *Union Carbide Data Sheet* 1968, Union Carbide Corp., New York, NY, USA.
8. *Gig. Sanit.* 1983, **48**(6), 28.
9. Gosselin, R. E. et al *Clinical Toxicology of Commercial Products* 5th ed., 1984, Williams & Wilkins, Baltimore, MD, USA.
10. Heinze, W. et al *Wiss. Z. Humboldt-Univ. Berlin, Math.-Naturwiss. Reihe* 1984, **33**(5), 513-517.
11. Heinze, W. et al *Wiss. Z. Humboldt-Univ. Berlin, Math.-Naturwiss. Reihe* 1982, **31**(6), 549-555.
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13. Bock, F. G. et al *J. Natl. Cancer Inst.* 1975, **55**, 1359-1361.
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16. Bulnes, C. et al *Rev. Salud Anim.* 1982, **4**(2), 59-65.
17. Li, C. et al *Yaoxue Tongbao* 1988, **23**(6), 345-348.
18. *S. I. 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

P52 perchloric acid

$HClO_4$

$ClHO_4$ **Mol. Wt.** 100.46 **CAS Registry No.** 7601-90-3

EINECS No. 231-512-4 **RTECS No.** SC 7500000

Uses Oxidiser in analytical chemistry and for separating potassium and sodium. Salts used for explosives or metal plating.

Physical properties

M. Pt. −112°C **B. Pt.** 19°C at 11 mmHg **Specific gravity** 1.768 at 22°C
Solubility Water: soluble

Occupational exposure

UN No. 1873 (>50%≤72% acid, by mass)

UN No. 1802 (≤50% acid, by mass) **HAZCHEM Code** 2P **Conveyance classification** oxidising substance, corrosive (>50%≤72% acid, by mass) **Conveyance classification** corrosive substance, fire intensifying hazard (≤50% acid, by mass)
Supply classification oxidising, corrosive
Risk phrases ≥50% – Heating may cause an explosion – Contact with combustible material may cause fire – Causes severe burns (R5, R8, 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 – Wear suitable

protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S26, S36, S45)

Ecotoxicity

Fish toxicity

LC_{20} (24 hr) goldfish 2000 ppm (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1100 mg kg^{-1} (2).
LD_{50} oral dog 400 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 250 mg kg^{-1} (2).

Irritancy

Direct contact causes lung and throat irritation in humans. Burns skin. Potential chronic skin rash from prolonged contact (3).

Other effects

Other adverse effects (human)

5/20 workers in a mineral analysis laboratory exposed to vapours including $HClO_4$ had bronchial hyperreactivity. Other symptoms included cough (2/5 workers), breathlessness (3/5 workers) and a history of chest tightness at work (4/5 workers), suggesting occupational asthma (4).

Other comments

Combines vigorously with water with evolution of heat.
Physical and chemical properties, hazards and French legislation reviewed (5).

References

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2. *Gig. Tr. Prof. Zabol.* 1973, **17**(8), 33.
3. *Dangerous Prop. Ind. Mater. Rep.* 1989, **9**(2), 70-73.
4. Musk, A. W. et al *Br. J. Ind. Med.* 1988, **45**(6), 381-386.
5. *Cah. Notes Doc.* 1987, (129), 683-686 (Fr.) (*Chem. Abstr.* **109**, 175482e)

P53 perchloryl fluoride

$FClO_3$

$ClFO_3$ **Mol. Wt.** 102.45 **CAS Registry No.** 7616-94-6

Synonyms chlorine fluoride oxide; chlorine oxyfluoride; trioxychlorofluoride

EINECS No. 231-526-0 **RTECS No.** SD 1925000

Uses In organic synthesis to introduce fluorine atoms into organic molecules; oxidising agent; insulator in high voltage systems.

Physical properties

M. Pt. –147.7°C **B. Pt.** –46.7°C **Specific gravity** 1.434 (liquid) at 20°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (inhalable dust fraction)
FR-VME 3 ppm (14 mg m^{-3})
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 3 ppm (13 mg m^{-3}) **UK-STEL** 6 ppm (26 mg m^{-3})
US-TWA 3 ppm (13 mg m^{-3}) **US-STEL** 6 ppm (25 mg m^{-3})

UN No. 3083 **Conveyance classification** toxic gas, fire intensifying hazard

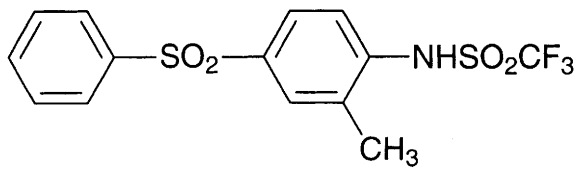
Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) inhalation mouse 630 ppm (1).

References

1. Pennsalt Chemicals Corporation, Technical Div., New Products, Philadelphia, PA, USA

P54 perfluidone



$C_{14}H_{12}F_3NO_4S_2$ **Mol. Wt.** 379.38 **CAS Registry No.** 37924-13-3

Synonyms 1,1,1-trifluoro-*N*-[2-methyl-4-(phenylsulfonyl)phenyl]methanesulfonamide; Destun; MBR 8251; SB 1528

EINECS No. 253-718-3 **RTECS No.** PB 0480000

Uses Superseded herbicide.

Physical properties

M. Pt. 138-139.5°C **Volatility** v.p. $<1 \times 10^{-5}$ mmHg at 25°C
Solubility Water: 60 mg l^{-1} at 22°C. Organic solvents: acetone, benzene, dichloromethane, methanol

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} (96 hr) bluegill sunfish, rainbow trout 312-318 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 633, 920 mg kg^{-1}, respectively (2,3).

LD_{50} dermal rabbit >4000 mg kg^{-1} (1).

Irritancy

Irritating to rabbit eye and skin (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).

References

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2. Thomson, W. T. *Agricultural Chemicals Book II* 1977, 215, Thomson Publications, Fresno, CA, USA.
3. *Farm Chemicals Handbook* 1980, D235, Meister Publishing Co., 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

P55 perfluorotributylamine

$$N(CF_2CF_2CF_2CF_3)_3$$

$C_{12}F_{27}N$ **Mol. Wt.** 671.10 **CAS Registry No.** 311-89-7

Synonyms 1,1,2,2,3,3,4,4,4-nonafluoro-*N*,*N*-bis(nonafluorobutyl)-1-butanamine; heptacosafluorotributylamine; tri(perfluorobutyl)amine; tris(nonafluorobutyl)amine; Fluorinert FC 43; Mediflor FC 43

EINECS No. 206-223-1 **RTECS No.** YA 1000000

Physical properties

B. Pt. 178°C **Specific gravity** 1.883

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 512 mg kg^{-1} (1).

Other effects

Any other adverse effects

2 ml intravenous doses to 28 dogs anaesthetised with pentobarbitone and artificially ventilated with air caused severe, significant, systematic hypotension with decreases in cardiac output and limb blood flow. Pulmonary and systemic vascular resistances were increased and body and limb muscle oxygen delivery and consumption decreased (2).

Produces irreversible toxic effects on the rabbit retina if used to replace the vitreous body for more than 1-2 wk, but temporary use during vitrectomy does not have harmful effects (3).

References

1. *Summary Tables of Biological Tests* 1951, **3**, 362.
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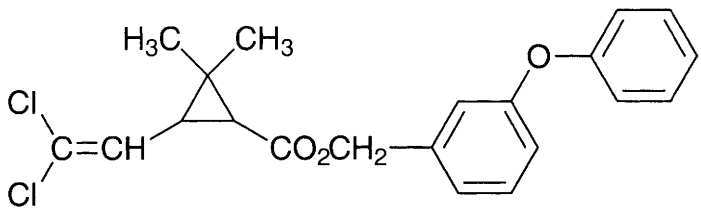
P56 permethrin



$C_{21}H_{20}Cl_2O_3$ **Mol. Wt.** 391.29 **CAS Registry No.** 52645-53-1

Synonyms cyclopropanecarboxylic acid, 3-(2,2-dichloroethenyl)-2,2-dimethyl-, (3-phenoxyphenyl)methyl ester; 3-phenoxybenzyl (1*RS*,3*RS*;1*RS*, 3*SR*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate; perméthrine; Permanone; Acsius; Biokill; Combinex; Dragnet; Epigon

EINECS No. 258-067-9 **RTECS No.** GZ 1255000

Uses Insecticide. Used to impregnate mosquito nets and to disinfect aircraft. Used to treat head pediculosis as 1% application and in treatment of scabies as 5% cream.

Physical properties

M. Pt. ~35°C; *cis*-isomers:63-65°C; *trans*-isomers 44-47°C **B. Pt.** 220°C at 0.05 mmHg **Flash point** >100°C
Specific gravity 1.190-1.272 at 20°C **Partition coefficient** log P_{ow} 6.1 (20°C) (1)
Volatility v.p. $<1 \times 10^{-6}$ mmHg at 50°C
Solubility Water: 0.2 mg l^{-1} at 20°C. Organic solvents: *n*-hexane, 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} (48 hr) rainbow trout, bluegill sunfish 5.4, 1.8 μg l^{-1}, respectively (2).
LC_{50} (96 hr) channel catfish, largemouth bass, brook trout, desert pupfish 1.1, 8.5, 3.2, 5.0 μg l^{-1}, respectively (3-5).
Embryos and hatched fry of sheepshead minnow, 1.25, 2.5, 5.0, 10, 20, 40 μg l^{-1} had no effect on embryo survival. Fry were unaffected by 10 μg l^{-1}, but only 19% survived at 20 μg l^{-1} (6).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 31.8 ppm Microtox test (7).
EC_{50} (48 hr) *Daphnia* 0.6 μg l^{-1} (8).
LC_{50} (96 hr) *Gammarus pseudolimnaeus* immature 0.17 μg l^{-1} (technical) (4).
LC_{50} (96 hr) *Procambarus clarkii* 0.39 μg l^{-1} (emulsifiable concentrate) (3).
Toxic to bees. LD_{50} (24 hr) oral 0.098, topical 0.029 μg bee^{-1} (8).

Toxicity to other species

LC_{50} (96 hr) *Rana catesbeiana* tadpole 7033 μg l^{-1} (3).

Bioaccumulation

Rainbow trout held in static water containing 5 μg l^{-1} ^{14}C-permethrin for 24 hr accumulated *cis* and *trans* isomers equally. Bioaccumulation ratios for radiocarbon in blood, muscle, liver and fat were 30, 30, 300 and 400, respectively (9).

Juvenile Atlantic salmon held in static water containing 22 μg l^{-1} for 96 hr had a bioconcentration ratio of 55 (10).

Bioaccumulation ratios of stone flies (*Pteronarcys dorsata*) exposed to running water containing 0.029-0.21 mg l^{-1} for 28 days ranged from 43-570 (11).

Environmental fate

Nitrification inhibition

Inconsistent decreases in available nitrogen seen during a study of soil with a high organic content treated with permethrin (12).

EC_{50} *Anabaena* sp. 1.4-2.5 mg l^{-1}. These cyanobacteria are significant nitrogen fixing organisms in wet tropical soils and were also susceptible to some breakdown products of permethrin (13).

Degradation studies

Degradation is microbial. Soils treated with ^{14}C-permethrin at 224 g ha^{-1} at 25°C. Rapidly degraded, *trans>cis* with $t_{1/2}$ <28 days in 4/5 soils. $^{14}CO_2$ was rapidly evolved. In waterlogged soil <0.3% CO_2 evolved. Similar effects with microbial growth inhibitor sodium azide (14).

Degradation in soil and water is rapid, $t_{1/2}$ <38 days (15).

Degraded more rapidly under oxidising conditions than reduced or weakly oxidising (16).

Degradation $t_{1/2}$ in Dubbs fine sandy loam soil for *trans* and *cis* isomers 14 and 55 days at 10°C, 5 and 12 days at 25°C and 4 and 27 days at 40°C, respectively (17).

Abiotic removal

When exposed to daylight, as a 0.2 mg cm^{-2} film near a window, 60% was undecomposed after 20 days (18).

Exposure of isomers on Dunkirk silt loam soil for 48 hr resulted in 55% lost in sunlight, 35% in dark (15).

Adsorption and retention

17.5 g active ingredient ha^{-1} sprayed onto a 640-ha forest persisted for <96 hr. Residues in streams peaked at 2.5 μg l^{-1} after 1 hr and persisted for <96 hr. Accumulation and persistence in bottom sediment were negligible, in pond sediment were minimal (5-8 mg kg^{-1}) and not found in stream sediment (19).

95% of permethrin in 6-42 μg l^{-1} aqueous solution was absorbed rapidly onto lake sediment in a laboratory study and not easily desorbed. Did not penetrate more than 2 cm of a sediment column when applied to surface in aqueous solution (20).

Mammalian & avian toxicity

Acute data

cis-Permethrin is more toxic than *trans*-permethrin. LD_{50} oral rat, mouse, guinea pig, rabbit ~4000 mg kg^{-1} (40:60 *cis:trans*); LD_{50} oral rat, mouse, guinea pig, rabbit ~6000 mg kg^{-1} (20:80 *cis:trans*) (2).

LD_{50} oral chicken, Japanese quail >3000, >13,500 mg kg^{-1}, respectively (40:60) (2).

LC_{50} inhalation rat 23.5 mg l^{-1} in air (duration and isomer ratio unspecified) (2).

LD_{50} dermal rat, rabbit >4000, >2000 mg kg^{-1}, respectively (isomers unspecified) (2).

Oral rat 4672->20,000 mg kg^{-1} (25:75), symptoms of acute poisoning developed within 12 hr, including muscular tremor, hypersensitivity to stimuli and staining of abdominal fur (21).

Sub-acute and sub-chronic data

♂, ♀ mice were fed 0, 200, 400, 2000 or 4000 mg kg^{-1} in diet for 28 day (group 1) or 80 mg kg^{-1} for 2 wk then 10,000 mg kg^{-1} for 2 wk (group 2). Group 1 had normal mortality, food utilisation and growth. Group 2 showed weight loss and poor food utilisation. Higher weight and organ-to-body weight ratios were seen in livers at mice fed ≥2000 mg kg^{-1} and in kidney, heart and spleen of ♂ mice fed 10,000 mg kg^{-1}. ♀ Mice fed 2000 and 10,000 mg kg^{-1} had gross tissue changes (1).

Sprague-Dawley rats fed 54, 108, 216, 432, 864 or 1728 mg kg^{-1} in diet for 14 days showed muscle tremors and increased liver-to-body weight ratios at 432 mg kg^{-1}. All except 1 ♀ died at the highest dose. NOEL was 216 mg kg^{-1} (22).
250 mg kg^{-1} body weight administered to beagles for 6 months produced no adverse effects (1).
No significant effects were observed in rabbits dermally exposed to 1.25 or 0.125 mg cm^{-2} for 3 wk (22).
No permanent changes were observed in guinea pigs exposed to aerosol concentrations of 125, 250, 500 mg m^{-3} 6 hr day^{-1}, 5 day wk^{-1} for 13 wk (23).
Charles River rats 0 or 6000 mg kg^{-1} for 14 days in diet showed clinical signs of poisoning. 1/12 survived. 4/5 showed fragmented and swollen sciatic nerve axons and myelin degeneration (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials rats receiving 100 mg kg^{-1} diet showed no ill-effects. No mutagenic, teratogenic or carcinogenic activity was observed (2).
Alpk:Ap rats were fed 0, 500, 1000 or 2500 ppm in diet for 2 yr and Swiss-derived mice 0, 500, 1000 or 2500 ppm for life. Rats showed tremors and hypersensitivity and liver hypertrophy but no carcinogenic effect at 2500 ppm. Mice showed decreased body weight gain and a slight elevation in benign lung tumour incidence in ♂ at 2500 ppm, but this was not considered to represent a carcinogenic effect (24).

Teratogenicity and reproductive effects
Pregnant ICR mice administered 0, 15, 50, 150 mg kg^{-1} body weight orally from day-7 to day-12 pregnancy and sacrificed on day-18 showed no maternal toxicity or teratogenicity (1).
Pregnant Sprague-Dawley rats administered 0, 10, 20, 50 mg kg^{-1} body weight from day 9-11 of pregnancy and sacrificed on day-20 showed toxic signs of poisoning, including ataxia, tremor and reduced body weight, but no teratogenic effects were observed (1).
Wistar rats fed 0, 500, 1000, 2000 mg kg^{-1} for 12 wk were mated to initiate a three-generation study. No abnormalities were seen in the third litter of the F_3 generation on day-12 of gestation (1).

Metabolism and toxicokinetics
Hydrolysis of the ester bond, hydroxylation and elimination as the glucuronide conjugate occurs in mammals (25,26).
40% of 1 mg kg^{-1} ^{14}C-*cis*-permethrin applied to skin of mice had moved from site of application within 5 min (27).
1.6-4.8 mg kg^{-1} [1*RS,trans*]- or [1*RS,cis*]-permethrin (^{14}C-labelled in the alcohol or acid moiety) administered to rats was rapidly metabolised and the products eliminated from the body within a few days. Radiocarbon from the *cis* isomer was eliminated in the urine (52-54%) and faeces (45-47%) whereas radiocarbon from the *trans* isomer appeared in the urine (79-82%) and faeces (16-18%) (28).
Major metabolites in the rat were dichlorovinyldimethylcyclopropanecarboxylic acid, free or conjugated with glucuronic acid, sulfate conjugate of 4'-hydroxy-3-phenoxybenzoic acid, free and conjugated forms of 3-phenoxybenzoic acid, and the glucuronide conjugate of the hydroxymethyl derivative of dichlorovinyldimethylcyclopropanecarboxylic acid (25,28).
Permethrin (0.05-23.5% wt/wt) was applied in four distinct ointments to single-pass perfused isolated rabbit ears. Permethrin absorption was not detected. The permeation coefficient calculated from the analytical detection limit for permethrin was $<7.5 \times 10^{-12}$ cm s^{-1} (29).
Milk of goats given 0.2-0.3 mg kg^{-1} body weight day^{-1} radiolabelled *cis*- and *trans*-permethrin contained parent compound, 3-phenoxybenzoic acid-glycine and 4'-hydroxy-3-phenoxybenzoic acid-glycine (30).

Irritancy
0.5 ml dermal rabbit (duration unspecified) caused no irritation (1).
0.1 ml instilled into rabbit eye (24 hr) caused no irritation (1).

Sensitisation
Dermal guinea pigs, 10% solution in dimethylformamide for 3 days then challenged with 0.1%, 1%, 10% solution in dimethylformamide after 4 days, only mildly or non-sensitising (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (1).

Escherichia coli reverse mutation test with and without metabolic activation negative (31).
In vitro Chinese hamster V79 cells with and without metabolic activation non-mutagenic (31).
In vitro human lymphocytes cell growth inhibition IC_{50} 54.7 mg l^{-1}, protein synthesis inhibition concentration IC_{50} 48.9 mg l^{-1} (32).
In vitro mouse L1210 lymphoblastoid cells IC_{50} cell growth 43.0 mg l^{-1}, IC_{50} protein synthesis 43.0 mg l^{-1} (32).
Drosophila melanogaster chromosome loss negative (33).
In vitro mouse lymphoma L5178Y tk^+/tk^- with and without metabolic activation negative (1).
In vivo rat bone marrow cells, no increase in chromosomal aberrations (1).

Other effects

Other adverse effects (human)
Major work-related symptoms in plant nursery workers exposed to permethrin were itching and burning of the skin, itching and irritation of the eyes and upper respiratory tract and increased nasal secretion (34).
Laboratory workers using permethrin, cypermethrin, fenvalerate and fenpropathrin reported a tingling or burning facial sensation but not with permethrin alone (35).
Medical surveillance of staff involved in bagging, mixing or spraying in Nigeria showed no effects attributable to permethrin. 2 mg was excreted within 24 hr of exposure, despite the use of protective clothing (1).

Any other adverse effects
No toxic effects on pipistrelle bats roosting in boxes treated with permethrin for up to 154 days (36).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (37).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (38).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (39).
WHO Toxicity Class II (40).
EPA toxicity Class II (Ambush), Class III (Pounce, Outflank) (8).
ADI 0.05 mg kg^{-1} (for nominal *cis:trans* 40:60 and 25:75 isomers) (8).

Other comments

Technical mixture contains *trans* and *cis* isomers in ratio 60:40 (1).
Toxicity and metabolism of pyrethroids reviewed (41).

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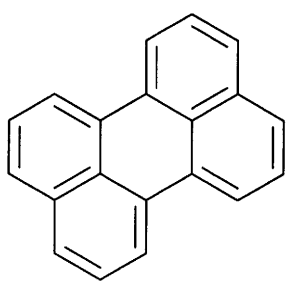
P57 perylene



$C_{20}H_{12}$ **Mol. Wt.** 252.32 **CAS Registry No.** 198-55-0

Synonyms dibenz[*de,kl*]anthracene; *peri*-dinaphthalene; perilene

EINECS No. 205-900-9 **RTECS No.** SE 3794000

Uses Activator (energy acceptor) of undirect chemiluminescence of peroxy esters. Used in the manufacture of organic semiconductors

Physical properties

M. Pt. 278-280°C **B. Pt.** 350-400°C (sublimes) **Specific gravity** 1.35 **Partition coefficient** log P_{ow} 6.25
Solubility Water: 4×10^{-4} mg l^{-1} at 25°C. Organic solvents: acetone, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
LC_{50} (0.76 day) (species unspecified) 0.6 µg mg l^{-1} (1).

Bioaccumulation
Rainbow trout sub-adult (25 day) 10 mg 5 day^{-1}. Not accumulated through dietary exposure due to combined effects of poor absorption efficiencies and rapid elimination rates (2).

Environmental fate

Adsorption and retention
300 mg kg^{-1} perylene was detected in sediment taken from a sewage sedimentation lagoon. 30% of a salamander population inhabiting the lagoon had neoplastic skin lesions (3).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (4).
Dermal (58-60 wk) 20 ♀ ICR/Ha Swiss mice, 6-8 wk of age, 800 µg in 200 µl benzene on clipped dorsal skin. No skin tumour was observed (5).

Teratogenicity and reproductive effects
A dose of 2 mg kg^{-1} egg^{-1} increased mortality among the embryos of chicken, turkey, domestic duck and common eider (6).

Genotoxicity

Subcutaneous ♂ rat (duration unspecified) 100 µg of perylene, no bioalkylation observed *in vivo* (7).
Escherichia coli SOS chromotest with and without metabolic activation negative (8).
In vitro postmitochondrial supernatants of C578L/6 mice, DBA/2 mice, Sprague-Dawley and Lewis rats with and without metabolic activation negative (9).
In vitro Chinese hamster V79 cells without metabolic activation chromosomal aberrations negative (10).

Other effects

Any other adverse effects
Benzo[*a*]pyrene hydroxylase activity of the rat placenta can be induced by perylene (11).
The growth rate of mouse ascites sarcomas cells in culture was not inhibited when perylene was added at a concentration of 1 µmol l^{-1} in dimethyl sulfoxide (12).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (14).

Other comments

Occurs in fossil fuel, car exhaust and cigarette smoke emissions.
Reviews on human health effects and experimental toxicity listed (15).
Daphnia magna model used to predict PAH toxicity (16).
PAH environmental toxicity to *Leiostomus xanthurus* reviewed (17).

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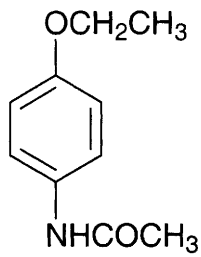
P58 phenacetin



$C_{10}H_{13}NO_2$ **Mol. Wt.** 179.22 **CAS Registry No.** 62-44-2

Synonyms *N*-(4-ethoxyphenyl)-acetamide; acetophenidin; 4-ethoxyacetanilide; *p*-acetophenetidide; Fenidina; Phenin; Kalmin

EINECS No. 200-533-0 **RTECS No.** AM 4375000

Uses Analgesic. Antipyretic.

Physical properties

M. Pt. 134-135°C

Solubility Water: 0.76 g l^{-1} (cold), 12.2 g l^{-1} (hot). Organic solvents: 71 g l^{-1} chloroform, 11 g l^{-1} diethyl ether, 357 g l^{-1} hot ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* concentration 111 ppm Microtox test (1).

Bioaccumulation

Confirmed to be non-accumulative or low accumulative (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral hamster, guinea pig, rabbit and rat 1690-3600 mg kg^{-1} (3-6).
LD_{50} oral mouse 866 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse, rat 540, 630 mg kg^{-1}, respectively (8).
LD_{50} subcutaneous rabbit 1 g kg^{-1} (9).
LD_{Lo} intravenous dog 260 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Intragastric (220 day) ♂ rat 2 g kg^{-1} 5 × wk^{-1}, 80% of the rats were sterile at 176 day (11).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals for analgesic mixtures containing phenacetin, IARC classification group 1. Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals for phenacetin, IARC classification group 2A (12).
Oral (duration unspecified) 30 BD 1 and BD 111 rats (sex unspecified) 40-50 mg $animal^{-1}$ daily. One rat died after 10 g had been administered and was found to have an osteochondroma. Mean age at death was 770 days. No tumours related to treatment were found (13).
Oral (88 or 110 wk) ♀ Sprague-Dawley rats 0 or 0.535%. In the 86-wk study, epithelial hyperplasia of renal papillae was found in 2/24 controls and in 21/38 treated animals (14).
In the 110-wk study urothelial hyperplasia of renal papillae was found in 26, dilation of vasa recta in 28, and epithelial hyperplasia in 1 animal, respectively. Carcinomas of the mammary gland in 5/30 animals and of the ear duct in 4/30 animals were observed (15).
Oral (18 month) Sprague-Dawley rats 1.25% or 2.5%; neoplasms were detected in 26/27 ♂ and 21/27 ♀ fed 2.5%, and in 20/22 ♂ and 19/25 ♀ fed 1.25%. Tumours of the nasal cavity were found in 16/27 ♂ and 7/27 ♀ fed 2.5%, and in 16/22 ♂ and 6/25 ♀ fed 1.25%. Malignant tumours of the urinary tract were detected in 13/27 ♂ and 4/27 ♀ fed 2.5%, and in 1/22 ♂ and 0/25 ♀ fed 1.25% (16).
Tumours of the ureter and bladder have been reported in patients with analgesic nephropathy and a history of analgesic abuse (17).
Gavage (2 wk) rats 100, 625 or 1250 mg kg^{-1} day^{-1} increased olfactory epithelial cell replication 62.4, 174 or 763%, respectively (18).
Oral (6 and 12 wk) 20 ♂ Sprague Dawley rats 0.5, 1.0 or 1.5% in feed. The 1.0 and 1.5% dose levels showed a marked proliferative effect on the urothelium (19).
Oral (73 wk) four groups of 15, 20, 20 and 24 ♂ albino rats,0, 0.5, 0.1 or 0.5%; of treated animals 11, 13 and 15 rats were still alive at the time of the appearance of the first tumour after 45, 45 and 38 wk, and 8/11, 13/13 and 15/15 developed liver tumours, compared with 0/15 controls (20).

Teratogenicity and reproductive effects

Oral rat 600-1200 mg kg^{-1} day^{-1} given from day 0 to day 20 of gestation, reduced foetal weight was observed. No increase in defect rate but some retardation in skeletal growth and an increase in supernumerary ribs occurred with doses of 150 mg kg^{-1} (21).
There was no increase in the congenital malformation rate observed in children of 5546 women who used phenacetin during the first 4 lunar months of pregnancy (22).

Metabolism and toxicokinetics

Oral rat 33-900 mg kg^{-1} caused a dose-dependent increase in urinary excretion of *p*-phenetidine from 0.031 to 0.527% and 2-hydroxyphenetidine sulfate from < 0.5% to 14%. The percentage excretion of unchanged phenacetin and *N*-acetyl-*p*-aminophenol did not change. 400 mg kg^{-1} divided into 5 equal portions and administered at 3-hr intervals did not affect the percentage excretion of unchanged phenacetin and *N*-acetyl-*p*-aminophenol, but significantly decreased the percentage excretion of metabolites. Metabolic pathways involve deethylation, *N*-deacetylation and ring hydroxylation (23).
In rats and dogs given 200 mg kg^{-1} body weight, 1% of the total dose was excreted as 4-acetaminophenoxyacetic acid in the urine of rats, and 0.13% in dogs (24).
Intestinal microflora in rats have been shown to deconjugate the metabolites *N*-acetyl-*p*-aminophenyl glucuronide excreted partly in bile, to the *N*-acetyl-*p*-aminophenol (25).

A reactive metabolite had been reported to have been generated by cytochrome P_{450} in hamster liver microsome (26).

Metabolites also found in the urine of rats, guinea pigs and rabbits are 2-hydroxyphenacetin and 3-[(5-acetamido-2-hydroxyphenyl)thio]aniline (27); the 2-hydroxyacetophenelidine-glucuronide conjugate has been found in the urine of dogs and cats (28).

In humans the major part of the dose is excreted in the urine as conjugated *N*-acetyl-*p*-aminophenol (~70-80%), some as free *N*-acetyl-*p*-aminophenol (3-5%), unchanged phenacetin (0.2%) and *p*-phenetidine (0.1%) (29).

In three men administered 2 g orally, 2% of the dose was excreted as *S*-(1-acetamido-4-hydroxyphenyl)cysteine in the urine (30).

Urinary excretion of 2-hydroxyphenetidine, *N*-acetyl-*p*-aminophenol, and their conjugates was significantly decreased when phenacetin was ingested in combination with aspirin, caffeine and codeine (31).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 and TA1537 with and without metabolic activation negative (32,33).

Bacillus subtilis repair test with and without metabolic activation negative (34).

Escherichia coli K12/343/113 with and without metabolic activation negative (33).

Drosophila melanogaster increased frequency of sex-linked recessive lethals negative (33).

In vitro C3H/10TI/2 clone 8 mouse embryo cells with metabolic activation increased potency (35).

SOS chromotest, *Escherichia coli* PQ37 with and without metabolic activation equivocal findings (36).

In vitro V79 Chinese hamster cells with metabolic activation weakly positive (37).

In vitro mouse lymphoma L5178Y cells with and without metabolic activation negative (positive after precipitation) (38).

Other effects

Other adverse effects (human)

Methaemoglobin and haemolytic anaemia have occurred in subjects ingesting phenacetin; methaemoglobinaemia has been associated with the excretion of increased amounts of 2-hydroxyphenetidine sulfate and the glucuronide or its oxidation products in the urine (39-41).

It may cause methaemoglobinaemia, sulfhaemoglobinaemia, and haemolytic anaemia. Prolonged administration of large doses in analgesics has been associated with renal papillary necrosis and transitional-cell carcinoma of the renal pelvis (42).

Of 189 primary tumours of the urinary tract of adult patients in the UK, 2/30 carcinomas of the renal body, 7/13 carcinomas of the renal pelvis, 0/2 carcinomas of the ureter and 2/144 carcinomas of the bladder occurred in people using large amounts of analgesics, including phenacetin-containing mixtures (43).

Of 320 patients in Denmark with chronic pyelonephritis, 101 had used large amounts of phenacetin-containing analgesics; 2 of these presented papillary necrosis and transitional-cell tumour of the renal pelvis (44).

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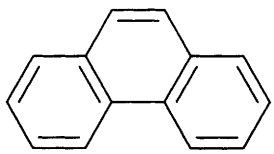
P59 phenanthrene



$C_{14}H_{10}$ **Mol. Wt.** 178.23 **CAS Registry No.** 85-01-8

EINECS No. 201-581-5 **RTECS No.** SF 7175000

Uses Dyestuffs. Explosives. Synthesis of drugs. Biochemical research.
Occurrence Crude oil and gasoline.

Physical properties

M. Pt. 99-101°C **B. Pt.** 340°C **Flash point** 171°C (open cup) **Specific gravity** 1.179 at 25°C
Partition coefficient log P_{ow} 4.52 **Volatility** v.p. 1 mmHg at 118.3°C ; v.den. 6.14
Solubility Water: 1.6 mg l^{-1} at 15°C. Organic solvents: benzene, diethyl ether, hot ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) larval rainbow trout 3.2 mg l^{-1} (1).

Exposure to 5 ppm was toxic to trout, bluegill sunfish and goldfish within 24 hr. Test conditions: temperature 30°C; dissolved oxygen 7.5 ppm; total hardness (soap method) 300 ppm; alkalinity 300 ppm (methyl orange); free carbon dioxide 5 ppm (2).

Invertebrate toxicity

LC_{50} (96 hr) ragworm in seawater 22°C: 0.6 ppm (3).

Perturbation levels *Gammarus pulex* 8000 mg l^{-1}, *Vorticella companula* 4000 mg l^{-1}, *Paramecium caudatum* 12,000 mg l^{-1} (4).

LC_{50} (96 hr) *Daphnia pulex* 0.1 mg l^{-1} (5).

EC_{50} (30 min) *Photobacterium phosphoreum* concentration 0.0726 ppm Microtox test (6).

LC_{50} (48 hr) *Daphnia magna* 0.350 mg l^{-1} (1).

LC_{100} (16 hr, dark) *Tetrahymena pyriformis* 7.0 μM, no observed effect concentration (16 hr, dark) 0.5 μM (7).

LC_{50} estuarine copepod *Schizopera knabeni* 473 μg sediment-associated phenanthrene g^{-1} dry sediment (8).

Bioaccumulation

Tissue burdens and behaviour of lipophilic polycyclic aromatic compounds (PAHs) in blue crab (*Callinectes sapidus*) were investigated. Highest concentrations were detected in hepatopancreas, ovarian and muscle tissues. Major contaminants in blue crabs were alkylated PAHs. Unsubstituted polynuclear aromatic hydrocarbons predominate in molluscs and sediments (9).

Environmental fate

Degradation studies

Pathway of phenanthrene degradation by a pseudomonad: phenanthrene → phenanthrene *cis*-3,4-dihydrodiol → 3,4-dihydroxyphenanthrene → *cis*-4-(1-hydroxynaphth-2-yl)2-oxobut-3-enoic acid → 4-(1-hydroxynaphth-2-yl)-2-oxo-4-hydroxybutyrate→1-hydroxy-2-naphthaldehyde → 1-hydroxy-2-naphthoic acid → 1,2-dihydroxynaphthalene (10).

Alcaligenes denitrificans WW1, isolated from contaminated soil, maximum degradation rate 0.3 mg ml^{-1} day^{-1} (11).

Pseudomonas fluorescens, Pseudomonas paucimobilis, Pseudomonas vesicularis and *Alcaligenes denitrificans* are capable of complete mineralisation of phenanthrene with doubling time of 2.9 to 35 hr (12).

Degradation time in groundwater from a petrol-contaminated aquifer was 150 hr at 10°C, initial concentration was 0.2-1 mg l^{-1} (13).

Concentrations before and after 5 wk of incubation with microorganisms, nutrients and surfactants, were 40 and 22 mg kg^{-1}, respectively (14).

Adsorption and retention

Sediment samples from the North Sea to locations in Norway and Sweden ranged from 1.51-10,700 ppb phenanthrene dry weight (15).

Polyaromatic hydrocarbons were detected at levels of 1.2-3.1 μg g^{-1} in sediments (depth 50-200 m) and 1 μg g^{-1} in bottom sediments (16).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 700 mg kg^{-1} (17).

LD_{50} intravenous mouse 56 mg kg^{-1} (18).

LD_{50} oral redwing blackbird 113 mg kg^{-1} (19).

Carcinogenicity and chronic effects

No adequate data on carcinogenicity to humans and inadequate evidcence for carcinogenicity to animals, IARC classification group 3 (20).

Injected into lungs (duration unspecified) 35 ♀ rats, 1, 3 or 10 mg. One squamous cell carcinoma developed at the highest dose (21).

Dermal (20 wk) 20 ♀ Swiss Ha/CR mice, 7-8 wk of age, 100 µl of a 0.1% solution in acetone ten times on alternate days. Treatment was followed 10 days later by thrice wkly applications of 2.5 µg 12-*O*-tetradecanoylphorbol-13-acetate in 100 µl of acetone. No skin tumours were found (22).
Subcutaneous (29 month) 40 C57B1 mice ♂/♀, 5 mg in 0.5 ml tricarprylin, 27 mice survived four months. No local tumours were observed (23).
Perinatal (62 wk) neonatal stock albino mice, 40 µg in 1% aqueous gelatine, 49 animals survived more than 50 wk. The incidence of tumours (pulmonary adenomas, hepatomas and skin papillomas) at 62 wk was not higher than that seen in controls (24).

Metabolism and toxicokinetics

In vitro and *in vivo* percutaneous absorption/metabolism guinea pigs at dose levels of 6.6 and 15.2 µg cm^{-2}, 89.7 and 79.1%, respectively, were absorbed into the skin. Metabolised to phenanthrene-9,10-dihydrodiol, phenanthrene-3,4-dihydrodiol, phenanthrene-1,2-dihydrodiol and traces of hydroxyphenanthrene (25).

Genotoxicity

Escherichia coli B/r WP2 (λ) with and without metabolic activation negative (26).
In vivo Chinese hamster bone-marrow cells aberrations without metabolic activation negative, sister chromatid exchanges without metabolic activation positive (27).
Saccharomyces cerevisiae mitotic recombination with metabolic activation negative (28).

Other effects

Any other adverse effects

The growth rate of mouse ascites sarcoma cells in culture was inhibited by 22% when phenanthrene was added at a concentration of 1 µgmol ml^{-1} in dimethyl sulfoxide (27).
Benzo[*a*]pyrene hydroxylase activity of the rat placenta can be induced by phenanthrene (29).
Intraperitoneal ♂ rats single unspecified dose increased serum glutamyl transpeptidase levels after 72 hr (30).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (31).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 µg l^{-1} (32).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (33).

Other comments

Has been detected in surface water, tapwater and wastewater.
Reviews on health effects, experimental toxicity and environmental effects listed (34).

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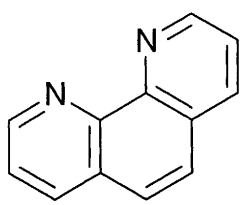
P60 1,10-phenanthroline



$C_{12}H_8N_2$ **Mol. Wt.** 180.21 **CAS Registry No.** 66-71-7

Synonyms Activ-8; 4,5-diazaphenanthrene; *o*-phenanthroline; 4,5-phenanthroline

EINECS No. 200-629-2 **RTECS No.** SF 8300000

Uses Indicator in oxidation reduction systems. Determination of nickel, ruthenium, iron, silver and other metals.

Physical properties

M. Pt. 114-117°C (anhydrous)

Solubility Water: soluble in 300 parts water. Organic solvents: diethyl ether, ethanol

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) – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S45)

Ecotoxicity

Invertebrate toxicity

LC_{100} (16 hr, dark) *Tetrahymena pyriformis* 11 μM, no-observed-effect concentration (16 hr, dark) 8.0 μM (1).

Environmental fate

Nitrification inhibition

9 mg l^{-1} caused ~50% inhibition of NH_3 oxidation by *Nitrosomonas* sp. (2).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 75 mg kg^{-1} (3).

LD_{50} intravenous mouse 18 mg kg^{-1} (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with and without metabolic activation negative (5).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Inactivated type A botulinum toxin when incubated at pH 7 for 30 min in 3600 mg l^{-1} (7).

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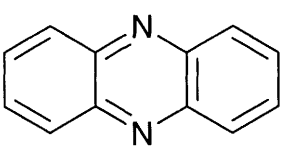
P61 phenazine



$C_{12}H_8N_2$ **Mol. Wt.** 180.21 **CAS Registry No.** 92-82-0

Synonyms azophenylene; 9,10-diazaanthracene; dibenzoparadiazine; dibenzopyrazine

EINECS No. 202-193-9 **RTECS No.** SG 1360000

Physical properties

M. Pt. 174-177°C **B. Pt.** >360°C

Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity

Threespine stickleback exposed to 10 mg l^{-1} experienced loss of equilibrium within 12-16 hr. Test conditions: temperature 15°C; total hardness 67-120 mg l^{-1}; alkalinity 151-183 mg l^{-1} (methyl orange); total dissolved solids 160-175 mg l^{-1} pH 7.1 (1).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* concentration 21.7 ppm Microtox test (2).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 400 mg kg^{-1} (3).

LD_{50} intravenous mouse 180 mg kg^{-1} (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

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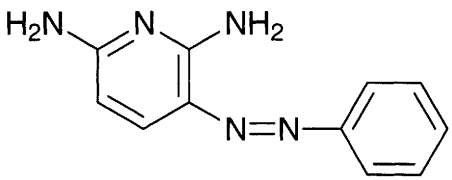
P62 phenazopyridine



$C_{11}H_{11}N_5$ **Mol. Wt.** 213.24 **CAS Registry No.** 94-78-0

Synonyms 3-(phenylazo)-2,6-pyridinediamine; 2,6-diamino-3-(phenylazo)-pyridine; Gastracid

EINECS No. 202-363-2 **RTECS No.** US 7700000

Uses Urinary tract analgesic. Used in stomach pH determination.

Physical properties

M. Pt. 225-226°C **Partition coefficient** log P_{ow} 1.73 (est.) **Volatility** v.p. 4.57×10^{-12} mmHg at 25°C

Solubility Water: 388 mg l^{-1} at 25°C

Ecotoxicity

Bioaccumulation

Bioconcentration factors 1.08 and 1.33 (est.) predict low potential for bioconcentration in aquatic organisms (1).

Environmental fate

Abiotic removal

Reacts with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 2 hr (concentration of hydroxyl radicals 5×10^5 cm^3 (2).

However, phenozopyridine is expected to exist almost entirely in the particulate phase in ambient air (3).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 560 mg kg^{-1} (4).

Carcinogenicity and chronic effects

It caused tumours in the intestine/colon of ♂ and ♀ rats and tumours in the liver of ♀ mice (5).

Metabolism and toxicokinetics

Urinary excretion is rapid in humans and guinea pig, but slower in rat and mouse and there was significant faecal excretion. The extent of azo bond cleavage was high in the mouse and guinea pig, moderate in the rat, and low in human. In human, 5-hydroxyphenazopyridine was the major metabolite (48.3% of the dose) (6).

Genotoxicity

In vitro L5178Y mouse lymphoma cell with metabolic activation positive, without metabolic activation negative (7).

In vitro Chinese hamster ovary cells sister chromatid exchanges with and without metabolic activation weakly positive and positive, respectively (8).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

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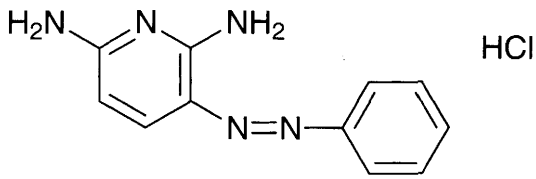
P63 phenazopyridine hydrochloride



$C_{11}H_{12}ClN_5$ **Mol. Wt.** 249.70 **CAS Registry No.** 136-40-3

Synonyms 3-(phenylazo)-2,6-pyridinediamine, monohydrochloride; Azodyne; Bisteril; phenazodine; pyridium; Urodine

EINECS No. 205-243-8 **RTECS No.** US 7875000

Uses Analgesic (urinary tract).

Physical properties

M. Pt. 235°C (decomp.)

Solubility Water: 3.3 g l^{-1}. Organic solvents: acetic acid, ethanol, ethylene glycol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 403 mg kg^{-1} (1).

LD_{50} intravenous mouse 180 mg kg^{-1} (2).

LD_{Lo} intraperitoneal rat 200 mg 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).

Oral (104-107 wk) 35 Fischer 344 rats and B6C3F1 of each sex. Dosed at 3700 or 7500 ppm for rats and 600 or 1200 ppm for mice. Dose administered for 78 wk in rats and 80 wk in mice then they were observed for 25-27 wk. Adenomas or adenocarcinomas of the large intestine were found in ♂ and ♀ rats. Hepatocellular adenomas and carcinomas were found in ♀ mice. Whilst in ♂ mice the incidence of hepatocellular adenomas and carcinomas were not significant (5).

Oral (80 wk) groups of 35 ♂/♀ B6C3F1 mice 0, 600 or 1200 mg kg^{-1} diet, 5 days wk^{-1}. All surviving animals were sacrificed at 105-107 wk. Incidences of hepatocellular adenomas and carcinomas were ♂ 5/15, 15/35 and 15/33 ♀ 2/15, 11/34, 19/32, respectively (6).

Oral (78 wk) groups of 35 ♂/♀ Fischer 344 rats 0, 3700 or 7500 mg kg^{-1}. All surviving animals were killed at 104-105 wk. The combined incidence of adenomas, adenocarcinomas and sarcomas of the colon and rectum; ♂ 0/14, 5/34 and 10/35; ♀ 0/14, 3/33 and 6/32, respectively, positive carcinogenicity (6).

Intraperitoneal (24 wk) groups of 10 ♂/♀ A/He mice given 0.310, 0.775 or 1.55 g kg^{-1} low survivors killed at 24 wk. The combined numbers of ♂ and ♀ mice that developed lung tumours were 6/20, 3/18 and 6/18, respectively (7).

Metabolism and toxicokinetics

Oral rabbits 150 mg kg^{-1}, body weight, 85% of the dose was eliminated in the urine during the first 12 hr. Aniline, *p*-aminophenol (as 50% of the dose); *N*-acetyl-*p*-aminophenol; *o*-aminophenol (as traces); 2,3, 6-triaminopyridine and phenazopyridine appeared in the urine (8).

Absorbed from the gastro-intestinal tract in humans. It is excreted mainly in the urine, up to 65% may be excreted as unchanged phenazopyridine (3).

Oral human 600 mg, ~80% is eliminated in the urine within 24 hr: 41-45% appears as conjugated phenazopyridine; 24-27% as *p*-aminophenol; 18-20% as conjugated *N*-acetyl-*p*-aminophenol; 7-8% as aniline and traces of *o*-aminophenol and 2,3,6-triaminopyridine (9,10).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 and TA1537 with and without metabolic activation negative (11).

Other effects

Other adverse effects (human)

It can cause gastro-intestinal side-effects, headache and rashes. Abnormalities in liver function, haemolytic anaemia, methaemoglobinaemia and acute renal failure (3).

Renal failure with acute tubular necrosis was reported in a 13-yr-old girl following ingestion of 2 g in a suicide attempt (12).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides: guide level 1 $\mu g\ l^{-1}$, approximate concentration above which effects might occur 200 $mg\ l^{-1}$ (13).

Other comments

Used in humans to relieve symptomatic pain and irritability in conditions such as cystitis, prostatitis and urethritis. During administration the urine is tinged either orange or red (3).

2,3,6-Triaminopyridine is more acutely toxic than phenazopyridine (12).

Reviews on human health effects and experimental toxicity listed (14).

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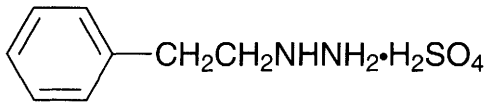
P64 phenelzine sulfate



$C_8H_{14}N_2O_4S$ **Mol. Wt.** 234.28 **CAS Registry No.** 156-51-4

Synonyms 1-hydrazino-2-phenylethane hydrogen sulfate; phenelzine dihydrogen sulfate; β-phenylethylhydrazine sulfate; Estinerval; Kalgan; Nardelzine; Nardil; Stinerval

EINECS No. 205-856-0 **RTECS No.** MV 8750000

Uses Antidepressant.

Physical properties

M. Pt. 164-168°C

Solubility Water: freely soluble. Organic solvents: practically insoluble in chloroform, ethanol, ether

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 156, 210 mg kg^{-1}, respectively (1).

LD_{50} subcutaneous, intravenous, intraperitoneal mouse 125, 157, 162 mg kg^{-1}, respectively (1-3).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (4).

Teratogenicity and reproductive effects

Implantation was partially suppressed in mice injected subcutaneously with 25 mg kg^{-1} daily over the first six days of gestation (5).

Metabolism and toxicokinetics

Rats injected intraperitoneally with 25 mg kg^{-1} excreted 62% of the dose in the urine within 24 hr. The major excretion product was phenylacetic acid. Monoamine oxidase is the first enzyme involved in the elimination (6).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (7).

Exhibited reactivity towards DNA in *Escherichia coli pol A+/A-*test and inactivated *Bacillus subtilis* transforming DNA, but showed no DNA-damaging potency in the liver and lung of intraperitoneally dosed (1 × 0.72 or 5 × 0.24 mmol kg^{-1}) ♂ Swiss white mice investigated by the alkaline elution technique (8-10).

Other effects

Other adverse effects (human)

Adverse effects include orthostatic hypotension and attacks of dizziness. Other common side-effects include headache, dryness of mouth, constipation and other gastro-intestinal disturbances and oedema. Also frequently reported are drowsiness, weakness and fatigue. CNS stimulation may occur and symptons include agitation, nervousness, euphoria, restlessness, insomnia and convulsions. Pyschotic episodes, with manic reactions, or toxic delirium may be induced in susceptible persons. Sweating and muscle tremors, twitching, or hyperreflexia may occur. Other reported reactions include blurred vision, urinary retention or difficulty in micturation, skin rashes, leucopenia, sexual disturbances, and weight gain with inappropriate appetite (11).

Other comments

Phenelzine sulfate is a monoamine oxidase inhibitor in humans (12).

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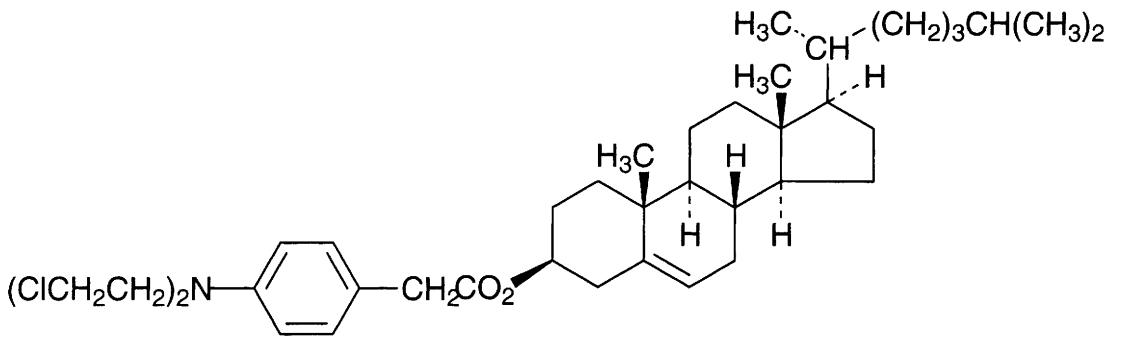
P65 phenesterine



$C_{39}H_{59}Cl_2NO_2$ **Mol. Wt.** 644.81 **CAS Registry No.** 3546-10-9

Synonyms cholest-5-en-3β-ol 4-[bis(2-chloroethyl)amino]benzeneacetate; β-phenylethylhydrazine; phenalzine; Fenesterin; Fenestrin; Phenesterin

RTECS No. AF 5457000

Uses Antineoplastic.

Physical properties

M. Pt. 90-90.5°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Caused tumours in the mammary gland of ♀ rats and tumours in the circulatory system of ♂/♀ mice (1). Gavage (84-85 wk) 35 Sprague-Dawley rats, 5 or 10 mg kg body weight^{-1}, 3 × wk^{-1} for 52 wk. In ♀ rats, a dose-related trend was present in adenocarcinomas of the mammary gland. No carcinogenicity was observed in ♂ rats (2).

Gavage (81-104 wk) 35 B6C3F1 mice 15 or 10 mg kg body weight^{-1}, 3 × wk^{-1} for 52 wk. In ♂ mice there were 18/40 alveolar/bronchiolar carcinomas and adenomas. In ♀ 15 alveolar/bronchiolar adenomas and carcinomas were found (2).

Genotoxicity

Drosophila melanogaster larvae (metabolic activation unspecified) negative (3).
Salmonella typhimurium TA98, TA100, TA1535 and TA1537 with and without metabolic activation negative (4).

References

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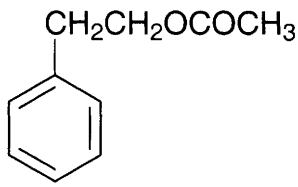
P66 phenethyl acetate



$C_{10}H_{12}O_2$ **Mol. Wt.** 164.20 **CAS Registry No.** 103-45-7

Synonyms 2-phenylethyl acetate; acetic acid, 2-phenylethyl ester; benzylcarbinyl acetate; 2-phenylethanol acetate; phenylethyl ethanoate

EINECS No. 203-113-5 **RTECS No.** AJ 2220000

Physical properties

M. Pt. 164.2°C **B. Pt.** 238-239°C **Flash point** 101°C **Specific gravity** 0.984 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 2.30
Solubility Organic solvents: ethanol, propylene glycol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, guinea pig 3670 mg kg^{-1} (1).
LD_{50} dermal rabbit 6210 mg kg^{-1} (2).

Other comments

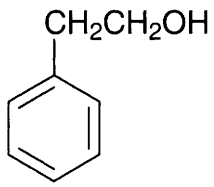
It is an ovipositional deterrent to *Delia antiqua* (3).
Reviews on human health effects, experimental toxicity and environmental effects listed (4).

References

1. *Vopr. Pitan.* 1974, **33**(5), 48.
2. *Food Cosmet. Toxicol.* 1974, **12**, 807.

3. Cowles, R. et al *J. Chem. Ecol.* 1990, **16**(8), 2401-2428.
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

P67 phenethyl alcohol



$C_8H_{10}O$ **Mol. Wt.** 122.17 **CAS Registry No.** 60-12-8

Synonyms 2-phenylethanol; benzeneethanol; phenethanol; benzyl carbinol; β-hydroxyethylbenzene; PEA; 2-phenylethyl alcohol; 2-phenethyl alcohol

EINECS No. 200-456-2 **RTECS No.** SG 7175000

Uses Pharmaceutical aid. Flavours and perfumery.

Physical properties

M. Pt. -27°C **B. Pt.** 219-221°C at 750 mmHg **Flash point** 102°C **Specific gravity** 1.017-1.019 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 1.36 **Volatility** v.den. 4.21
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 5.33 ppm Microtox test (1).

Environmental fate

Degradation studies
Degraded by *Xanthobacter* sp. 124X to phenylacetaldehyde and phenylacetic acid (2).
Pseudomonas T12 degrades 2-phenylethyl alcohol to the 2,3-dihydroxy derivative (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig, mouse, rat, rabbit 400, 800, 1790 and 2000 mg kg^{-1}, respectively (4-6).
LD_{50} intraperitoneal mouse 250 mg kg^{-1} (4).
LD_{50} dermal rabbit, guinea pig 790, 5000 mg kg^{-1}, respectively (7,4).

Irritancy
May cause eye irritation in humans (dose unspecified) (8).

Other comments

Interaction with other compounds such as non-ionic surfactants may reduce activity (8).
Toxicity reviewed (9).
Antibacterial activity is related to the compound's lipophilicity (10).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Hartmans, S. et al *Appl. Environ. Microbiol.* 1989, **55**(11), 2850-2855.
3. Renganathan, V. et al *Appl. Microbiol. Biotechnol.* 1989, **31**(4), 419-421.
4. Patty, F. A. (Ed.) *Industrial Hygiene and Toxicology* 2nd rev. ed., 1963, Interscience Publishers, New York, NY, USA.
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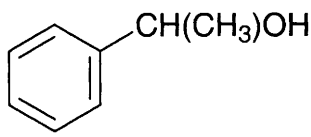
7. *Toxicol. Appl. Pharmacol.* 1974, **28**, 313.
8. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
9. *BIBRA Toxicity Profile* 1991, British Industrial Biological Research Association, Carshalton, UK.
10. Lucchini, J. J. et al *Res. Microbiol.* 1990, **141**(4), 499-510

P68 *sec*-phenethyl alcohol



$C_8H_{10}O$ **Mol. Wt.** 122.17 **CAS Registry No.** 98-85-1

Synonyms 1-phenylethanol; α-methylbenzenemethanol; α-methylbenzyl alcohol; α-hydroxyethylbenzene; methylphenyl carbinol; α-phenethyl alcohol; styrallyl alcohol; 1-phenylethyl alcohol

EINECS No. 202-707-1 **RTECS No.** DO 9275000

Uses Cosmetic ingredient. Food flavouring agent.

Physical properties

M. Pt. 20°C **B. Pt.** 204°C at 745 mmHg **Flash point** 85°C **Specific gravity** 1.015 at 20°C with respect to water at 20°C **Volatility** v.p. 0.1 mmHg at 20°C ; v.den. 4.21
Solubility Organic solvents: glycerin, fixed oils, propylene glycol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 400 mg kg^{-1} (1).
LD_{50} dermal rabbit 2500 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 250 mg kg^{-1} (3).
LD_{Lo} intravenous dog 200 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Body weight gain in F344/N rats was reduced at 1500 mg kg^{-1} gavage in 13-wk study. The only effects were ataxia, laboured breathing and lethargy for 30 min after dosing in rats and B6C3F1 mice and increases in liver weight to body weight ratios for rats (5).

Carcinogenicity and chronic effects
National Toxicology Program tested gavage F344/N rat and B6C3F1 mouse 375 or 750 mg kg^{-1} 5 days wk^{-1} for 103 wk. Some evidence of carcinogenic activity (renal tubular cell adenomas and adenomas or adenocarcinomas (combined)) for ♂ rat. No evidence of carcinogenic activity in ♀ rat or mice (both sexes). In a 2-yr study, significant reduction in body weight gain commenced at weeks 20-30 in high-dose rats. Renal nephropathy was

enhanced, particularly in ♂ rats, as ageing occurred. Non-neoplastic lesions (parathyroid hyperplasia, fibrous osteodystrophy of bone and calcification of the heart and glandular stomach) were found in ♂ rats. Mice only showed a reduction in body weight gain at the highest dose (5).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate to severe erythema and moderate oedema (2).
2 mg instilled into rabbit eye caused severe irritation (6).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).
In vitro mouse lymphoma L5178Y tk^+/tk^- without metabolic activation positive for induction of trifluorothymidine resistance (5).
In vitro Chinese hamster ovary cells with metabolic activation chromosomal aberrations positive, without metabolic activation negative. Sister chromatid exchange was not observed (5).

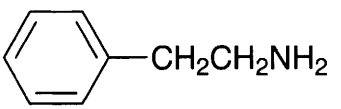
Other comments

Reviews on experimental toxicology and human health effects listed (8).

References

1. *J. Ind. Hyg. Toxicol.* 1944, **26**, 269.
2. *Food Cosmet. Toxicol.* 1974, **12**, 995.
3. *Arch. Int. Pharmacodyn. Ther.* 1958, **116**, 154.
4. *J. Pharmacol. Exp. Ther.* 1920, **15**, 129.
5. Dieter, M. P. *National Toxicology Program Report* 1990, NTP-TR-369, NIH/PUB-89-2824, NIEHS, Research Triangle Park, NC, USA.
6. *Am. J. Ophthalmol.* 1946, **29**, 1363.
7. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
8. *BIBRA Toxicity Profile* 1991, British Industrial Biological Research Association, Carshalton, UK

P69 phenethylamine



$C_8H_{11}N$ **Mol. Wt.** 121.18 **CAS Registry No.** 64-04-0

Synonyms benzenethanamine; β-(aminoethyl)benzene; 2-phenylethylamine

EINECS No. 200-574-4 **RTECS No.** SG 8750000

Occurrence Present in oil of bitter almonds; found in trace amounts in human urine (30 μg l^{-1}).

Physical properties

B. Pt. 197-200°C **Flash point** 90°C **Specific gravity** 0.964 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.41
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 400 mg kg^{-1} (1).
LD_{Lo} oral rat 800 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 320 mg kg^{-1} (3).
LD_{50} intravenous mouse 100 mg kg^{-1} (4).
LD_{Lo} intraperitoneal rat 100 mg kg^{-1} (2).

Teratogenicity and reproductive effects

Mouse embryos (24 hr) concentrations of 121 and 1210 mg l^{-1} were embryo lethal, neural tube closure defects were observed in 67% of the embryos at 12 mg kg^{-1} (5).

Other effects

Other adverse effects (human)

Skin irritant and possible sensitiser (6).

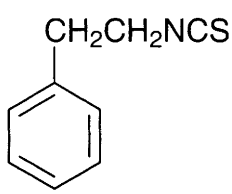
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

References

1. *J. Appl. Am. Chem. Soc.* 1941, **63**, 602.
2. *Naunyn-Schmiedeberg's Arch. Exp. Pathol. Pharmakol.* 1940, **195**, 647.
3. *Arzneim.-Forsch.* 1957, **7**, 620.
4. *J. Pharmacol. Exp. Ther.* 1952, **106**, 341.
5. Denno, K. M. et al *Teratology* 1990, **42**(5), 565-570.
6. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
7. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

P70 phenethyl isothiocyanate



C_9H_9NS **Mol. Wt.** 163.24 **CAS Registry No.** 2257-09-2

Synonyms (2-phenylethyl isothiocyanate)benzene; benzene, (2-isothiocyanatoethyl)-; isothiocyanic acid, phenethyl ester; phenethyl mustard oil

EINECS No. 218-855-5 **RTECS No.** NX 9115000

Physical properties

B. Pt. 139-140°C at 11 mmHg **Flash point** >110°C **Specific gravity** 1.094

Mammalian & avian toxicity

Acute data

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

Metabolism and toxicokinetics

Gavage mice 5 μmol of [^{14}C]-2-phenylethyl isothiocyanate. 50% of the total radioactivity was excreted within 24 hr, with nearly 80% of radioactivity found in urine and faeces at 72 hr (2).

Other effects

Any other adverse effects

Intragastric 0.25 or 1.00 mmol kg^{-1}, 2 hr before sacrifice in mice and 24 hr before sacrifice in rat. Mouse and rat lung microsomal activities were inhibited by ~40% and 90% by the low and high dose, respectively (3).

Other comments

Inhibits *N*-nitrosodimethylamine demethylase activity (4-6).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. Eklind, K. I. et al *Carcinogenesis (London)* 1990, **11**(11), 2033-2036.
3. Guo, Z. et al *Cancer Res.* 1991, **51**(18), 4798-4803.
4. Ishizaki, H. et al *Xenobiotica* 1990, **20**(3), 255-264.
5. Stoner, G. D. et al *Cancer Res.* 1991, **51**(8), 2063-2068.
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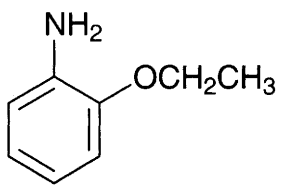
P71 *o*-phenetidine



$C_8H_{11}NO$ **Mol. Wt.** 137.18 **CAS Registry No.** 94-70-2

Synonyms 2-ethoxyaniline; 2-ethoxybenzenamine; 2-aminophenetole

EINECS No. 202-356-4 **RTECS No.** SI 6465300

Uses Manufacture of dyestuffs.

Physical properties

M. Pt. <20°C **B. Pt.** 228-230°C **Flash point** 80°C **Specific gravity** 1.051 at 20°C with respect to water at 4°C
Solubility Organic solvents: ethanol

Occupational exposure

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 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)

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation equivocal (1).

Other effects

Any other adverse effects

Compound does not act as a co-substrate during horseradish peroxidase/H_2O_2-mediated oxygenation of arachidonic acid (2).

Absorbed through skin; vapour hazardous (3).

Other comments

Compound is a breakdown product of iminocyclohexadienylidene, formed by thermal or photochemical degradation of benzotriazole (4).

Biodegradability reviewed (5).

References

1. Zeiger, E. *Environ. Mol. Mutagen.* 1988, **11** (Suppl. 12), 1-157.
2. Lehmann, F. M. *Biochem. Pharmacol.* 1989, **38**(8), 1209-1216.
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4. Haruo, S. *J. Phys. Chem.* 1987, **91**(7), 1793-1797.
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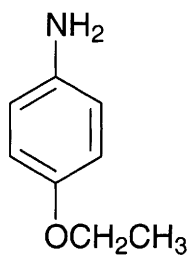
P72 *p*-phenetidine



$C_8H_{11}NO$ **Mol. Wt.** 137.18 **CAS Registry No.** 156-43-4

Synonyms 4-ethoxyaniline; 4-ethoxybenzenamine; 4-aminophenetole; *p*-aminophenetole; 4-phenetidine

EINECS No. 205-855-5 **RTECS No.** SI 6465500

Physical properties

M. Pt. 3°C **B. Pt.** 253-255°C **Flash point** 115°C **Specific gravity** 1.0652 at 16°C with respect to water at 4°C

Volatility v.p. 3.48 mm Hg at 25°C ; v.den. 4.73

Solubility Organic solvents: ethanol

Occupational exposure

UN No. 2311 **HAZCHEM Code** 3X **Conveyance classification** harmful 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 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)

Environmental fate

Degradation studies
6% degradation occurred in a 7 day period. Test concentration at 100 mg l^{-1} incubated at 35°C in the presence of anaerobic sludge inoculum (1).
Modified AFNOR test (50 day) 83% degradation occurred. This aerobic degradation followed the attempt to degrade anaerobically (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} dermal rabbit 500 mg kg^{-1} (2).
LD_{Lo} (45 min) eye rabbit 100 mg kg^{-1} (2).

Metabolism and toxicokinetics
Absorbed through the skin (2).
Metabolism is peroxidase catalysed (3).
Metabolised by isolated rat hepatocytes to *N*-(4-ethoxyphenyl)-*p*-benzoquinone imine which interacts with GSH to form mono and diglutathione conjugates as well as GSSG. Reduction occurs both in microsomes and cytosol (4,5).

Irritancy
Skin and eye irritant (species unspecified) (2).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (6).
Inactive in transformation assay using clone 9 mouse embryo cells at concentrations ≥ cytotoxic doses (4).
Decreased cell survival of V79 Chinese hamster cells exposed to 0.4 g l^{-1} for 30 min (7).

Other effects

Any other adverse effects
Chemical intermediate, particularly in the manufacture of dyestuffs.
Cytotoxic to hepatocytes (5,8).
Acts as a co-substrate during horseradish peroxidase H_2O_2-mediated oxygenation of arachidonic acid to yield free radicals that may cause cytotoxic, mutagenic or carcinogenic effects (9).

Other comments

Biodegradability reviewed (10).

References

1. Brown, D. *Chemosphere* 1987, **16**(7), 1539-1553.
2. *Food Chem. Toxicol.* 1982, **20**, 563.
3. Larsson, R. et al *Metabol. Xenobiot.* [Pap. Eur. Meeting. Issx] 2nd ed. 1987, Gorrod, J. W. (Ed.), Taylor & Francis, London, UK.
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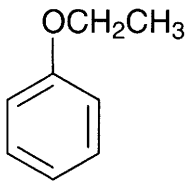
8. Larsson, et al *Chem.-Biol. Interact.* 1986, **60**(3), 317-330.
9. Lehmann, F. M. *Biochem. Pharmacol.* 1989, **38**(8), 1209-1216.
10. Wellens, H. Z. *Wasser/Abwasser Forsch.* 1990, **23**(3), 85-98 (Ger.) (*Chem. Abstr.* **113**, 137899w)

P73 phenetole



$C_8H_{10}O$ **Mol. Wt.** 122.17 **CAS Registry No.** 103-73-1

Synonyms ethyl phenyl ether; ethoxybenzene; phenoxyethane; phenyl ethyl ether

EINECS No. 203-139-7 **RTECS No.** SI 7700000

Physical properties

M. Pt. -30°C **B. Pt.** 171-173°C **Flash point** 62.8°C **Specific gravity** 0.967 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.51 **Volatility** v.p. 1.7 mmHg at 25°C ; v.den. 4.2
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* concentration 7.53 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 2200 mg kg^{-1} (2).
LD_{Lo} subcutaneous rat 3500 mg kg^{-1} (3).

Metabolism and toxicokinetics
Hydroxylated in the *p*-position and excreted as the glucuronide and ethereal sulfate (4).

Irritancy
Dermal rabbit (dose and duration unspecified) caused slight irritation (5).

Legislation

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

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. *J. Pharmacol. Exp. Ther.* 1946, **88**, 400.
3. *Rev. Med. Suisse Romande* 1895, **15**, 561.

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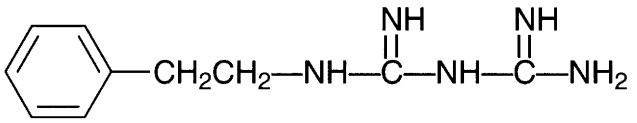
P74 phenformin



$C_{10}H_{15}N_5$ **Mol. Wt.** 205.26 **CAS Registry No.** 114-86-3

Synonyms *N*-(2-phenylethyl)imidodicarbonimidic diamide; 1-phenethylbiguanide; Azucaps; fenformin; Glyphen; Retardo

EINECS No. 204-057-4 **RTECS No.** DU 2100000

Uses Oral hypoglycemic; antidiabetic.

Physical properties

M. Pt. 175-178°C (as hydrochloride)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1650 mg kg^{-1} (1).
LD_{50} oral mouse 830 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 140 mg kg^{-1} (2).
LD_{50} subcutaneous guinea pig 16 mg kg^{-1} (3).
LD_{Lo} intravenous 30 mg kg^{-1} (4).

Metabolism and toxicokinetics

Metabolised in rats to 4-hydroxyphenformin (both free and glucuronic acid conjugated) and some unchanged phenformin. Amount of metabolism varied with dose and route of administration. Excreted in urine. Oral guinea pig (unspecified dose) 47% of 24 hr urinary radioactivity (17% of initial dose) existed in an unidentified metabolite and its glucuronide (5).
Single dose, oral human 50 mg kg^{-1}, major urinary metabolite *p*-hydroxyphenformin detected after 26 hr in phenotypically extensive metabolisers. Not observed in phenotypically poor metabolisers (6).

Other effects

Other adverse effects (human)

Causes lactic acidosis in humans. A study by the University Group Diabetes Program reported increased incidence of cardiovascular mortality after treatment with phenformin hydrochloride (7).
In humans, doses >200 mg day^{-1} may cause metallic taste, nausea, anorexia, vomiting, diarrhoea and cramps (8).

Any other adverse effects

When added to *in vitro* rat hepatocytes of normal rat, induction of δ-aminolevulinic acid synthase and ferrochelatase activities and cytochrome P_{450} content was observed only in the presence of added dibutyl cyclic AMP (9).

Legislation

The US FDA has classified phenformin hydrochloride as hazardous to human health (10,11).

Other comments

Administered as phenformin hydrochloride (RN 834-28-6) used in the treatment of non-insulin dependent diabetes mellitus. Lactic acidosis side-effects reviewed (12-15).

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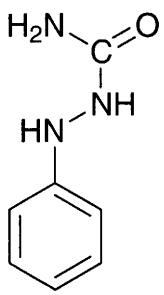
P75 phenicarbazide



$C_7H_9N_3O$ **Mol. Wt.** 151.17 **CAS Registry No.** 103-03-7

Synonyms 2-phenylhydrazinecarboxamide; 1-phenylsemicarbazide; 1-carbamyl-2-phenylhydrazine; 1-carbamoyl-2-phenylhydrazine; 2-phenyldiazenecarboxamide

EINECS No. 203-072-3 **RTECS No.** FD 0575000

Uses Antipyretic, analgesic

Physical properties

M. Pt. 172°C

Solubility Water: Very soluble in hot water, dissolves with difficulty in cold. Organic solvents: acetone, ethanol, methanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 10.7 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

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

Carcinogenicity and chronic effects

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

Oral ♂ and ♀ mice (continuous administration in drinking water, daily intake ♀ 20.4 mg, ♂ 25 mg) produced lung tumours and angiomas and/or angiosarcomas in liver (4).

Genotoxicity

Escherichia coli DNA damage 250 µg $well^{-1}$ (5).

Salmonella typhimurium TA97, TA102 negative (6).

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 negative (7,8).

Rat and mouse hepatocyte DNA repair tests negative (9).

Other comments

Incompatible with strong oxidising agents, strong acids, acid chlorides and acid anhydrides.

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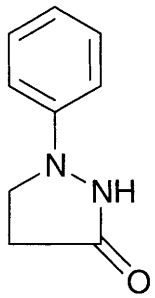
P76 phenidone



$C_9H_{10}N_2O$ **Mol. Wt.** 162.19 **CAS Registry No.** 92-43-3

Synonyms 1-phenyl-2-pyrazolin-3-ol; 1-phenyl-3-pyrazolidinone; Fenidon

EINECS No. 202-155-1 **RTECS No.** UQ 8750000

Uses Photographic developer.

Physical properties

M. Pt. 122-123°C

Solubility Water: 100 g l^{-1} boiling water

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

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 3.02 ppm Microtox test (1).

Environmental fate

Abiotic removal

Wastewater containing phenidone was oxidised using Fentons reaction; oxidation was completed by ~120 min with >97% being removed (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 200 mg kg^{-1} (3).

LD_{50} intraperitoneal 200 mg kg^{-1} (3).

Other effects

Any other adverse effects

Inhibited DNA synthesis in SENCAR and NMRI mice *in vivo* and *in vitro* (4).

Other comments

Showed antiarthritic potency in the murine collagen-induced arthritis model (5).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

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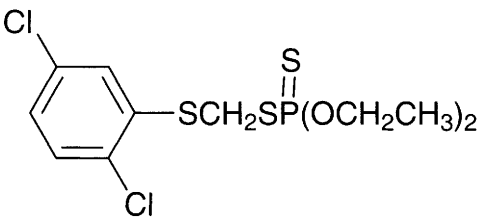
P77 phenkapton



$C_{11}H_{15}Cl_2O_2PS_3$ **Mol. Wt.** 377.32 **CAS Registry No.** 2275-14-1

Synonyms phosphorodithioic acid, *S*-[[(2,5-dichlorophenyl)thio]methyl] *O*,*O*-diethyl ester; CMP; ENT 25585; phencapton; phenudin; phenudine

EINECS No. 218-892-7 **RTECS No.** TD 5775000

Uses Superseded insecticide and acaricide.

Physical properties

B. Pt. 120°C at 0.001 mmHg **Specific gravity** 1.35 (liquid) at 21°C **Volatility** v.p. 4.1×10^{-8} mmHg at 20°C

Occupational exposure

Supply classification toxic, dangerous for the environment

Risk phrases 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 (R23/24/25, 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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S13, S45, S61)

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling >178 mg kg^{-1} (1).

LD_{50} oral rat, mouse, chicken 61, 220, 886 mg kg^{-1}, respectively (2-4).

LD_{50} dermal rat 652 mg kg^{-1} (5).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Limited under EC Directive on Drinking Water Quality 80/778/EEC.

Pesticides: maximum admissible concentration 0.1 μg l^{-1} (7).

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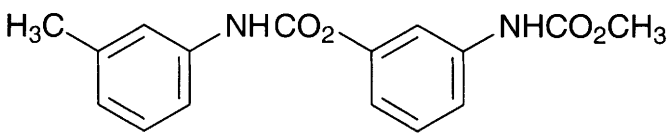
P78 phenmedipham



$C_{16}H_{16}N_2O_4$ **Mol. Wt.** 300.31 **CAS Registry No.** 13684-63-4

Synonyms 3-methylphenylcarbamic acid, 3-[(methoxycarbonyl)amino]phenyl ester; Betanal; Fenmedipham; SN 38584

EINECS No. 237-199-0 **RTECS No.** FD 9050000

Uses Herbicide. Inhibits photosynthesis.

Physical properties

M. Pt. 139-142°C (tech.~144°C) **Specific gravity** 0.34-0.54 at 20°C **Partition coefficient** log P_{ow} 3.59 at pH 4 (1)
Volatility v.p. 9.97×10^{-12} mmHg at 25°C
Solubility Water: 4.7 mg l^{-1} (25°C). Organic solvents: acetone, benzene, chloroform, cyclohexanone, hexane, methanol

Occupational exposure

UN No. 2757

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) harlequin fish 16.5 mg l^{-1} (1).
LOEC rainbow trout 1.6 mg l^{-1} (2).
LOEC carp 2.4 mg l^{-1} (2).
LC_{50} (96 hr) bluegill sunfish 3.98 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (96 hr) *Daphnia magna* 3.2 mg l^{-1} (2).
LD_{50} oral, contact bee >23, 50 μg bee^{-1}, respectively (2).

Bioaccumulation
Estimated bioconcentration factor 260 predicts bioconcentration in aquatic organisms may occur (3).

Environmental fate

Nitrification inhibition
Heterotrophic nitrogen fixation inhibited at 100 μg g^{-1} soil (4).

Carbonaceous inhibition
Dehydrogenase activity was inhibited at 100 μg g^{-1} soil (4).

Degradation studies
$t_{1/2}$ in soil 25 days (5).
Metabolites include methyl *N*-(3-hydroxyphenyl)carbamate and *m*-aminophenol and subsequently complexes with soil components (6).

Abiotic removal
Hydrolysed in neutral and alkaline media. At 22°C, 50% hydrolysis occurs in 70 days at pH 5, in 24 hr at pH 7 and in 10 min at pH 9 (1).

Adsorption and retention
Sorption on sodium montmorillonite was 0.099 g kg^{-1} (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck, chicken 2100, 3000 mg kg^{-1}, respectively (1).
LD_{50} oral rat 4 g kg^{-1} (8).
LD_{50} oral guinea pig, dog, rat, mouse >4000->8000 mg kg^{-1} (1).
LD_{50} dermal rats >4000 mg kg^{-1} (1).
LD_{50} intraperitoneal rats >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral mallard duck and bobwhite quail >10,000 mg kg^{-1} (1).
In 90-day feeding trials, no-effect level in rats and dogs was 100 mg kg^{-1} diet (1).

Metabolism and toxicokinetics
In mammals, following oral administration, 97% was excreted in urine within 24 hr (1).

Other effects

Any other adverse effects
Intragastric administration of a vitamin mixture and methionine 30 min before phenmedipham increased urinary excretion and moderated the damage of peripheral leukocytes, liver, kidney and stomach as compared with rats treated by phenmedipham only. Prophylactic administration of vitamins and methionine increases animal resistance against phenmedipham poisoning (9).
Chronic inhalation and internal administration in albino rats induced changes in the ECG and integral rheograms of the cardiovascular system (10).

Legislation

Included in Schedule 4 (Release into Air: 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).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (13).
WHO Toxicity Class Table 5 (14).
EPA Toxicity Class (formation) IV (2).
ADI 0.03 mg kg^{-1} (2).

Other comments

Increased nitrate reductase activities at 0.3 and 0.03 g l^{-1} (15).
Metabolic pathways reviewed (16).

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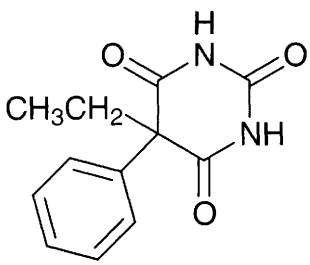
P79 phenobarbitone



$C_{12}H_{12}N_2O_3$ **Mol. Wt.** 232.24 **CAS Registry No.** 50-06-6

Synonyms 5-ethyl-5-phenyl-2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione; 5-ethyl-5-phenylbarituric acid; Adonal; Barbital; Lepinal; Phob; Somonal; Phenobarbital

EINECS No. 200-007-0 **RTECS No.** CQ 6825000

Uses Anticonvulsant. Sedative. Hypnotic.

Physical properties

M. Pt. 174-178°C

Solubility Water: 1 g l^{-1}. Organic solvents: 1.43 g l^{-1} benzene, 25 g l^{-1} chloroform, 77 g l^{-1} diethyl ether, 125 g l^{-1} ethanol

Ecotoxicity

Fish toxicity

Exposure to 5 ppm was toxic to trout causing distress within 1 hr; and was fatal to yellow perch within 23 hr. Test conditions: temperature 30°C; dissolved oxygen 7.5 ppm; total hardness (soap method) 300 ppm; alkalinity 310 ppm (methyl orange); free carbon dioxide 5 ppm (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 100 mg kg^{-1} (2).
LD_{50} oral mouse, dog, rat 137-162 mg kg^{-1} (3-5).
LD_{50} subcutaneous rat, mouse 200, 228 mg kg^{-1}, respectively (6,7).
LD_{50} intravenous rat, mouse 209, 218 mg kg^{-1}, respectively (8,9).
LD_{50} intraperitoneal mouse, rat 128, 151 mg kg^{-1}, respectively (7,10).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (11).
Oral (12 month) 4- or 12-wk-old C3H mice, incidence of liver tumours in untreated was 7/17 in ♂ and 1/16 in ♀. Addition of 500 mg kg^{-1} in diet raised these incidences to 16/17 and 10/16 respectively (12).
Intraperitoneal (life) 36 ♂/♀ Sprague-Dawley rats 2 mg kg^{-1} wk^{-1}. Mean survival times were 80 wk in ♂ and 85 wk in ♀. Among 32 ♂ and 30 ♀ surviving 200 or more days, 2 tumours were observed, 1 malignant tumour of the adrenal gland and 1 carcinoma of the nasal cavity (13).

Metabolism and toxicokinetics

Intravenous rat 50 mg kg^{-1} body weight ^{14}C-phenobarbitone, concentration in liver was higher than in other internal organs and elimination in the urine reached a peak after 6-8 hr (14).
The major metabolite in humans is the *p*-hydroxy derivative, which is excreted in the urine partly as the sulfate conjugate (15).
In vitro human placenta. No evidence for metabolism to its *p*-hydroxylated form was found in either perfused lobules or incubations with placental microsomes. It was readily transferred across the placenta after addition to either maternal or foetal perfusates (16).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1530 and TA1537 with and without metabolic activation negative (17).
Drosophila melanogaster weakly mutagenic (18).
In vitro V79 Chinese hamster cells 50% reduction in protein values (3 day) 366 μg ml^{-1}; (4 hr) >1000 μg ml^{-1} (metabolic activation unspecified) (19).

Other effects

Other adverse effects (human)

31,877 infants born between 1965 and 1971 were studied in Cardiff; 245 mothers in this series had a history of epilepsy. Among the 111 births to epileptic mothers not on anticonvulsant therapy, the malformation rate was 2.7%, compared with 2.8% of infants in the total population. In contrast, 6.7% of 134 infants born to mothers receiving anticonvulsant therapy had malformations. One child had a hare lip but no cleft palate among 53 born to mothers treated with phenobarbitone alone; whereas 6 children were born with malformations among 60 births to mothers treated with phenobarbitone and phenytoin (20).
Of 7 patients orignally described as developing pseudolymphomas following phenobarbitone and/or phenytoin treatment, two died, one from multiple myeloma with an unknown survival time after diagnosis and another from malignant lymphoma, within 4 yr (21).

Any other adverse effects

Phenobarbitone-induced microsomal enzymes are characterised by a low substrate specificity. They are involved in the metabolism of a large variety of endogenous and exogenous substances; in the detoxification and activation of chemical carcinogens (22).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).

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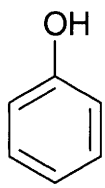
P80 phenol



C_6H_6O **Mol. Wt.** 94.11 **CAS Registry No.** 108-95-2

Synonyms benzenol; carbolic acid; hydroxybenzene; phenyl alcohol; phenylic acid; Satocide

EINECS No. 203-632-7 **RTECS No.** SJ 3325000

Uses Disinfectant. Manufacturing of colourless or light coloured artificial resins. Reagent in chemical analysis. Many medical and industrial organic compounds and dyes. Pharmaceutical aid; antibacterial agent.

Occurrence Animal wastes, decomposition of organic wastes (1).

Physical properties

M. Pt. 40.6°C **B. Pt.** 181.9°C **Flash point** 79°C (closed cup) **Specific gravity** 1.072

Partition coefficient log P_{ow} 1.50 **Volatility** v.p. 1 mmHg at 40°C ; v.den. 3.24

Solubility Water: 66.7 g l^{-1}. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

FR-VME 5 ppm (19 mg m^{-3})
JP-OEL 5 ppm (19 mg m^{-3})
SE-LEVL 1 ppm (4 mg m^{-3}) **SE-STEL** 2 ppm (8 mg m^{-3})
UK-LTEL 5 ppm (20 mg m^{-3}) **UK-STEL** 10 ppm (39 mg m^{-3})
US-TWA 5 ppm (19 mg m^{-3})

UN No. 2312 (molten)

UN No. 1671 (solid)

UN No. 2821 (solution) **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic in contact with skin and if swallowed – Causes burns (R24/25, R34)
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 followed by polyethylene glycol (mol. wt. 300) for at least 30 minutes – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S45)

Ecotoxicity

Fish toxicity
LC_{50} (25, 50 hr) bluegill sunfish >15, >10 mg l^{-1}, respectively (2).
LC_{50} (25, 50 hr) sailfin molly 63, 22 mg l^{-1}, respectively (2).
LC_{50} (24, 96 hr) mosquito fish 56, 23 mg l^{-1}, respectively (3).
LD_{50} (24 hr) goldfish 46 mg l^{-1} modified ASTM-D 1345 (4).
LC_{50} (48 hr) snakehead fish 46 mg l^{-1} (static bioassay) (5).
LC_{50} (24 hr) guppy 30 ppm at pH 7.3 (6).
LC_{50} (24 hr) rainbow trout 5.6-11.3 mg l^{-1} (7).
LC_{50} (96 hr) juvenile rainbow trout 0.15 mg l^{-1} (8).
LC_{50} (24 hr) eggs, embryo rainbow trout 5 mg l^{-1} (9).
LC_{50} (96 hr) fathead minnow 25.3 mg l^{-1} (10).
Brown and rainbow trout 0.005 mg l^{-1} raised from the stage of fertilised egg to the adult. Apart from the increased mortality of eggs no other differences were observed (11).

Invertebrate toxicity
Cell multiplication inhibition tests: *Pseudomonas putida* 64 mg l^{-1}, *Scenedesmus quadricauda* 7.5 mg l^{-1}, *Entosiphon sulcatum* 33 mg l^{-1} (12), *Microcystis aeruginosa* 4.6 mg l^{-1} (13).
Perturbation level *Paramecium caudatum* 10 mg l^{-1}, *Vorticella campanula* 3 mg l^{-1} (14).
LC_{50} (2 day) *Tanytarsus dissimilis* >51.1 mg l^{-1} (10).
EC_{50} (4 hr) *Selenastrum capricornutum* 290 mg l^{-1} (15).
LC_{50} (48 hr) *Daphnia magna* 23 mg l^{-1}; EC_{50} (16 day) *Daphnia magna* 10 mg l^{-1} (16).
EC_{50} (30 min) *Photobacterium phosphoreum* concentration 35.8 ppm Microtox test (17).

Bioaccumulation
Bioconcentration factor goldfish 1.9 (18), *Daphnia magna* 277 (19), gold orfe (20), *Chlorella fusca* 200 (20); *Scenedesmus quadricauda* 3.5 (21).

Environmental fate

Nitrification inhibition
Inhibits nitrification process in non-adapted activated sludge from 5.6 mg l^{-1} upwards (22).
75% inhibition of NH_3 oxidation in activated sludge (5.6 mg l^{-1}) (23,24).
1.0 mg l^{-1} was the limit concentration for inhibition of nitrification in Agar test (25).
Threshold inhibition of denitrification in rotating disc was 0.500 mg l^{-1} (26).

Carbonaceous inhibition

Inhibits degradation of glucose by *Pseudomonas fluorescens* at 20 mg l^{-1}; inhibition of degradation of glucose by *Escherichia coli* at >1000 mg l^{-1} (27).

1500 ppm inhibited cellulose degradation by natural soil populations (17 hr 98.4%, 200 hr 60.3%); 1500 ppm inhibited starch degradation by natural soil populations (20 hr 97.4%, 140 hr 85.1%) (28).

Escherichia coli inhibitory concentration 25.4 g l^{-1}, bacteriocidal concentration 140 g l^{-1}. *Pseudomonas aeruginosa* inhibitory concentration 16 g l^{-1}, bacteriocidal concentration 87 g l^{-1}. *Staphylococcus aureus* inhibitory concentration 15 g l^{-1}, bacteriocidal concentration 126 g l^{-1}. *Enterococcus faecium* inhibitory concentration 42 g l^{-1}, bacteriocidal concentration 162 g l^{-1} (29).

Anaerobic effects

C I_{50} (concentration at which bioactivity was 50% of control) was 1750, 1000, and 1700 mg l^{-1} phenol for acetate-, propionate-, and benzoate-degrading (upflow anaerobic sludge blanket) biogranules, respectively (30).

Degradation studies

The maximum rate of degradation obtained was 1 g l^{-1} day^{-1} by *Methanospirillum* and *Methanococcus* spp. (31).

BOD_5 33% ThOD; 90% biological oxidation, fresh dilution water; 55% biological oxidation, salt dilution water (2).

BOD_5 1.68 mg O_2 l^{-1} NEN 3235-5.4; COD 2.33 mg O^2 l^{-1} NEN 3235-5.3 (4).

TOC: 100% ThOD (32).

Degradation by adapted culture 500 mg l^{-1} 100% after 48 hr incubation feed (33).

Degradation of 500 ppm phenol by acclimated activated sludge after 12 hr aeration; 33% ThOD (2).

Degradation by *Pseudomonas* sp. 500 mg l^{-1} at 30°C; parent strains 100% ring disruption in 25 hr; mutant strains 100% ring disruption in 8 hr (34).

Partial inhibition has been noted at concentrations as low as 50 ppm in aerobic reactors using industrial wastewater seed and activated sludge seed (35).

95% degradation in 1 to 2 days using cultures obtained from garden soil, compost, river mud, and/or sediment from petroleum refinery waste lagoon; the microorganisms present were common to each of the cultures utilised (36).

Degradation is somewhat slower in salt water; $t_{1/2}$ 9 days in (estuarine river) (37).

Mineralisation in an alkaline para-brown soil under aerobic conditions was 45.5%, 48% and 65% after 3, 7, and 70 days, respectively (38).

In two silt loam soils degradation $t_{1/2}$ 2.7 and 3.5 hr, (low concentrations) of phenol present (39).

Good source of carbon for *Azotobacter* sp. strain GPI (40).

The $t_{1/2}$ in ground water, river water and harbour water were 20, 11 and 3 days, respectively (41).

[^{14}C]-labelled phenol in an OECD screening test, 75% degradation occurred within 28 days.

In an oxygen consumption inhibition test, the inhibitory threshold was 100 mg l^{-1} (42).

Abiotic removal

Photoxidation by UV light in aqueous medium at 50°C caused ~11% degradation to carbon dioxide after 24 hr (43).

Autoxidation at 25°C: $t_{1/2}$ 286 hr at pH 9.0, 629 hr at pH 7.0 (44).

Reacts with hydroxyl radicals in air, estimated $t_{1/2}$ 15 hr (45).

Reaction with nitrate radicals during night-time may be a significant removal process based on a rate constant of 3.8×10^{-12} cm^{-3} molecule-sec (46), which corresponds to a $t_{1/2}$ of 15 min at an atmospheric concentration of 2×10^8 nitrate radicals cm^{-3} (47).

Natural sunlight caused degradation in water (48).

Degrades on sand by a surface-catalysed reaction (38).

Reacts with photochemically produced singlet oxygen in surface waters contaminated by humic substances, estimated $t_{1/2}$ 83 days (49).

0.161 g removed g^{-1} activated carbon (50).

Adsorption and retention

Low adsorbicity to clay soils and silt loam reported (51).

K_{oc} values for two silt loams were 39 and 91. Based on the reported and estimated K_{oc} values, phenol is expected to exhibit high to very high mobility in soil and may therefore leach to ground water (52,53).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 113 mg kg^{-1} (54).
LD_{Lo} oral human infant 10 mg kg^{-1}, oral adult 140 mg kg^{-1} (55).
LD_{50} oral mouse, rat 270, 370 mg kg^{-1}, respectively (56,57).
LD_{50} dermal rat, rabbit 670, 850 mg kg^{-1}, respectively (58,59).
LC_{50} by inhalation (duration unspecified) mouse, rat 117, 316 mg m^{-3}, respectively (60).
LD_{50} subcutaneous rat 460 mg kg^{-1} (61).

Sub-acute and sub-chronic data

Rats, mice and monkeys exposed by inhalation to 25 ppm, 8 hr day^{-1}, 5 day wk^{-1} for 90 day, showed no significant adverse effects (62).
Guinea pigs exposed by inhalation to 25 ppm 6 hr day^{-1}, 5 day wk^{-1} showed excessive 42% mortality after 28-day exposure. Rabbits exposed to the same concentrations for 88 days showed no external signs of toxicity, but pathological changes were noted in the lungs, liver and kidney. Rats appeared to show no signs of toxicity, internally or externally, after 74-day exposure (63).

Carcinogenicity and chronic effects

Papillomas and carcinomas have been observed in sensitive mice pretreated with 7, 12-dimethylbenz[*a*]anthracene, indicating a strong tumour promoting activity, whilst in Swiss mice pretreated with benz[*a*]pyrene only a weak tumour promoting activity was demonstrated (64).
Oral (103 wk) ♂, ♀ rats and mice 2500 or 5000 ppm in drinking water, statistically significant increases in pheochromocytomas, leukaemias and lymphomas were observed in the low doses ♂ rats, but not the high-dose groups, nor in the ♀ rats or in the mice of either sex. It was concluded that there was insufficient evidence to classify phenol as a carcinogen (65).

Teratogenicity and reproductive effects

Increased incidence of preimplantation loss and early postnatal death has been reported in the offspring of rats exposed throughout pregnancy at 0.13 or 1.3 ppm (66).
Oral (days 6-15 of gestation) CD rat doses of 0, 30, 60 or 120 mg kg^{-1} day^{-1}; dose-related decreases in foetal body weight but no signs of structural malformations (67).
Placental changes were recorded in women exposed to phenol as an air pollutant at 14× the control limit. Pregnancies and neonates were otherwise normal (68).

Metabolism and toxicokinetics

Absorbed from the gastro-intestinal tract, skin and mucous membranes in humans. Metabolised to phenylglucuronide and phenyl sulfate, small amounts are oxidised to catechol and quinol conjugates. The metabolites are excreted in the urine; on oxidation to quinones they may tint the urine green (69).
In human volunteers exposed to phenol vapour for 8 hr at concentrations up to 6.8 mg m^{-3}, phenol excretion in the urine increased up to a maximum of 100 mg total phenol l^{-1}. Exposure to phenol vapour via inhalation or skin resulted in a urinary excretion rate constant $k = 0.2\ hr^{-1}$, corresponding to a half-life of approximately 3.5 hr for a one-compartment model (70).

Irritancy

Contact with the eyes causes severe damage, including conjunctival swelling, opacification and hypoethesia of the cornea and blindness (71).
5% solution instilled into the eyes of rabbits produced severe damage, including corneal opacities. The duration of these opacities was reduced by washing the chemical out of the eye 30 sec after instillation (72).

Genotoxicity

5 ppm (19 mg m^{-3}) (under review) *Escherichia coli* B/Sd-4 assay (0.1-0.2% phenol) mutagenic (73).
Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (74).
Salmonella typhimurium TA98 with metabolic activation positive; *Drosophila melanogaster* sex-linked recessive lethal mutations negative; *in vivo* mouse bone marrow micronuclei, chromosal aberrations negative (75).

In vitro HGPRT locus of the V79 Chinese hamster fibroblast cell line with metabolic activation positive (76).
A significant increase in sister chromatid exchanges was observed with metabolic activation in human lymphocytes (77).
Increases in sister chromatid exchanges were also observed in peripheral blood T-cell lymphocytes along with decreases in mitotic indices and inhibition of cell cycle kinetics following a single oral dose of 250 mg kg^{-1} to male mice (78).
Inhibition of DNA synthesis was produced with metabolic activation in HeLa cells (79).
Ultrastructural changes were observed in HeLa cells treated with ≥0.5% phenol ≥10 mins (80).

Other effects

Other adverse effects (human)

Exposure can cause extensive local corrosion with pain, nausea, vomiting, sweating, and diarrhoea. There is depression of the central nervous system, with circulatory and respiratory failure which may lead to death. Acidosis may develop and occasionally there is haemolysis and methaemoglobinaemia with cyanosis. The urine may become green. Pulmonary oedema and myocardial damage may develop, and damage to the liver and kidneys may lead to organ failure. Absorption of phenol from unbroken skin or wounds may cause poisoning. It causes blanching and corrosion when applied to skin. Aqueous solution as dilute as 10% may be corrosive. Toxic symptoms may also occur through absorption of phenol vapour by the skin or lungs (69).
Contamination of drinking water supplies have led to an increase in the incidence of gastro-intestinal disturbance (81).
A 41-yr-old man developed acute renal failure due to cutaneous absorption of phenol after falling into a vat of industrial solvent. No ingestion occurred. 50% body-surface burns, cold extremities, nausea, vomiting and respiratory distress were also observed (82).
A number of poisonings have been reported in workers exposed to phenol at 2-3 ppm, through contaminated quenching water in a coke oven plant (83).
A study of humans exposed to controlled conditions of phenol, 1.5-5.2 ppm for 8 hr with two 30 min breaks, showed no adverse effects from inhalation or skin absorption, and urinary phenol returned to normal within 16 hr of exposure (70).
A case of phenol marasmus was reported in a laboratory technician who was exposed to the vapours and through spills on the skin for 13.5 yr. On examination he was found to be emaciated, with an enlarged liver and altered liver function, and dark urine. Recovery was gradual after removal from exposure (84).
A technical assistant was sprayed with liquid phenol over ~25% of his body. He collapsed and died 10 min after the exposure (85).
Accidental death was reported in a person who died after being painted with benzyl benzoate as a scabicide with a brush which had been disinfected with 80% phenol (86).
Acute renal failure was reported in a man after accidental skin absorption of phenol (87).
Doses as low as 1 g have resulted in death (88).
Chronic oral exposures were reported in a group of people exposed after an accidental spill caused ground water contamination. Estimated doses were 10-240 mg day^{-1} for ~1 month. Most significant symptoms were diarrhoea, mouth sores and dark urine. No long-term effects were noted after 6 months (89).
Exposure to phenol in the wood working industry has been associated with increased incidence of respiratory cancer (90).
Atrophy of the papilla of the tongue has been observed in workers exposed to phenol and formaldehyde in the plastics industry, and it is suggested that the papilla may even undergo malignant transformation (91).

Any other adverse effects

Chronic exposures in rats, 0.02-1 ppm for 2 months produced changes in blood enzyme activity and time for excitation of extensor muscles and, at the higher exposure, decreases in body weight (92).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (93).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phenols: maximum admissible concentration 0.5 μg l^{-1}, excluding natural phenols which do not react to chlorine (94).

Other comments

Occurs in wastewater discharges from its use in manufacture, including iron and steel, leather tanning, aluminium works, foundries, pharmaceuticals and paints and inks industries (1).
Found in cigarette smoke and car exhaust fumes (95).
Taste and odour of fish is affected at 15-25 mg l^{-1} (2).
Aqueous solutions up to 1% are bacteriostatic while stronger solutions are bacteriocidal (69).
Its biological hazards have been reviewed (96).
It has been reported as a possible factor in cardiovascular disease (97).
Reviews on human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (98).
Autoignition temperature 715°C.

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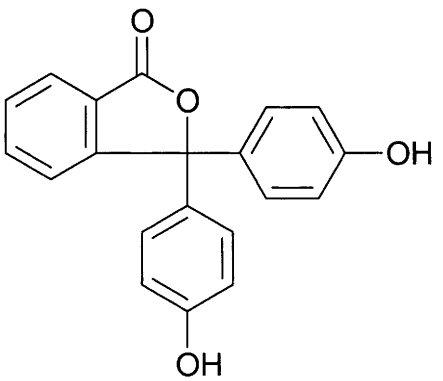
P81 phenolphthalein



$C_{20}H_{14}O_4$ **Mol. Wt.** 318.33 **CAS Registry No.** 77-09-8

Synonyms 3,3-bis(4-hydroxyphenyl)-1(3*H*)-isobenzofuranone; Phenolax; Prulet

EINECS No. 201-004-7 **RTECS No.** SM 8380000

Uses Indicator for titrations. Cathartic. Laxative, human and animal.

Physical properties

M. Pt. 261-263°C **Specific gravity** 1.277 at 32°C with respect to water at 4°C
Solubility Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
Proteus mirabilis, Azospirillum brasilense 0.5 mg ml^{-1} caused inhibition of swarming (1).
Bacillus thuringiensis 0.1 mg ml^{-1} caused growth inhibition (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} intraperitoneal rat 500 mg kg^{-1} (2).

Carcinogenicity and chronic effects
The National Toxicology Program tested rats and mice via feed. Clear evidence for carcinogenicity in ♂ rats and ♂ and ♀ mice, some evidence for carcinogenicity in ♀ rats (3).

Metabolism and toxicokinetics
Has been detected in human urine after the ingestion of 1 laxative tablet containing phenolphthalein (4).

In humans 15% is absorbed after oral administration. Enterohepatic circulation occurs. It is excreted in bile as the glucuronide with some excretion also occurring in the urine (5).

Sensitisation

Skin reactions or eruptions caused by hypersensitivity have been observed in patients undergoing treatment (5).

Other effects

Other adverse effects (human)

♂ who accidently ingested 2 g developed acute pancreatitis from which he completely recovered (6).

♀ who ingested a fatally large unknown amount of laxatives containing phenolphthalein developed widespread organ damage with disseminated intravascular coagulation, pulmonary oedema, myocardial damage, massive liver injury and renal failure (7).

Patients being treated with phenolphthalein have developed adverse effects such as cardiac and respiratory distress, renal damage and abdominal discomfort (5).

Other comments

Phenolpthalein is used as a test for liver function. Injection into the jugular of femoral veins of rats showed significant differences in the appearance of phenolphthalein in the bile, dependent on injection site (8).

Toxicity and mutagenicity of phenolphthalein reviewed (9).

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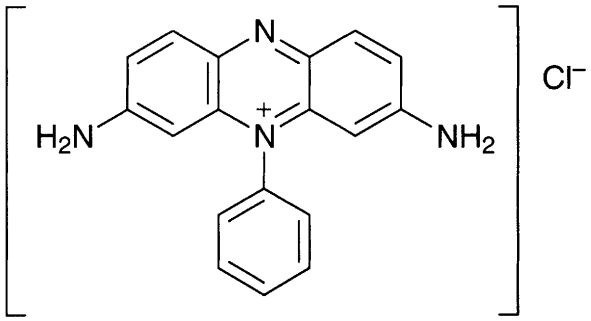
P82 phenosafranin



$C_{18}H_{15}ClN_4$ **Mol. Wt.** 322.80 **CAS Registry No.** 81-93-6

Synonyms 3,7-diamino-5-phenylphenazinium chloride; Safranin B Extra; Schultz no.958; phenosafranine; C.I. 50200

EINECS No. 201-387-0 **RTECS No.** SG 1630000

Uses Biological stain.

Physical properties

M. Pt. >300°C

Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 112 mg kg^{-1} (1).

LD_{50} intravenous mouse 18 mg kg^{-1} (2).

Genotoxicity

Eschericha coli Q13 DNA-cell-binding assay without metabolic activation positive with metabolic activation equivocal (3).

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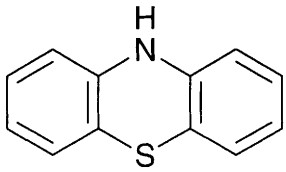
P83 phenothiazine



$C_{12}H_9NS$ **Mol. Wt.** 199.28 **CAS Registry No.** 92-84-2

Synonyms 10*H*-phenothiazine; thiodiphenylamine; dibenzothiazine; Phenoverm; Nemazine

EINECS No. 202-196-5 **RTECS No.** SN 5075000

Uses Pharmaceutical manufacture. Insecticide. Anthelmintic for animals.

Physical properties

M. Pt. 180-187°C **B. Pt.** 371°C **Partition coefficient** log P_{ow} 4.15

Solubility Organic solvents: benzene, diethyl ether, hot acetic acid

Occupational exposure

FR-VME 5 mg m^{-3}

US-TWA 5 mg m^{-3}

Ecotoxicity

Invertebrate toxicity

EC_{50} (5, 15, or 30 min) *Photobacterium phosphoreum* 19.9 ppm Microtox test (1).

Intestinal worm of sheep and goats *Oesophagostomum columbianum* in incubation medium EC_{50} 3.2-4.7 mg l^{-1} ♂, ♀ parasitic adult, EC_{50} 2.5 mg l^{-1} free living stage (2).

Phenothiazine was not toxic at saturation to *Tetrahymena pyriformix* in the dark, but was phototoxic under illumination with UVb radiation (100% mortality after 368 minutes) (3).

Environmental fate

Anaerobic effects

Phenothiazine in combination with chloronaphthalene and polychlorinated biphenyl was applied to an anaerobic microbial population collected from subsurface soil of grass prairie. Enzyme activities of this population were adversely effected by treatment (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling >100 mg kg^{-1} (5).

LD_{50} oral mouse 5000 mg kg^{-1} (6).

LD_{50} intravenous mouse 178 mg kg^{-1} (7).

Sensitisation

Sensitisation responses were observed in animal fodder workers who had not used phenothiazine for over 2 yrs (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).

Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (11).
The effect of tobacco smoking on the pharmacological action and pharmokinetics of phenothiazine are reviewed (12).
Unmodified it is too toxic for use in human medicine, but its derivatives are used in antihistamines and neuroleptics (13).

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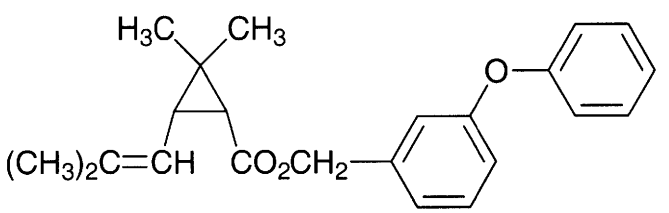
P84 phenothrin



$C_{23}H_{26}O_3$ **Mol. Wt.** 350.46 **CAS Registry No.** 26002-80-2

Synonyms cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-, (3-phenoxyphenyl)methyl ester; cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methylpropenyl)-, *m*-phenoxybenzyl ester; 3-phenoxybenzyl *cis,trans*-chrysanthemate; phenoxythrin; OMS 1809; OMS 1810; Sumithrin

EINECS No. 247-404-5 **RTECS No.** GZ 1975000

Uses Insecticide, mainly used in household aerosols. Control of human lice, incorporated into soaps, shampoos etc.

Physical properties

B. Pt. >290°C **Specific gravity** 1.058-1.061 at 25°C with respect to water at 25°C
Volatility v.p. 1.2032×10^{-6} mmHg at 20°C
Solubility Water: 9.7 μg l^{-1}. Organic solvents: acetone, xylene

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) killifish 200 μg l^{-1} (racemic) (1).
LC_{50} (96 hr) rainbow trout, bluegill sunfish 2.7, μg l^{-1} (racemic), respectively (2).

Invertebrate toxicity

LC_{50} (3 hr) *Daphnia pulex* 50 mg l^{-1} (racemic) (1).

Bioaccumulation

Levels of 0.2 μg g^{-1} were detected in bodies of poisoned honey bees (3).

Environmental fate

Degradation studies

[^{14}C]-[1*R*,*cis*]- or -[1*R*, *trans*]-phenothrin rapidly degraded in soils under upland conditions with initial $t_{1/2}$ 1-2 days, under flooded conditions $t_{1/2}$ 2-4 wk and 1-2 months for the *trans*- and *cis*-isomers, respectively (4). The degradation products found soil included: 3-(4-hydroxyphenoxy)benzoic acid, 3-(4-hydroxyphenoxy)benzyl alcohol, and 3-hydroxybenzyl 2,2-dimethyl-3-(2,2-dimethylvinyl)cyclopropanecarboxylate as well as the unchanged parent compound. These products did not persist and underwent further degradation to carbon dioxide (4).

Abiotic removal

[1*RS*,*trans*]-phenothrin in an oxygenated benzene solution under UV light or in a thin film under sunlight is rapidly photodegraded. Exposure to sunlight resulted in a 30% conversion, the major products being the alcohol, aldehyde and epoxides (5).

Adsorption and retention

In laboratory soil column investigations, < 2% of the applied phenothrin moved when leaching was started either immediately or 14 days after treatment (4).

Mammalian & avian toxicity

Acute data

LC_{50} oral bobwhite quail >2500 mg kg^{-1} diet (1*R*)-(*cis*-*trans*-isomers) (6).
LD_{50} oral rat, mouse >5000 mg kg^{-1} (racemic) (1).
LC_{50} (4 hr) inhalation rat, mouse >1210 mg m^{-3} (racemic) (1).
LD_{50} dermal rat, mouse >5000 mg kg^{-1} (racemic) (1).
LD_{50} subcutaneous rat, mouse >5000 mg kg^{-1} (racemic) (1).
LD_{50} intravenous ♂, ♀ mouse 265-317 mg kg^{-1} (racemic) (1).
LD_{50} intraperitoneal rat, mouse >5000 mg kg^{-1} (racemic) (1).

Sub-acute and sub-chronic data

Inhalation (4 wk) rat, mouse 0, 43 or 220 mg m^{-3} 4 hr day^{-1} 5 day wk^{-1} (racemic) no adverse toxicological effects were observed (1).
Oral (6 month) rat 0, 1, 3 or 10 g kg^{-1} diet (*d*-phenothrin) no significant effect on mortality, clinical signs, opthalmology, urinalysis or histopathological findings. Raised serum albumin levels were found after 3 months in ♂ fed 10 g kg^{-1} and ♀ 3 or 10 g kg^{-1}. Absolute and relative liver weights were increased in ♂ and ♀ fed 3 or 10 g kg^{-1} (1).
Oral (26 wk) dog 0, 100, 300 or 1000 mg kg^{-1} (*d*-phenothrin) diet no abnormal findings were observed except for raised alkaline phosphatase activity in ♂ fed ≥ 300 mg kg^{-1} and ♀ fed 1000 mg kg^{-1} (1).
Oral (52 wk) dog 0, 100, 300, 1000 or 3000 mg kg^{-1} diet (*d*-phenothrin) no significant effects on clinical signs, body weight, food consumption, opthalmology or urinalysis. The 3000 mg kg^{-1} dose group showed decreased haemoglobin concentration, haematocrit, erythrocyte count and total blood protein and increased liver weight. ≥1000 mg kg^{-1} caused focal degeneration of the adrenal cortex with cytoplasmic deposition of crystalline material in some animals (1).

Carcinogenicity and chronic effects
Oral rat (105-118 wk) 0, 300, 1000 or 3000 mg kg^{-1} diet (*d*-phenothrin). No oncogenic activity was observed (1).
Oral mouse (18 month) 0, 300, 1000 or 3000 mg kg^{-1} diet (racemic) no significant increase in tumours was observed (1).

Teratogenicity and reproductive effects
Oral New Zealand White rabbits 3-30 mg kg^{-1} day^{-1} (racemic) on days 6-18 of gestation 30 mg caused a slight decrease in maternal body weight, foetal weight and the number of live young. No teratogenic effects were observed (1).
Oral ICR mice, 30-3000 mg kg^{-1} day^{-1} (*d*-phenothrin) on days 7-12 of gestation, no teratogenic or embryotoxic effects were observed (1).
A three-generation reproduction study in rats fed racemic phenothrin at 200-2000 mg kg^{-1} diet. No adverse effects on reproduction were observed (1).

Irritancy
♂ volunteers had *d*-phenothrin (talc powder formulation with Span 80 as a stabiliser) applied to their head and pudenda hair 32 mg man^{-1} day^{-1} for 3 days, the powder was left on the hair for 1 hr and then washed off. No dermal irritation was observed and no *d*-phenothrin was detected in the blood (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (*d*-phenothrin) (1).
Escherichia coli WP2*uvr* with and without metabolic activation negative (*d*-phenothrin) (1).
In vitro Chinese hamster ovary cells with and without metabolic activation chromosome aberrations negative (*d*-phenothrin) (1).
In vivo mouse bone marrow cells chromosome aberrations negative (*d*-phenothrin) (1).

Other effects

Any other adverse effects
In rats, changes were observed in carbohydrates and proteins but it did not cause chromosomal aberrations (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).
WHO Toxicity class table 5 (10).
EPA Toxicity class IV (formulation) (2).
ADI 0.07 mg kg^{-1} body weight for *d*-phenothrin (2).

Other comments

Racemic phenothrin (CAS RN 26002-80-2) is a mixture of 4 stereoisomers: [1*R*,*trans*], [1*R*,*cis*], [1*S*,*trans*] and [1*S*,*cis*]. The only commercially available phenothrin, *d*-phenothrin is a 1:4 mixture of [1*R*,*cis*] and [1*R*,*trans*] isomers (1).
Toxic to bees (6).

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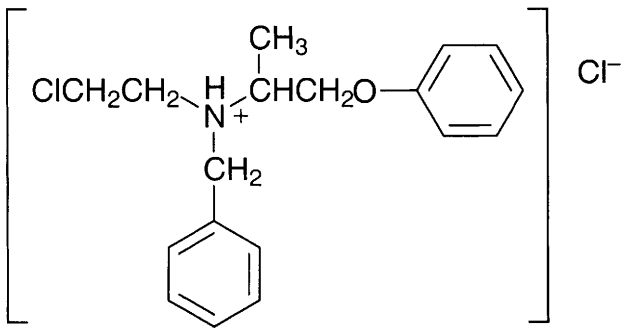
P85 phenoxybenzamine hydrochloride



$C_{18}H_{23}Cl_2NO$ **Mol. Wt.** 340.29 **CAS Registry No.** 63-92-3

Synonyms benzenemethanamine, *N*-(2-chloroethyl)-*N*-(1-methyl-2-phenoxyethyl)-, hydrochloride; benzylamine, *N*-(2-chloroethyl)-*N*-(1-methyl-2-phenoxyethyl)-, hydrochloride; dibenzyline chloride; dibenzyline hydrochloride; phenoxybenzamine chloride

EINECS No. 200-569-7 **RTECS No.** DP 3750000

Uses Adrenergenic blocker used in the treatment of peripheral vascular disorders including Raynaud's disease, frostbite sequelae and acrocyanosis. Antihypertensive.

Physical properties

M. Pt. 137.5-140°C
Solubility Organic solvents: chloroform, ethanol, propylene glycol

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig, mouse 500, 900 mg kg^{-1}, respectively (1,2).
LD_{Lo} oral rat 800 mg kg^{-1} (3).
LD_{50} intravenous mouse 63.75 mg kg^{-1} (4).
LD_{50} subcutaneous mouse 105 mg kg^{-1} (5).
LD_{50} intraperitoneal mouse 228 mg kg^{-1} (6).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (7).
Intraperitoneal (85 wk) ♂, ♀ B6C3F_1 mice 12.5 or 25 mg kg^{-1} 3 × wk in phosphate-buffered saline containing 0.05% polysorbate 80 for the first 10 wk and then in 6% propylene glycol in saline for 42 wk (1 ml 100 g^{-1} body weight), the mice were observed for the remainder of the experimental period. All of the high-dose group ♂ died by 50 wk. Of the high-dose groups 17/21 ♂ and 16/20 ♂ developed abdominal cavity (peritoneal) sarcomas. The

low-dose groups and control developed no such tumours (8).
Intraperitoneal (85 wk) ♂, ♀ Sprague-Dawley rat 5 or 10 mg kg^{-1} body weight 3 × wk^{-1} in phosphate-buffered saline containing 0.05% polysorbate 80 for 13 wk and then in 6% propylene glycol in saline for 37 wk (0.25 ml 100 g^{-1} body weight. In the high-dose groups 16/20 ♂ and 16/30 ♀ and in the low-dose groups 11/31 ♂ and 0/35 ♀ developed abdominal cavity (peritoneal) sarcomas (8).

Teratogenicity and reproductive effects
Oral rat 10 mg kg^{-1} day^{-1} on the first 5 days of gestation and intraperitoneal rat 20 mg kg^{-1} day^{-1} on days 2-5 of gestation had no effect on implantation (9,10).

Metabolism and toxicokinetics
[^{14}C]phenoxybenzamine hydrochloride (0.54 mg) injected intravenously into mice remained in the blood for 40 min. Radioactivity was found widely distributed in tissues (notably the heart and central nervous system). Radioactivity remained for 4 days, biliary excretion provided an important route for elimination (11).
[^{14}N]phenoxybenzamine hydrochloride administered intraperitoneally or orally to rats and orally to dogs. The principal urinary metabolite in both species was *N*-benzyl-*N*-(*p*-hydroxyphenoxy)isopropylamine, minor metabolites included *N*-benzyl-*N*-phenoxyisopropylamine in dogs and intraperitoneally injected rats, phenoxyisopropylamine in dogs and 2-benzylamino-1-propanol in intraperitoneally injected rats (12).
The metabolite *N*-benzyl-*N*-(*p*-hydroxyphenoxy)isopropylamine was identified in the urine of treated patients (12).
In humans, absorption from the gastro-intestinal tract is variable and incomplete. Following intravenous administration a maximum effect is obtained after 1 hr whilst oral administration leads to a slower effect, 3-4 hr after administration which persists for up to 4 days. The plasma $t_{1/2}$ ~24 hr in humans (13).
It is metabolised in the liver and excreted in the bile and urine (human) (13).

Other effects

Other adverse effects (human)
Adverse effects occurring in patients undergoing treatment include reflex tachycardia, dizziness, nasal congestion, miosis, postural hypertension and inhibition of ejaculation (12).

Other comments

In humans it blocks α-adrenergenic receptors with action on the peripheral vascular system (14).
Reviews on human health effects and experimental toxicology listed (15).
Has been shown to be mutagenic in *in vitro* tests (species not specified) (13).

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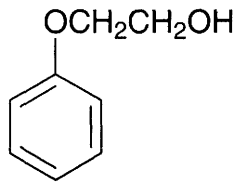
P86 2-phenoxyethanol



$C_8H_{10}O_2$ **Mol. Wt.** 138.17 **CAS Registry No.** 122-99-6

Synonyms ethylene glycol monophenyl ether; β-hydroxyethyl phenyl ether; phenoxethol; β-phenoxyethyl alcohol; phenyl cellosolve; Dowanol EP; 1-hydroxy-2-phenoxyethane

EINECS No. 204-589-7 **RTECS No.** KM 0350000

Uses Topical antiseptic. In organic synthesis. Insect repellent. Perfume fixative. Fish anaesthetic. Preservative in pharmaceutical and cosmetic preparations.

Physical properties

M. Pt. 11-13°C (98% pure) **B. Pt.** 237°C (98% pure) **Flash point** 110°C (98% pure)
Specific gravity 1.102 at 22°C with respect to water at 4°C
Solubility Water: 26.7 g l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 20 ppm (110 mg m^{-3})
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) – 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 345 g l^{-1} (1).
Carp (~ 600 g in weight) 400-800 ppm (duration unspecified). 400 ppm caused deep sedation, an increase in ventilation frequency, tachycardia and a slight decrease in oxygen consumption, at 600 ppm the tachycardia had disappeared and there was a decrease in all respiratory parameters. Fish exposed to 400 or 600 ppm recovered when placed in fresh water. 800 ppm caused progressive bradycardia, an increase in the time elements of the electrocardiogram reading and a drop to almost zero in respiratory parameters owing to cessation of ventilation movement, fish did not recover. Death was due to anoxia induced by paralysis of the respiratory centre (2).
Rainbow trout exposed to 2-phenoxyethanol (duration unspecified) developed severe hypoxia accompanied by a cessation of breathing in deep anaesthesia. There was a fall in blood pH and a rise in adrenaline levels and carbon dioxide partial pressure (3).
In rainbow trout tranquilised with 2-phenoxyethanol it was rapidly excreted, biological $t_{1/2}$ ~30 min. It was found distributed especially in the cerebellum and also the gall bladder, kidneys, liver and brain (4).

Invertebrate toxicity
LC_{50} (5 min) *Photobacterium phosphoreum* 32.4 ppm Microtox test (5).
Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecium minimum inhibitory concentration (growth) 2.44-7.32 mg l^{-1} (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1.26 g kg^{-1} (7).

LD_{50} dermal rabbit 5000 mg kg^{-1} (8).

Teratogenicity and reproductive effects

Dermal pregnant rabbits 300, 600 or 1000 mg kg^{-1} day^{-1} on days 6-18 of gestation. Dose-related maternal toxicity was observed at 600 and 1000 mg kg^{-1} day^{-1} with some deaths in the higher dose group. Examination of embryos showed no embryotoxic, foetotoxic or teratogenic effects (9).

Oral ♂, ♀ Swiss CD-1 mice 0.04, 2.0 or 4 g kg^{-1} day^{-1} in feed. They were dosed for 7 days prior to and during a 48-day cohabitation. During the continuous breeding period there was no alteration in the ability to produce 5 litters. In the high-dose group there was a significant reduction (10-15%) in the number of pups $litter^{-1}$ and pup weight. It was indicated that ♀s were susceptible to reproductive toxicity. Severe neonatal toxicity was observed; in the mid- and high-dose groups after 21 days only 8/40 litters had at least 1 ♂ and 1 ♀ $litter^{-1}$ (10).

Oral ♂, ♀ CD-1 mice 2.50% in diet. The mice were kept separately during the first 7 days of treatment and were then randomly paired and kept together for the next 9 days, during which treatment was continued. ♂ body weight was decreased but there was no change in ♂ organ weight, or in sperm motility, concentration or sperm numbers (11).

Metabolism and toxicokinetics

Absorption through unoccluded rat skin *in vitro* in the static diffusion cell 64 ± 4.4% at 24 hr and through unoccluded human skin 59.3 ± 7.0% at 6 hr. Post mitochondrial fraction of rat skin metabolised phenoxyethanol to phenoxyacetic acid at 5% of the rate for liver, but first-pass metabolism of phenoxyethanol to phenoxyacetic acid was not detected during percutaneous penetration through viable rat skin in the flow-through system (12).

Irritancy

Dermal (24 hr) rabbit 500 mg caused moderate irritation and 250 µg instilled into the eye (24 hr) caused severe irritation (13).

Dermal human caused mild stinging in 10 volunteers. When combined with cosmetic ingredients, strong stinging was reported in 17 volunteers, especially in an aqueous solution of 2% 2-phenoxyethanol, 10% ethanol and 0.3% methylparaben (14).

Sensitisation

Dermal human 5% in patch test, 1/501 patients developed an allergic reaction (15).

Other effects

Any other adverse effects

Escherichia coli grown in culture with 2-phenoxyethanol showed marked decrease in thymidine, uracil and glucose uptake and utilisation, which was comparable with a decrease in growth rate (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).

Other comments

Toxicity reviewed (19).

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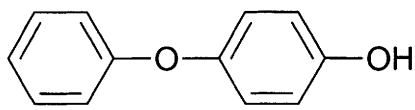
P87 4-phenoxyphenol



$C_{12}H_{10}O_2$ **Mol. Wt.** 186.21 **CAS Registry No.** 831-82-3

Synonyms *p*-phenoxyphenol; 4-hydroxydiphenyl ether; *p*-hydroxydiphenyl ether

EINECS No. 212-611-1

Physical properties

M. Pt. 83-85°C

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 4.56 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (5, 15 or 30 min) *Photobacterium phosphoreum* 6.17 ppm Microtox test (2).

Environmental fate

Degradation studies

Erwinia sp. mutants isolated from sewage by enrichment on methanol and lignin could degrade 4-phenoxyphenol in the presence of copper ions (3).

References

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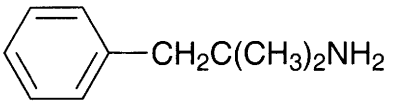
P88 phentermine



$C_{10}H_{15}N$ **Mol. Wt.** 149.24 **CAS Registry No.** 122-09-8

Synonyms α,α-dimethylphenethylamine; phenyl-*tert*-butylamine; α-benzylisopropylamine; 1,1-dimethyl-2-phenylethanamine; Duromine; Lipopill; Ionamin; Mirapront; Wilpo; α,α-dimethylbenzeneethanamine; α,α-dimethylphenethylamine

EINECS No. 204-522-1 **RTECS No.** SH 4025000

Uses Ingredient of phentermine resins. Anorexic.

Physical properties

Solubility Organic solvents: chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 105 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 71 mg kg^{-1} (2).
LD_{50} intravenous mouse 14 mg kg^{-1} (3).
TD_{Lo} oral man 1429 μg kg^{-1} (4).

Metabolism and toxicokinetics

p-Hydroxyphentermine was isolated as the hydrochloride from urine of rats dosed with phentermine, indicating that *p*-hydroxylation of phentermine is a primary metabolic reaction (5).

Genotoxicity

Aspergillus nidulans P and P_1 used to detect non-disjunction and crossing over showed positive mutagenicity (6).

Other effects

Any other adverse effects

Urticaria may occur with use (7).

References

1. *Arch. Int. Pharmacodyn. Ther.* 1969, **178**, 62.
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3. *Report No. NX 03232* US Army Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals (Aberdeen Proving Ground), MD, USA.
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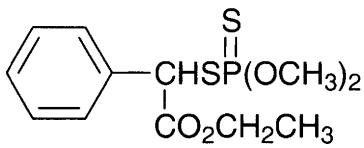
P89 phenthoate



$C_{12}H_{17}O_4PS_2$ **Mol. Wt.** 320.37 **CAS Registry No.** 2597-03-7

Synonyms *O,O*-dimethyldithiophosphorylphenylacetic acid, ethyl ester; *O,O*-dimethyldithiophosphorylbenzeneacetic acid, ethyl ester; *S*-[α-(ethoxycarbonyl)benzyl] *O,O*-dimethyl phosphorodithioate; ethyl 2-dimethoxyphosphinothioyl(phenyl) acetate; ethyl α-[(dimethoxyphosphinothioyl)thio]benzeneacetate; ethylmercaptophenyl acetate (*S*)-ester with *O,O*-dimethylphosphorodithioacetate; Elsan; Rogodial; Phendal

EINECS No. 219-997-0 **RTECS No.** AI 7875000

Uses Non-systemic insecticide. Acaricide.

Occurrence Residues have been detected in crops, dairy products and meat. Environmental pollutant. Food contaminant.

Physical properties

M. Pt. 17-18°C **Flash point** 165-170°C **Specific gravity** 1.226 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.69 (1) **Volatility** v.p. 4.0×10^{-5} mmHg at 40°C
Solubility Water: 11 mg l^{-1} at 24°C. Organic solvents: acetone, benzene, carbon disulfide, carbon tetrachloride, cyclohexane, diethyl ether, ethanol, *n*-hexane, petroleum spirit, xylene

Occupational exposure

UN No. 2783 (solid)

UN No. 3018 (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) – Do not breathe dust – Wear suitable protective clothing and gloves (S2, S22, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) mosquito fish, goldfish, carp, minnow 0.12-2.5 mg l^{-1} (1-3).
Phenthoate acts synergistically with carbamate antichlolinesterases such as carbaryl to enhance their toxicity to fish (4).

Invertebrate toxicity
LC_{50} (96 hr) tiger shrimp (nauplius and zoea stages) 5 ppm. Toxicity increased through larval stages, especially after metamorphosis when it increased by >800-fold (5).
LC_{50} (acute survival) *Daphnia pulex* 0.002 mg l^{-1} (3).
LD_{50} bee, 0.306 μg bee^{-1} (1).

Bioaccumulation
Calculated bioconcentration factor is 31 (6).
Topmouth gudgeon kept under continuous flow conditions in water containing 5-20 mg l^{-1} accumulated phenthoate (7).

Environmental fate

Degradation studies

In plants, there is oxidation to phosphorothioate followed by hydrolysis; metabolites detected include, phosphoric acid dimethyl phosphate, and monomethyl phosphate (8).

Abiotic removal

Hydrolysis in water $t_{1/2}$ ~12 days at pH 8. Major hydrolysis products are phenthoate acid, dimethylphenthoate and dimethylphenthoate oxon (9).

Degradation products formed on exposure to sunlight were unchanged phenthoate, phenthoate oxon, demethylphenthoate, mandelic acid bis[α-(carbethoxy)benzyl] disulfide, *O,O*-dimethylphosphorothioic acid and phosphorodithioic acid (9).

Adsorption and retention

Calculated K_{oc} 240 indicates that significant adsorption to soil and sediments is unlikely (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken, quail 36, 300 mg kg^{-1}, respectively (10,11).

LD_{50} oral rat 76-116 mg kg^{-1} (10).

LD_{50} oral rat, mouse 300-400 mg kg^{-1} (8).

Oral rat, 20-40 mg inhibited blood and brain acetylcholinesterase and caused hypothermia (12).

LC_{50} (4 hr) inhalation rat >800 mg m^{-3} (1,8).

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

LD_{50} dermal rat, mouse 2100, >5000 mg kg^{-1}, respectively (8).

Dermal buffalo calves 125 or 250 mg kg^{-1}. Blood samples taken at intervals for up to 8 hr showed cholinesterase activity was inhibited dose-dependently; hyperglycaemia was also observed (13).

LD_{50} subcutaneous mouse 1470 mg kg^{-1} (14).

Carcinogenicity and chronic effects

In a 20-month feeding trial to rats a no-effect level of 10 mg kg $diet^{-1}$ was established (8).

Irritancy

Non-irritant to skin of rabbits (dose, duration unspecified) (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (15).

Escherichia coli WP2hcr reverse mutation assay negative (16).

Other effects

Any other adverse effects

Concentrations in the region of 0.38 g l^{-1} inhibited acetylcholinesterase activity by 50% (5).

In mammals a low dose which was capable of inhibiting cholinesterase activity had no effect on glutamic oxalactic transaminase or glutamic pyruvic transaminase activity in serum, but at higher doses the levels of both enzymes was raised indicating liver damage (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).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (20).

WHO Toxicity Class II (21).

EPA Toxicity Class II (1).

ADI 0.003 mg kg^{-1} body weight (1).

Other comments

Genotoxicity reviewed (22).

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19. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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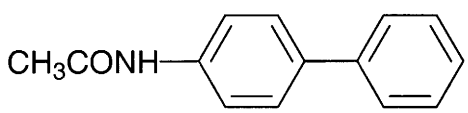
P90 4-phenylacetanilide



$C_{14}H_{13}NO$ **Mol. Wt.** 211.26 **CAS Registry No.** 4075-79-0

Synonyms *p*-phenylacetanilide; 4-acetylaminobiphenyl; (1,1'-biphenyl-4-yl)acetamide; 4-acetamidobiphenyl

RTECS No. AE 6125000

Uses In genotoxicity and cytotoxicity testing.

Physical properties

M. Pt. 170-172°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

A single subcutaneous injection of 25-100 μg 4-phenylacetanilide induced hepatoma, pulmonary adenoma and lymphoma in neonatal ICR/Ha mice, duration of study 1 yr (1).

In ♀ rats, 0.025% dietary dose as a supplement for 12-15 months induced distant tumours at one or more unspecified sites (2).
8-10 month feeding trials in rats (concentrations unspecified) induced a high number of adenocarcinomas of the mammary glands in ♀ rats and a small number of adenocarcinomas of the small intestine and squamous cell carcinomas and sebaceous gland carcinomas of the earduct in both ♂ and ♀ mice (3).

Metabolism and toxicokinetics

In rabbits, 4-phenylacetanilide administered orally and intraperitoneally was excreted in urine as the glucuronide and *N*-hydroxy derivatives (4).
Intraperitoneal rat 186 mg kg^{-1}, 4-phenylacetanilide appeared slowly in the blood, accompanied by the appearance of aminobiphenyl and 4-hydroxyacetylaminobiphenyl. After 4 hr the concentration of 4-phenylacetanilide and aminobiphenyl were in dynamic equilibrium with the *N*-deacetylation of 4-phenylacetanilide and the acetylation of aminobiphenyl (5).
A single oral dose of 100 mg kg^{-1} in the rat was metabolised to arylamine, *N*-arylformamide and *N*-arylacetamide. The compounds were excreted in the urine and faeces. Percentages of arylamine, *N*-arylformamide and *N*-arylacetamide excreted in urine were 0.25%, 0.01% and 0.44%, respectively. Percentages excreted in the faeces were 0.29%, 0.04% and 8.21%, respectively (6).
The metabolism of 4-phenylacetanilide was followed by *in situ* guinea pig perfusion using a recirculation method. The results demonstrated that the compound was metabolised by a combination of *N*-acetylation, *C*- and *N*-hydroxylations, as well as glucuronidation (7).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation induced frameshift and base-pair mutations (8).
4-Phenylacetanilide reduced the survival of *Escherichia coli Uvr* endonuclease-deficient strains and reduced the ability of PBR322 plasmid DNA to transform the *Escherichia coli* strains (9).
Inactive in cytotoxicity tests using Xeroderma pigmentosum human cells (10).

References

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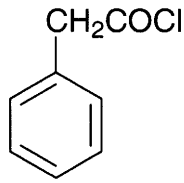
P91 phenylacetyl chloride



C_8H_7ClO **Mol. Wt.** 154.60 **CAS Registry No.** 103-80-0

Synonyms benzeneacetyl chloride; phenylacetic acid chloride; α-phenylacetyl chloride

EINECS No. 203-146-5

Physical properties

B. Pt. 104-105°C at 24 mmHg **Flash point** 102°C **Specific gravity** 1.1682 at 20°C

Solubility Water: hydrolyses in water. Organic solvents: ether

Occupational exposure

UN No. 2577 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (5, 10, 15 min) *Photobacterium phosphoreum* 3.38 ppm Microtox test (1).

References

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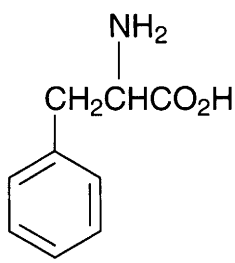
P92 L-phenylalanine



$C_9H_{11}NO_2$ **Mol. Wt.** 165.19 **CAS Registry No.** 63-91-2

Synonyms (*S*)-α-aminobenzenepropanoic acid; α-aminohydrocinnamic acid; β-phenylalanine; antibiotic FN 1636; phenylalanine; 3-phenylalanine

EINECS No. 200-568-1 **RTECS No.** AY 7535000

Uses An essential amino acid, required in human diet but not synthesised by humans. Biochemical research. Laboratory reagent. Dietary supplement.

Occurrence Whole eggs and skin (5.4 and 5.1%, respectively).

Physical properties

M. Pt. 275-283°C (decomp.)
Solubility Water: 19.8 g l^{-1} at 25°C. Organic solvents: slightly soluble, diethyl ether, ethanol, methanol

Environmental fate

Degradation studies
Activated sludge treatment: 6 hr, 2.3% of ThOD; 12 hr, 5.6% of ThOD; and 24 hr, 16.4% of ThOD (1).
Activated sludge, fed 333 mg l^{-1} (at 20°C), 15 days acclimation 99% was removed (2).
Anaerobic metabolism by the denitrifying bacterium *Thauera aromatica* was studied using phenylalanine as the sole carbon source. Evidence was found that biodegredation proceeded via benzoyl-CoA as the central aromatic intermediate. Phenylpyruvate, phenylacetaldehyde, phenylacetate, phenylacetyl-CoA, and phenylglyoxalate were intermediates in the oxidation of phenylalanine to benzoyl-CoA (3).

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal rat 5287 mg kg^{-1} (4).

Teratogenicity and reproductive effects
In vitro rat embryo limb bud cells, inhibited chondrogenesis which indicates a positive teratogenic effect (5).
Logistic regression and discriminant analysis were used to predict L-phenylalanine's developmental toxicity. It was predicted to be positive for humans and primates (6).
In vitro neurulating mouse embryos 1.65-1650 mg l^{-1} for 24 hr. 1650 mg l^{-1} inhibited cranial neural tube closure in 82% of embryos; concentrations below this had no teratogenic effects (7).

Metabolism and toxicokinetics
[^{14}C]Phenylalanine fed to rats in diet containing 0, 5, 10, 15 or 30% of protein calories (4100 kcal of metabolisable energy kg^{-1} diet). >80% of the dose groups of 0 and 5% protein calories were incorporated into body protein 12 hr after injection; incorporation decreased gradually at higher levels (8).
Oral Senegal baboon 5, 150 or 450 mg kg^{-1}. 1-4 hr after the highest dose was given peak plasma levels were ~330 mg l^{-1}. The plasma L-phenylalanine:large neutral amino acid ratio increased ~30-fold (9).
p-[^{125}I]Iodo-DL-phenylalanine, mouse pancreas *in vivo* and *in vitro*. It showed a high affinity for the pancreatic cell membrane active transport system, which was indicated by a high and specific accumulation in the pancreas followed by rapid clearance (10).
Radiofluorolabelled-L-phenylalanine injected into the tail vein of mice, ~2% accumulated in the brain (11).

Other comments

Serum collected from rats that had been intraperitoneally injected was added *in vitro* to HIV-infected T-cells. It inhibited HIV virus growth (12).
Did not show attractant reactions to crucian carp at $1.65 \times 10^{-5} - 1.65 \times 10^{-3}$ g l^{-1} (13).
Toxicity to developing chick embryos reviewed (14).
Used (successfully) in conjunction with UVA/sunlight in the treatment of patients with vitiligo (15).

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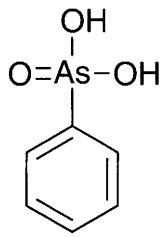
P93 phenylarsonic acid



$C_6H_7AsO_3$ **Mol. Wt.** 202.04 **CAS Registry No.** 98-05-5

Synonyms benzenearsonic acid; phenylarsenic acid

EINECS No. 202-631-9 **RTECS No.** CY 3150000

Uses Reagent for tin. In the preparation of carbarsone (an antiamoebic agent in humans). Veterinary medicine. In the preparation of tryparsamide.

Physical properties

M. Pt. 160°C **Specific gravity** 1.760
Solubility Water: 25 g l^{-1}

Occupational exposure

UK-LTEL MEL 0.1 mg m^{-3} (as As)

Ecotoxicity

Fish toxicity
Exposure to 5 ppm caused trout to die within 23 hr (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 583 mg l^{-1} Microtox test (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 50 mg kg^{-1} (3).
LD_{50} intravenous rabbit 16 mg kg^{-1} (4).

Metabolism and toxicokinetics
Major excretory route (species unspecified) urine (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50μg l^{-1} As (6).

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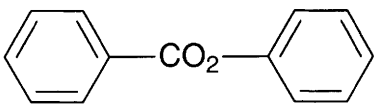
P94 phenyl benzoate



$C_{13}H_{10}O_2$ **Mol. Wt.** 198.22 **CAS Registry No.** 93-99-2

Synonyms benzoic acid, phenyl ester; phenol benzoate

EINECS No. 202-293-2 **RTECS No.** DH 6299500

Uses Manufacture of plastics, plasticisers and perfume. Insecticide.

Physical properties

M. Pt. 69-71°C **B. Pt.** 298-299°C **Specific gravity** 1.235 at 20°C **Partition coefficient** log P_{ow} 3.59
Volatility v.p. 1 mmHg at 106.8°C
Solubility Organic solvents: diethyl ether, hot ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 1.44 ppm Microtox test (1).

Environmental fate

Adsorption and retention
Sorption coefficients were determined for 3 soil types. The K_{oc} values determined were: 2646 podzol, 798 alfisol, and 848 sediment (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 1225 mg kg^{-1} (3).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendment) (4).
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).

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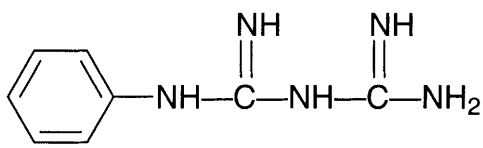
P95 1-phenylbiguanide



$C_8H_{11}N_5$ **Mol. Wt.** 177.21 **CAS Registry No.** 102-02-3

Synonyms *N*-phenylimidodicarbonimidic diamide; phenylbiguanide; *N*-phenyl-*N'*-guanylguanidine

EINECS No. 202-998-5 **RTECS No.** DU 2450000

Physical properties

M. Pt. 135-142°C
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 500 mg kg^{-1} (1).

References

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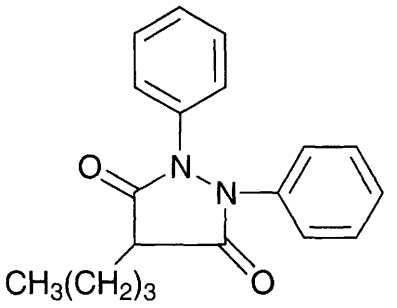
P96 phenylbutazone



$C_{19}H_{20}N_2O_2$ **Mol. Wt.** 308.38 **CAS Registry No.** 50-33-9

Synonyms 4-butyl-1,2-diphenyl-3,5-pyrazolidinedione; Arthrizon; Butalidon; diphebuzol; flexazone; Reumuzol

EINECS No. 200-029-0 **RTECS No.** UQ 8225000

Uses Anti-inflammatory. Analgesic.

Physical properties

M. Pt. 105°C

Solubility Water: 0.7 mg ml^{-1} at 22.5°C. Organic solvents: chloroform, diethyl ether

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂, ♀ rat 1311, 647 mg kg^{-1}, respectively (1).
LD_{50} oral rat, mouse, dog, guinea pig 245-332 mg kg^{-1} (2-5).
LD_{50} oral rabbit, hamster 781, 1260 mg kg^{-1}, respectively (4,6).
LD_{50} subcutaneous rat, mouse 230 mg kg^{-1} (7,8).
LD_{50} intraperitoneal mouse, rat 128-142 mg kg^{-1} (9,10).
LD_{50} intravenous mouse, rat, cat, dog, rabbit 90-146 mg kg^{-1} (11-14).
LD_{50} intramuscular rat, mouse 220, 430 mg kg^{-1}, respectively (12,15).

Sub-acute and sub-chronic data

Gavage (19 day) F344/N rat, B6C3F1 mouse ≤600 mg kg^{-1}. The deaths of 3/5 ♂ and 4/5 ♀ rats receiving 600 mg kg^{-1} and 2/5 ♀ receiving 300 mg kg^{-1} were considered to be related to treatment. The body weights of rats receiving 300 or 600 mg kg^{-1} were 14-15% and 46%, respectively, lower than the controls. No compound-related deaths or body weight reductions were recorded in mice (16).

Gavage (13 wk) F344/N rat ≤300 mg kg^{-1}, B6C3F1 mouse ≤600 mg kg^{-1}. Most of the rats receiving 300 mg kg^{-1} and 1/10 ♂, 2/10 ♀ that received 200 mg kg^{-1} died early, with the final body weight of the 300 mg kg^{-1} group ♂ rats being 31% lower than the controls. Liver weight to body weight ratios were increased in the 200 and 300 mg kg^{-1} group rats. Lesions observed were mainly in the kidney and included papillary oedema and necrosis and multifocal mineralisation. 5/10 ♂ and 4/10 ♀ mice receiving 600 mg kg^{-1} died early, lower doses did not cause death. Liver weight to body weight ratios were increased in mice in the 300 and 600 mg kg^{-1} groups, but no histopathological effects were observed (16).

Carcinogenicity and chronic effects

Insufficient evidence for carcinogenicity to humans, no adequate evidence for carcinogenicity to animals, IARC classification group 3 (17).

Gavage (2 yr) rat, 0, 50 or 100 mg kg^{-1} (in corn oil) 5 × wk^{-1} for 103 wk. Mean body weights of the high-dose

group were 6-11% lower than controls. Survival of the low-dose group ♂ were reduced compared with the controls, whilst survival for the other groups was not statistically different from the controls. There was equivocal evidence for carcinogenicity in ♂ rats as characterised by the occurrence of small numbers of renal tubular cell adenomas or carcinomas. There was some evidence for carcinogenicity in ♀ rats as characterised, primarily, by the occurrence of two rare transitional cell carcinomas in the high-dose group (16).
Gavage (2 yr) mice 0, 150 or 300 mg kg^{-1} (in corn oil) 5 × wk^{-1} for 103 wk. Mean body weights of high dose ♀ were 4-11% lower than controls, all others were not significantly different than controls. Tubular cell adenomas were observed in ♀ mice, however there was no evidence of carcinogenicity. In ♂ there was an increased incidence of hepatocellular adenomas or carcinomas (combined) (16).

Teratogenicity and reproductive effects
Treatment of ♂ rabbits (route, dose unspecified) for 9 consecutive days reduced the seminal concentrations of prostaglandin E_2 and prostaglandin $E_2\alpha$; sperm motility, fertility and volumes of ejaculate were increased (18).
♀ rats (immature) had ovulation induced by treatment with pregnant mare's serum gonadotrophin and human gonadotrophin. Treatment with phenylbutazone (dose, route unspecified) inhibited the ovulation rate and the normal increase in ovarian prostaglandin E during ovulation (19).

Metabolism and toxicokinetics
Plasma $t_{1/2}$ 6, 5, 3 hr in dog, guinea pig, rabbit, respectively (20).
In cattle following intravenous administration of 4.4 mg kg^{-1}, plasma disposition was described by a three-compartment open model; mean elimination $t_{1/2}$ 35.9 hr and clearance value 2.77 ml kg^{-1} hr^{-1}. Longer (unspecified) $t_{1/2}$ values were obtained following oral and intramuscular administration. Intramuscular dosing led to more complete absorption than oral dosing (21).
In cattle, two metabolites γ-hydroxyphenylbutazone and oxyphenbutazone were detected in trace amounts in the plasma for 72 hr and in higher concentrations in the urine for 168 hr. Urine:plasma concentration ratios (U/P) for the metabolites were similar to and were occasionally greater than the U/P ratio for exogenous creatinine, indicating reabsorption was poor (21).
In humans, it is readily absorbed from the gastro-intestinal tract, peak plasma concentrations are found within 2 hr of ingestion. Elimination $t_{1/2}$ ~70 hr. It is found bound to plasma proteins (98% of dose) (22).
In humans, metabolism is slow with the accumulation of oxyphenbutazone in plasma. The metabolites oxyphenbutazone and γ-hydroxyphenylbutazone are excreted in urine (20).
It is metabolised in the liver via oxidation and conjugation with glucuronic acid. The initial metabolites formed by oxidation are: oxyphenbutazone, γ-hydroxyphenbutazone and *p*-γ-dihydroxyphenylbutazone, however these are not excreted in the urine and are further metabolised (unspecified). ~1% of the dose is excreted unchanged in the urine and ~10% is excreted in the bile as metabolites (22).
In humans, it can cross the placental barrier and has been found in breast milk (22).

Irritancy
100 mg instilled into rabbit eye (duration unspecified) caused moderate irritation (23).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (16,24,25).
Aspergillus nidulans without metabolic activation, induction of non-disjunction or crossing-over negative (26).
In vitro mouse lymphoma assay with and without metabolic activation positive (16).
In vitro Chinese hamster ovary cells with metabolic activation chromosomal aberrations positive, without metabolic activation negative; with and without metabolic activation sister chromatid exchanges negative (16).
In vivo Chinese hamster bone marrow or rat bone marrow chromosomal abnormalities negative (27,28).
In vivo mouse dominant lethal test negative (29,30).

Other effects

Other adverse effects (human)
Cultured human peripheral leucocytes from patients who had been treated for rheumatic disorders with 100-500 mg day^{-1} for ≥3 month had a significant increase in the number of chromosomal abnormalities caused by chromosome breakage events (31).

A number of cases of leukaemia have been reported in patients treated with phenylbutazone, the IARC group did not consider the evidence available to be sufficient to associate treatment and subsequent development of leukaemia (32).
Minor side-effects caused by treatment include: skin rashes, nausea, vomiting, headache, diarrhoea, epigastric distress and blurred vision. More serious effects are: gastric irritation with ulceration and gastro-intestinal bleeding, jaundice, hepatitis, ulcerative stomatitis, renal failure, haematuria, nephritis, pancreatitis, ocular toxicity and goitre. It may precipitate heart failure and cause acute pulmonary syndrome. The most serious adverse reactions are related to bone-marrow depression including aplastic anaemia, agranulocytosis, haemolytic anemia, leucopenia, pancytopenia and thrombocytopenia can also occur (22).

Any other adverse effects

Dogs given intramuscular injections of 3.6-35.2 g over 10-103 day developed gastric ulcerations (33).
Administration orally to rats caused gastric ulcers, when given intravenously or rectally they produced less severe lesions in the stomach (34).
Had little or no effect on delayed hypersensitivity models in mice (35).

Other comments

Toxicity reviewed (32).
Binding to bovine and human serum albumin are discussed (36).

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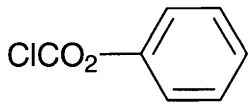
P97 phenyl chloroformate



$C_7H_5ClO_2$ **Mol. Wt.** 156.57 **CAS Registry No.** 1885-14-9

Synonyms carbonochloridic acid, phenyl ester; chloroformic acid, phenyl ester; phenyl chlorocarbonate

EINECS No. 217-547-8 **RTECS No.** FG 3850000

Physical properties

B. Pt. 74-75°C at 13 mmHg **Flash point** 75°C **Specific gravity** 1.248

Occupational exposure

UN No. 2746 **HAZCHEM Code** 2W **Conveyance classification** toxic substance, corrosive

Ecotoxicity

Invertebrate toxicity

EC_{50} (5, 15 or 30 min) *Photobacterium phosphoreum* 5.68 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1410 mg kg^{-1} (2).

LC_{Lo} (4 hr) inhalation rat 44 ppm (2).

LD_{50} dermal rabbit 3970 mg kg^{-1} (2).

Irritancy

Dermal (24 hr) rabbit 500 mg caused mild irritation and 50 μg instilled into rabbit eye (24 hr) caused severe irritation (3).

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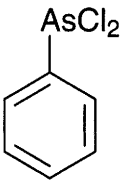
P98 phenyldichloroarsine



$C_6H_5AsCl_2$ **Mol. Wt.** 222.93 **CAS Registry No.** 696-28-6

Synonyms phenyl arsenous dichloride; phenylarsine dichloride; dichlorophenylarsine

EINECS No. 211-791-9 **RTECS No.** CH 5425000

Physical properties

B. Pt. 255-275°C **Specific gravity** 1.654 at 20°C **Volatility** v.p. 0.021 mmHg at 20°C ; v.den. 7.7

Occupational exposure

UK-LTEL MEL 0.1 mg m^{-3} (as As)

UN No. 3280 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LC_{50} (10 min) inhalation mouse 3300 mg m^{-3} (1).

LD_{50} dermal guinea pig, mouse, rabbit, rat 4-16 mg kg^{-1} (1,2).

LD_{50} intravenous mouse, rabbit 500 μg kg^{-1}, 500 mg kg^{-1}, respectively (2).

Other effects

Any other adverse effects

Phenyldichloroarsine-treated mouse skin *in vivo* and human skin xenografts developed histopathological changes including: degeneration of epidermal cell nuclei, loss of epidermal cytoplasmic basophilia, epidermal cytoplasmic vacuolisation and cleft formation within the basement membrane (3).

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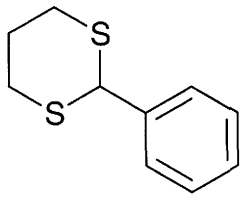
P99 2-phenyl-1,3-dithiane



$C_{10}H_{12}S_2$ **Mol. Wt.** 196.34 **CAS Registry No.** 5425-44-5

Synonyms 2-phenyl-*m*-dithiane

EINECS No. 226-568-1 **RTECS No.** JO 5277000

Physical properties

M. Pt. 72-74°C

Mammalian & avian toxicity

Acute data

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

References

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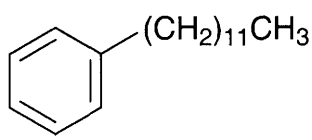
P100 1-phenyldodecane



$C_{18}H_{30}$ **Mol. Wt.** 246.44 **CAS Registry No.** 123-01-3

Synonyms dodecylbenzene; Nalkylene 500; Aikylate P1; Detergent Alkylate No.2

EINECS No. 204-591-8 **RTECS No.** CZ 9540000

Occurrence Measured in sediments of Port Phillip Bay, Australia (1).

Physical properties

B. Pt. 290-410°C **Flash point** 140.56°C **Specific gravity** 0.9 at 20°C with respect to water at 4°C

Volatility v.den. 8.47

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Dermal (78 wk) mice ≤ 80% dissolved in acetone twice wkly with or without pretreatment with 9, 10-dimethyl-1,2-benzanthracene (DMBA). At 80% it weakly induced tumours but they were not malignant. It tended to slightly enhance DMBA-initiated carcinogenesis, i.e. it appeared to act as a weak promoter of DMBA-initiated carcinogenesis (2).

Metabolism and toxicokinetics
90% of a single oral dose was metabolised to alcohols and carboxylic acids which were excreted in urine, 10% remained in the body tissues (3).

Irritancy
Repeated contact (species unspecified) may cause dermatitis, this is probably caused by delipidation of the skin (4).

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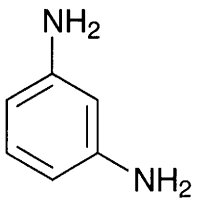
P101 *m*-phenylenediamine



$C_6H_8N_2$ **Mol. Wt.** 108.14 **CAS Registry No.** 108-45-2

Synonyms 1,3-benzenediamine; 3-aminoaniline; *m*-benzenediamine; C.I. Developer 11; Developer H; *m*-diaminobenzene; Direct Brown BR

EINECS No. 203-584-7 **RTECS No.** SS 7700000

Uses Ion exchange resins, dyes, textile fibres, urethanes, corrosion inhibitors, rubber chemicals manufacture. In photography. In hair dye preparations to produce brown, golden-blond, blue and grey shades.

Physical properties

M. Pt. 62-63°C **B. Pt.** 284-287°C **Flash point** 187°C **Specific gravity** 1.139 **Volatility** v.p. 1 mmHg at 99.8°C ; v.den. 3.7
Solubility Water: soluble. Organic solvents: benzene, diethyl ether, dioxane, ethanol, methanol

Occupational exposure

US-TWA 0.1 mg m^{-3}

UN No. 1673 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R43, 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 – 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, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) goldfish 5.74 mg l^{-1} (1).

Trout, bluegill sunfish, goldfish, yellow perch 5 ppm for 24 hr was not toxic. Test conditions: pH 5; 7.5 ppm dissolved oxygen; total hardness (soap method) 310 ppm; methyl orange alkalinity 310 ppm; 12.8°C; free carbon dioxide 5 ppm, phenolphthalein alkalinity 0 (2).

Bioaccumulation

Non- or low accumulative (3).

Environmental fate

Degradation studies

Total decomposition by soil microflora >64 days (4).

Activated sludge with compound as sole carbon source (at 20°C), 60% removal after 120 hr (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral quail 562 mg kg^{-1}; redwing blackbird, starling, house sparrow >1000 mg kg^{-1} (6).

LD_{50} oral rat 650 mg kg^{-1} (7).

LD_{Lo} oral cat, rabbit 300 mg kg^{-1} (8).

LD_{Lo} dermal rabbit 5000 mg kg^{-1} (7).

LD_{50} intraperitoneal rat 283 mg kg^{-1} (7).

LD_{Lo} subcutaneous rat, rabbit 30, 200 mg kg^{-1}, respectively (8,9).

LD_{Lo} intravenous dog 17 mg kg^{-1} (8).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (10).

Subcutaneous rat 9 or 18 mg kg^{-1} on alternate days, 5 months for the high-dose group and 11 months for the low-dose group. 1 fibrosarcoma was observed in the 9 mg kg^{-1} group, but none was observed in the 18 mg kg^{-1} or control groups (11).

Oral (78 wk) mouse 0.02-0.04% in drinking water induced no neoplastic changes apart from a deposition of brown pigment in some tissues (12).

Metabolism and toxicokinetics

In humans, it is excreted unchanged with little absorption (13).

Sensitisation

Rat, rabbit and guinea pig caused skin sensitisation but no local irritation (dose, duration unspecified) (14).

Genotoxicity

Salmonella typhimurium TA1538 with metabolic activation positive (15).

Salmonella typhimurium TA97, TA98, TA100 without metabolic activation negative, with metabolic activation positive. TA1535 without metabolic activation negative, with metabolic activation equivocal (16).

Escherichia coli WP2s(λ) microscreen assay without metabolic activation positive (17).

In vitro Chinese hamster lung cells without metabolic activation chromosomal aberrations equivocal, with metabolic activation weakly positive (18).

In vitro Chinese hamster ovary cells chromosomal aberrations without metabolic activation positive, with metabolic activation negative (18).

In vitro Chinese hamster cells (metabolic activation unspecified) induced chromosome breakages, especially chromatid type aberrations, but not changes in chromosome number (19).

In vitro primary rat hepatocytes DNA repair test negative (20).

In vivo rat intraperitoneal administration, no dominant lethal effects (21).

Other effects

Other adverse effects (human)

Workers exposed occupationally for 5-10 yr, 13.4% suffered from dysuria. A scratch test was positive for 8% of the workers studied, they also displayed eosinophiluria. Analysis of urine showed levels of 0.3-40 μg 100 ml^{-1} (22). Exposure can cause skin irritation, staining and sensitisation and also headache, methaemoglobinaemia, cyanosis and asthma (23).

Legislation

Suggested maximum allowable workplace air concentrations (USSR), based on allergenic potential and toxicity 0.1 mg m^{-3} (24).

Other comments

Reviews on human health effects, experimental toxicity, environmental effects and ecotoxicity listed (25).

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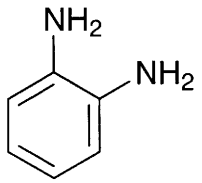
P102 *o*-phenylenediamine



$C_6H_8N_2$ **Mol. Wt.** 108.14 **CAS Registry No.** 95-54-5

Synonyms 1,2-benzenediamine; 2-aminoaniline; C.I. Oxidation Base 16; 1,2-diaminobenzene; orthamine; C.I. 76010

EINECS No. 202-430-6 **RTECS No.** SS 7875000

Uses Dye manufacture.

Physical properties

M. Pt. 103-105°C **B. Pt.** 256-258°C **Flash point** 156°C

Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

SE-LEVL 0.1 mg m^{-3} **SE-STEL** 0.3 mg m^{-3}

US-TWA 0.1 mg m^{-3}

UN No. 1673 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification toxic

Supply classification dangerous for the environment

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R43, 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

Invertebrate toxicity

EC_{50} (60 hr) *Tetrahymena pyriformis* 48 mg l^{-1} (reproductive effects) (1).

Inhibitory to the growth of *Escherichia coli, Klebsiella pneumoniae, Salmonella enteritidis,* and *Shigella sonnei* in the well-diffusion assay (2).

Environmental fate

Degradation studies

Decomposition by soil microflora >64 days (3).

Activated sludge with compound as sole carbon source (at 20°C), 33% COD removal after 120 hr (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral house sparrow, redwing blackbird, starling 100, 133, >1000 mg kg^{-1}, respectively (5).

LD_{50} oral rat 1070 mg kg^{-1} (6).
LD_{Lo} dermal rabbit 5000 mg kg^{-1} (6).
LD_{50} intraperitoneal rat 516 mg kg^{-1} (6).
LD_{50} subcutaneous mouse 450 mg kg^{-1} (7).

Sensitisation

In guinea pigs, sensitisation was induced by topical application with 10 μg of a 19.4 mg l^{-1} solution. When the animals were challenged 4 days later with 10 μl of a 9.7 mg l^{-1} solution, 30% showed sensitisation reactions (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 without metabolic activation negative, with metabolic activation positive. TA1535 with and without metabolic activation negative (9).
Escherichia coli WP2s(λ) microscreen test without metabolic activation negative (10).
In vitro Chinese hamster lung cells chromosomal aberrations without metabolic activation weakly positive, with metabolic activation negative (11).
In vitro Chinese hamster ovary cells chromosomal aberrations with and without metabolic activation positive (11).

Legislation

Suggested maximum allowable workplace air concentrations (former USSR), based on allergenic potential and toxicity, 0.5 mg m^{-3} (12).

Other comments

Carcinogenicity, mutagenicity and toxicity reviewed (13).
Reviews on human health effects, experimental toxicology, environmental effects and ecotoxicology listed (14).

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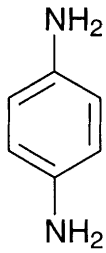
P103 *p*-phenylenediamine



$C_6H_8N_2$ **Mol. Wt.** 108.14 **CAS Registry No.** 106-50-3

Synonyms 1,4-benzenediamine; 4-aminoaniline; *p*-diaminobenzene; Developer PF; Pelagon D; Fourrine D

EINECS No. 203-404-7 **RTECS No.** SS 8050000

Uses Dye manufacture. Dye developer to obtain black and brown shades. Black and white photography developer. In hair dyes.

Physical properties

M. Pt. 143-145°C (99+% pure) **B. Pt.** 267°C **Flash point** 156°C **Volatility** v.p. <1 mmHg at 21°C ; v.den. 3.72
Solubility Water: In 100 parts cold water. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.1 mg m^{-3}
SE-LEVL 0.1 mg m^{-3} **SE-STEL** 0.3 mg m^{-3}
UK-LTEL 0.1 mg m^{-3}
US-TWA 0.1 mg m^{-3}

UN No. 1673 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R43, 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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – 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 (S1/2, S28, S45, S36/37, S60, S61)

Ecotoxicity

Fish toxicity
Fatal concentration (48 hr) goldfish 5.74 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (60 hr) *Tetrahymena pyriformis* 74 mg l^{-1} (effect on reproduction) (2).
EC_{50} (30 min) *Photobacterium phosphoreum* 37.5 ppm Microtox test (3).
Inhibitory to the growth and nitrogenase activity of *Azobacter vinelandii* (4).

Environmental fate

Degradation studies

Activated sludge with compound as sole carbon source (20°C), 80% removal after 210 hr (5).

Abiotic removal

Adsorption onto Amberlite XAD-2 ion exchange resin; influent 0.9 ppm; effluent 0.02 ppm; 98% retention efficiency (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, quail 100 mg kg^{-1}, house sparrow, starling 422, 562 mg kg^{-1}, respectively (7).
LD_{50} oral rat 80 mg kg^{-1} (8).
LD_{Lo} oral rat, rabbit 100, 250 mg kg^{-1}, respectively (9).
LD_{Lo} dermal rabbit 5000 mg kg^{-1} (8).
LD_{50} intraperitoneal rat 37 mg kg^{-1} (8).
LD_{Lo} intravenous dog, rat 17, 50 mg kg^{-1}, respectively (9,10).

Sub-acute and sub-chronic data

Hair-dye formulations containing 1, 2, 3 or 4% along with several aromatic amine derivatives were applied dermally to rabbits, 1 ml kg^{-1} 2 × wk for 13 wk. Blood and urine parameters and organ weights were not different from the controls (11).
Dermal guinea pig 0.1 ml day^{-1} of 1% w/v solution for 1, 3, 5 and 7 days. It was absorbed by the skin and caused significant increases in histamine content and lipid peroxidation in the skin. Dose-related degenerative changes in the liver and hyperkeratosis, together with infiltration of the cells in the dermis, were observed (12).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (13).
Oral (8 month) rat 0.06, 0.3 or 10 mg kg^{-1} day^{-1}, no tumours developed in the treated groups or in controls (14).
Dermal (20 wk) mice 1 drop of a 5% solution 2 × wk, no tumours were observed (15).
Subcutaneous (7 months) rat 12.5 or 20 mg kg^{-1} day^{-1}. Fibrosarcomas were produced at the injection site in 2/5 rats that received 12.5 mg kg^{-1}, no tumours were seen in the 20 mg kg^{-1} group or in the controls (14).

Teratogenicity and reproductive effects

Commercial hair-dye formulations containing 1, 2, 3, or 4% along with several aromatic amine derivatives were applied dermally to ♀ rats, 2 ml kg^{-1} on days 1, 4, 7, 10, 13, 16 and 19 of gestation. No abnormal foetal or maternal effects were observed, except for one group treated with a formulation containing 2% that had skeletal changes in 9/169 live foetuses (11).
Gavage rat 5-30 mg kg^{-1} day^{-1} on day 6-15 of gestation caused no teratogenicity (16).

Metabolism and toxicokinetics

In dogs the metabolite *N,N'*-diacetyl-*p*-phenylenediamine has been detected in urine (17).

Irritancy

Dermal (24 hr) human, mouse, pig, guinea pig 250 mg caused mild irritation (18).

Sensitisation

May cause eczematoid contact dermatitis in humans (19).
Hypersensitivity reactions have been reported in humans. It commonly provokes contact sensitisation of the skin (20).
2903 patients suffering from eczema were patch tested with 2% solution; 10.6% reacted positively (21).
In vitro murine lymph node assay for contact allergen detection positive (22).
Guinea pig maximization test positive (23).
Allergic contact dermatitis has been reported in occupationally exposed workers, including those working in the metallurgic and beauty industries (24).
Dermal guinea pig 10 µl of a 19.4 mg l^{-1} solution was used to induce sensitisation, the animals were challenged 4 days later with 10 µl of a 9.7 mg l^{-1} solution. Within 48 hr 70% had shown sensitisation responses. Guinea pigs were challenged with *o*-phenylenediamine in the same dose, 30% showed cross-sensitisation responses (25).

Genotoxicity

Salmonella typhimurium TA1538 with metabolic activation positive (26).
Salmonella typhimurium (strain unspecified) with metabolic activation negative (27).
Salmonella typhimurium TA98 without metabolic activation negative, with metabolic activation positive (28).
Escherichia coli WP2s(λ) microscreen test without metabolic activation positive (29)
In vitro Chinese hamster cells with or without metabolic activation induced sister chromatid exchanges (28).
In vivo mouse bone marrow cells micronuclei negative (30).
Drosophila melanogaster weakly mutagenic (31).
In vivo rat no dominant lethal effects (8).

Other effects

Other adverse effects (human)
A woman who regularly dyed her hair with a commercial preparation experienced *p*-phenylenediamine poisoning; symptoms included liver and spleen enlargement followed by progressive neurological symptoms prior to death 11 wk after hospital admission (32).
Accidental ingestion (dose unspecified) caused acute poisoning, the symptoms of which included oedema, respiratory distress and kidney damage in 1/2 cases (33).
Pregnant women who were occupationally exposed have higher incidences of complications during pregnancy and childbirth (34).

Legislation

Under the Federal Occupational Safety and Health the US Occupational Health and Safety Administration are amending existing air containment standards and permissible exposure limits (35).
Suggested maximum allowable workplace air concentrations former USSR, based on allergenic potential and toxicity, 0.05 mg m^{-3} (36).

Other comments

Toxicity, cancer studies, production and use reviewed (20).
Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicity, epidemiology, workplace experience, exposure conditions listed (37).

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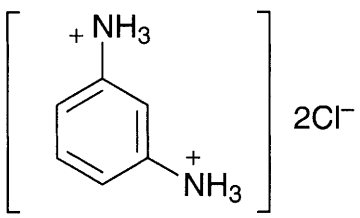
P104 *m*-phenylenediamine dihydrochloride



$C_6H_{10}Cl_2N_2$ **Mol. Wt.** 181.06 **CAS Registry No.** 541-69-5

Synonyms 1,3-benzenediamine dihydrochloride; 1,3-diaminobenzene dihydrochloride; *m*-phenylenediammonium dichloride

EINECS No. 208-790-0 **RTECS No.** SS 9800000

Uses Production of dyes. Curing agent for epoxy resins. Production of heat resistant fibres.

Physical properties

M. Pt. 277-278°C

Solubility Water: freely soluble in water. Organic solvents: diethyl ether, ethanol

Occupational exposure

Supply classification toxic

Supply classification dangerous for the environment

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R43, 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 – In case of accident or if you feel unwell, seek medical advice

immediately (show label where possible) – 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 (S1/2, S28, S45, S36/37, S60, S61)

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse, rat 100, 325 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous mouse 90 mg kg^{-1} (3).

Metabolism and toxicokinetics

In humans it is excreted rapidly and unchanged with little absorption (4).

Genotoxicity

Salmonella typhimurium TA1538 with metabolic activation positive (5,6).

Other effects

Other adverse effects (human)

Exposure unspecified (5-10 yr) workers aged 30-50 yr old. 13.4% complained of dysuria, a scratch test was positive in 8% and they also displayed eosinophiluria. 0.3-40 μg 100 ml^{-1} was found in the urine of workers. Cystoscopy showed oedema of mucosa, polypous swelling and infiltration of the area of the triangle and cervix of the urinary bladder. The eosinophilic character of these formations was confirmed cytologically (7).
Toxic effects included changes in central nervous system, decreased detoxifying activity of the liver and dermatitis at the site of application (3,8-10).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (11).

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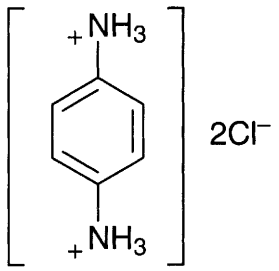
P105 *p*-phenylenediamine dihydrochloride



$C_6H_{10}Cl_2N_2$ **Mol. Wt.** 181.06 **CAS Registry No.** 624-18-0

Synonyms 1,4-benzenediamine dihydrochloride; C.I. 76061; Durafur Black RC; Pelagol CD

EINECS No. 210-834-9 **RTECS No.** ST 0350000

Uses In photochemical measurements. Dyeing furs. Vulcanisation.

Physical properties

M. Pt. 275°C

Solubility Water: freely soluble in water. Organic solvents: diethyl ether, ethanol

Occupational exposure

Supply classification toxic

Supply classification dangerous for the environment

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R43, 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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – 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 (S1/2, S28, S45, S36/37, S60, S61)

Ecotoxicity

Toxicity to other species

LD_{50} subcutaneous frog 10 mg kg^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 147, 316 mg kg^{-1}, respectively (2).

LD_{Lo} subcutaneous dog, rabbit, mouse 10, 20, 50 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects

Oral rats and mice (105 wk) 625 or 1250 ppm, no significant positive associations between concentrations administered and mortality, no evidence of carcinogenicity (3).

Genotoxicity

Salmonella typhimurium with metabolic activation positive (4).

In vitro Chinese hamster ovary cells chromosomal aberrations positive with and without metabolic activation,

sister chromatid exchanges positive without metabolic activation, negative with (4).
In vitro mouse lymphoma L5178Y tk^-/tk^+ without metabolic activation positive (4).
TK6 human cell lymphoblast assay without metabolic activation positive (4).

Other effects

Any other adverse effects

Intraperitoneal rabbits, cats and guinea pigs a characteristic oedema of the head and neck was caused by 190, 120 and 120-150 mg kg^{-1}, respectively (5).
Subcutaneous rat 3 mg induced skeletal muscle lesions: rhabdomyolysis with infiltration of myophages, necrosis with calcifications, accumulation of neutral lipids and dilation of sarcoplasmic reticulum (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

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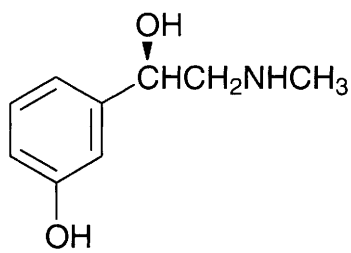
P106 phenylephrine



$C_9H_{13}NO_2$ **Mol. Wt.** 167.21 **CAS Registry No.** 59-42-7

Synonyms (*R*)-3-hydroxy-α-[(methylamino)methyl]benzenemethanol; isophrin; metaoxedrin; metasympatol; metasynephrine

EINECS No. 200-424-8 **RTECS No.** DO 7175000

Uses Sympathomimetic. Vasoconstrictor. Mydriatic. Nasal decongestant.

Physical properties

M. Pt. 169-172°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 350 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 60 mg kg^{-1} (2).
LD_{50} intravenous mouse 38 mg kg^{-1} (3).
LD_{50} subcutaneous rat 28 mg kg^{-1} (4).
LD_{50} subcutaneous mouse 875 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Oral rat, mouse (14 day) 2000 ppm no toxic effects were observed. Oral ♂ rat (14 wk) 5000 ppm 10% died (6).

Carcinogenicity and chronic effects

Oral ♂ and ♀ F344/N rat (104 wk) 0, 620 or 1250 ppm and $B6C3F_1$ mouse (104 wk) 0, 1250 and 2500 ppm, no evidence of carcinogenicity. Inflammation was observed in the liver and prostate gland of dosed ♂ rats (7).
Oral ♂ and ♀ rat (104 wk) mouse, 1250 and 2500 ppm, respectively. Carcinogenicity negative (8).

Metabolism and toxicokinetics

Low oral bioavailability due to irregular absorption and first-pass metabolism by monamine oxidase activity in the gut and liver (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 and TA1537 with and without metabolic activation negative (10).
In vitro L5178Y mouse lymphoma cell mutation assay without metabolic activation positive (as hydrochloride) (11).

Other effects

Other adverse effects (human)

Hypertension and hypertension with pulmonary oedema have been described in infants after the use of 10% eye drops (12,13).

Any other adverse effects

Chemical lesion of serotonergic afferents to the hippocampus resulted in a potentiation of phenylephrine stimulation of cyclic AMP formation in rat hippocampal slices (14).

Other comments

Usually administered as the hydrochloride (CAS Reg. No. 61-76-7).
α-adrenoreceptor agonist (15).

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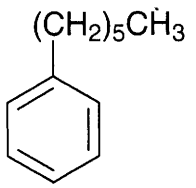
P107 1-phenylhexane



$C_{12}H_{18}$ **Mol. Wt.** 162.27 **CAS Registry No.** 1077-16-3

Synonyms hexylbenzene

EINECS No. 214-070-7

Physical properties

M. Pt. –61°C **B. Pt.** 226°C **Flash point** 83°C **Specific gravity** 0.861 **Partition coefficient** log P_{ow} 5.52
Solubility Organic solvents: benzene, petroleum ether, miscible with diethyl ether

Occupational exposure

UN No. 3082

Environmental fate

Degradation studies
ThOD for 100 mg was 326 mg O_2 l^{-1} (1).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 with metabolic activation negative. *Salmonella typhimurium* TA97, TA98, TA100, TA1535 and TA1537 with metabolic activation negative (2).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (3).

References

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2. Burghadtova, K. et al *Cesk. Hyg.* 1986, **31**(6), 361-365, (Slo.).
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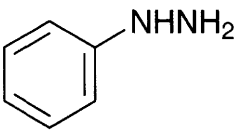
P108 phenylhydrazine



$C_6H_8N_2$ **Mol. Wt.** 108.14 **CAS Registry No.** 100-63-0

Synonyms hydrazinobenzene; monophenylhydrazine

EINECS No. 202-873-5 **RTECS No.** MV 8925000

Uses Manufacture of dyes. Antipyrine and nitron, a stabiliser for explosives. Haemolytic.

Physical properties

M. Pt. 19.5°C **B. Pt.** 243.5°C decomp. **Flash point** 88°C **Specific gravity** 1.432 at 20°C with respect to water at 4°C **Volatility** v.p. 1 mmHg at 71.8°C ; v.den. 3.7

Solubility Organic solvents: miscible with benzene, chloroform, diethyl ether, ethanol

Occupational exposure

US-TWA 0.1 ppm (0.44 mg m^{-3})

UN No. 2572 **HAZCHEM Code** 3X **Conveyance classification** toxic substance

Supply classification toxic, dangerous for the environment

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Irritating to the eyes – Very toxic to aquatic organisms (R23/24/25, R36, 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 – 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, S45, S61)

Ecotoxicity

Invertebrate toxicity

EC_{50} (5, 15 or 30 min) *Photobacterium phosphoreum* 66.7 ppm Microtox test (1).

Flavin-containing monooxygenase activity was induced after the addition of phenylhydrazine to microsomes from the digestive gland of *Cryptochiton stelleri* (2).

Mammalian & avian toxicity

Acute data

Intravenous Japanese quail 0.6, 6 or 60 mg kg^{-1}. Haemolytic anemia was induced within 24 hr post-injection this was still present at 72 hr post-injection. The specific changes in the blood included lymphocytosis, monocytopenia and heteropenia (3).

LD_{50} oral guinea pig, rabbit, rat 80-188 mg kg^{-1} (4-6).

Dermal (24 hr) single exposure rabbit, rat produced haematoxic effects including methaemoglobin formation, anaemia and reticulocytosis. Phenylhydrazine was lethal to rabbits but not to rats (dose unspecified) (7).

LD_{Lo} subcutaneous rat, rabbit, mouse 40-170 mg kg^{-1} (5,6).

LD_{Lo} intravenous dog 120 mg kg^{-1} (8).

100% of mice given 180 mg kg^{-1} subcutaneously died. Symptoms prior to death included irregular respiration, progressive cyanosis and increasing dyspnea, degenerative lesions were also seen in the liver (9).

Dogs given 20 mg kg^{-1} (1/10 of lethal dose) subcutaneously developed severe anaemia caused by haemolysis (10).

Metabolism and toxicokinetics

Oral rabbit 50 mg kg^{-1} [^{14}C]phenylhydrazine. 30-50% was excreted in urine by 48 hr while 40-60% was excreted by 4 days. Metabolites included *p*-hydroxyphenylhydrazine and the phenylhydrazones of pyruvic acid and α-oxoglutaric acid. 5-10% of [^{14}C]-label was found in the erythrocytes of animals killed after 4 days (11).

Irritancy

Rabbit eyes (duration unspecified) instilled with a 50% solution developed septic conjunctivitis (12).
In humans, occupational exposure has led to the development of eczematous contact dermatitis (13).

Sensitisation

Causes skin sensitisation in humans (13).

Genotoxicity

Salmonella typhimurium TA102 without metabolic activation weakly positive (14).
Escherichia coli without metabolic activation, WP2 *uvrA* (pkM101) positive, WP2 (pkM101) weakly positive (14).
Phenylhydrazine hydrochloride *in vitro* rat, mouse primary hepatocytes, DNA Repair Test positive (15).

Other effects

Other adverse effects (human)

Haemolytic anemia is its principal toxic effect, often associated with kidney and liver damage (16,17).

Other comments

Human health effects, experimental toxicology, physico-chemical properties reviewed (18).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Schlenk, D. et al *Mar. Biol. (Berlin)* 1990, **104**(1), 47-50.
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4. *Hyg. Sanit. (USSR)* 1965, **30**, 199.
5. *Naunyn-Schmiedeberg's Arch. Exp. Pathol. Pharmakol.* 1936, **182**, 118.
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14. Wilcox, P. et al *Mutagenesis* 1990, **5**(3), 285-291.
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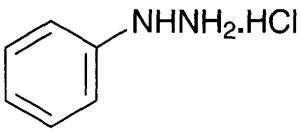
17. Ikuo, Y. et al *J. Toxicol. Sci.* 1977, **2**(3), 251-259.
18. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

P109 phenylhydrazine hydrochloride



$C_6H_9ClN_2$ **Mol. Wt.** 144.60 **CAS Registry No.** 59-88-1

Synonyms phenylhydrazine monohydrochloride; *N*-phenylhydrazine hydrochloride

EINECS No. 200-444-7 **RTECS No.** MV 9000000

Uses Haemolytic agent.

Physical properties

M. Pt. 243-246°C

Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2100 mg kg^{-1} (1).

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

LD_{50} subcutaneous rabbit, mouse 25, 89 mg kg^{-1}, respectively (2,3).

LD_{50} intraperitoneal rat 161 mg kg^{-1} (4).

Other effects

Any other adverse effects

It has been shown to be porphyrinogenic in animals and in *in vitro* systems (5).

References

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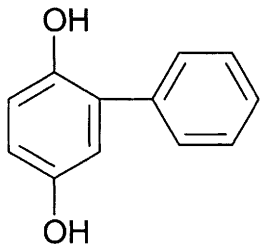
P110 phenylhydroquinone



$C_{12}H_{10}O_2$ **Mol. Wt.** 186.21 **CAS Registry No.** 1079-21-6

Synonyms 2-phenyl-1,4-benzenediol; [1,1'-diphenyl]-2,5-diol; 2,5-biphenyldiol; 2,5-dihydroxybiphenyl

EINECS No. 214-091-1 **RTECS No.** DV 4550000

Physical properties

M. Pt. 102-103°C

Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

Oral rat 700 or 1400 mg kg^{-1} caused toxic effects to the kidney and liver (1).

Metabolism and toxicokinetics

Metabolised by prostaglandin(H) synthase to phenylbenzoquinone, the disappearance of phenylhydroquinone with time was stoichiometric with phenylbenzoquinone formation. In the absence of the enzyme 10% was converted into phenylbenzoquinone, indicating that autooxidation may have a minor role in metabolism (2).

Genotoxicity

Incubation with supercoiled pUC18 DNA (form 1) resulted in DNA strand scission; cleavage seemed to occur at guanine residues (3).

In vitro Chinese hamster ovary cells with metabolic activation induced cytotoxic cell-progression delay and cytogenic effects (4).

In vivo ♂ rat induced DNA damage in urinary bladder epithelium (5).

Other effects

Any other adverse effects

Single intravesical injection to rats of 0.05% or 0.1% induced epithelial hyperplasia of the bladder epithelium by 5 days (5).

Oral rat 700 or 1400 mg kg^{-1} caused (unspecified) toxic effects to liver and kidneys, but these effects were less than phenyl-*p*-benzoquinone which is also a metabolite of *o*-phenylphenol (1).

Other comments

It is the major metabolite (in rats) of the fungicide *o*-phenylphenol, which is a known bladder carcinogen (3).

References

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2. Kolachana, P. et al *Carcinogenesis (London)*, 1991, **12**(1), 145-149.

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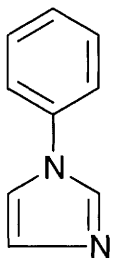
P111 1-phenylimidazole



$C_9H_8N_2$ **Mol. Wt.** 144.18 **CAS Registry No.** 7164-98-9

Synonyms 1-phenyl-1*H*-imidazole; *N*-phenylimidazole

Physical properties

M. Pt. 13°C **B. Pt.** 142°C at 15 mmHg **Flash point** >110°C **Specific gravity** 1.140
Solubility Organic solvents: chloroform, diethyl ether

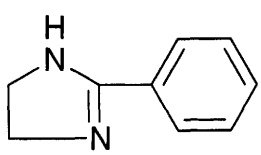
Other comments

A cytochrome P_{450} inhibitor (1).

References

1. Zijlstra, J. A. et al *Mutat. Res.* 1988, **198**, 73-83

P112 2-phenyl-2-imidazoline



$C_9H_{10}N_2$ **Mol. Wt.** 146.19 **CAS Registry No.** 936-49-2

Synonyms 4,5-dihydro-2-phenyl-1*H*-imidazole; 2-phenyl-4,5-dihydroimidazole

EINECS No. 213-313-4 **RTECS No.** NJ 4395500

Physical properties

M. Pt. 94-99°C

Mammalian & avian toxicity

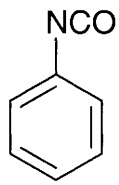
Acute data

LD_{Lo} intravenous mammal (species unspecified) 67 mg kg^{-1} (1).

References

1. *Arch. Exp. Pathol. Pharmakol.* 1939, **192**, 141

P113 phenyl isocyanate



C_7H_5NO **Mol. Wt.** 119.12 **CAS Registry No.** 103-71-9

Synonyms isocyanatobenzene; isocyanic acid, phenyl ester; phenylcarbimide; carbanil; phenyl carbonimide; Mondur P

EINECS No. 203-137-6 **RTECS No.** DA 3675000

Physical properties

M. Pt. —30°C **B. Pt.** 163°C **Flash point** 55°C **Specific gravity** 1.0887 at 25.9°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 10.6°C
Solubility Water: decomp. Organic solvents: diethyl ether

Occupational exposure

SE-LEVL 0.005 ppm (0.02 mg m^{-3}) **SE-CEIL** 0.01 ppm (0.05 mg m^{-3})
UK-LTEL MEL 0.02 mg m^{-3} (as NCO) **UK-STEL** MEL 0.07 mg m^{-3} (as NCO)

UN No. 2487 **HAZCHEM Code** 3W **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

LC_{50} (5, 15 or 30 min) *Photobacterium phosphoreum* 20.2 ppm Microtox test (1).

Environmental fate

Degradation studies

500 mg l^{-1} at 20°C (unspecified) microorganisms caused 90% ring disruption in 48 hr, (unspecified) mutant microorganisms caused 100% ring disruption in 8 hr (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 940 mg kg^{-1} (3).
LD_{50} dermal rabbit 7130 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Inhalation ♂ rat (6 hr day^{-1}, 5 days week^{-1} for 2 weeks) 0-10 mg m^{-3}. Chronic airway inflammation and induction of asthma were observed at 7 and 10 mg m^{-3} levels (5).

Irritancy

Irritating to human eyes (duration, dose unspecified) (6).

Sensitisation

The dose predicated to sensitise 50% of mice, determined with the mouse ear swelling test, was 0.04 μmol kg^{-1} body weight compared with 0.5 μmol kg^{-1} of hexamethylene diisocyanate, 2.1 μmol kg^{-1} of diphenylmethane diisocyanate and 30.4 μmol kg^{-1} of toluene diisocyanate (TDI) which are recognised diisocyanate sensitisers. Antibody titres to phenyl isocyanate (PI), were more than 10-fold greater than those induced by TDI, with mean hapten-specific immunoglobin G titres of 1.4×10^4 and 1.3×10^3, respectively. The anti-PI immunoglobin G_1 antibody titre, 1.2×10^4, was significantly higher than the anti-TDI immunoglobin G_1 titre, 6.4×10^2. Hapten-specific immunoglobin E was not detected with either isocyanate. The results indicated that PI is a potent inducer of cellular and humoral immune responses (7).

Other comments

Reviews on human health effects, experimental toxicology and work place experience listed (8).

References

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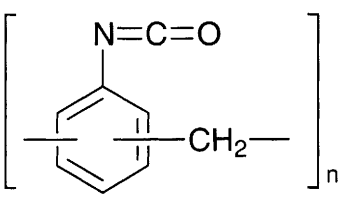
P114 phenyl isocyanate formaldehyde polymer



CAS Registry No. 9016-87-9

Synonyms polymethylene polyphenyl isocyanate; isocyanic acid, polymethylene polyphenylene ester; poly(methylene phenylene isocyanate); polymeric MDI; Isocyanate 390P; Modur MRS; Thanate P 210

RTECS No. TR 0350000

Uses Production of polyurethane rigid foam, flexible foams and elastomers.

Physical properties

B. Pt. 329°C (decomp.) **Flash point** 215-218°C **Specific gravity** 1.2 at 20°C with respect to water at 20°C
Volatility v.p. $<10^{-4}$ mmHg at 25°C ; v.den. 8.6

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)
Supply classification harmful
Risk phrases Harmful by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by inhalation (R20, R36/37/38, R42)
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 – 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) (S2, S26, S28, S38, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂ rat >10,000 mg kg^{-1} body weight (1).
Inhalation ♂ rat (8 hr) 0.2 ppm, no adverse effects reported up to 14 days (2,3).
Inhalation ♂ rat (7 hr) 0.2 ppm, no adverse effects reported (4).
LD_{50} dermal rabbit >5 ml kg^{-1} (5).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans or animals, IARC classification group 3 (6).

Irritancy
Dermal rabbit (24 hr) 2.5, 3.9, 6.0, 9.4 mg kg^{-1} body weight, minor local skin changes (7).
In three groups of three rabbits each, application in eyes left unwashed and in eyes that were washed at two or four seconds after application produced circumcorneal injection of the iris and irritation of the conjunctivae that cleared in 24 hr. Purulent ocular discharge occurred in four of the nine animals. This had disappeared within seven days (8).

Other effects

Other adverse effects (human)
The prevalence of occupational asthma was assessed in paint shops of an assembly plant where 51 employees were exposed to several types of isocyanates, including polymethylene polyphenyl isocyanate. The diagnosis of occupational asthma was confirmed in six subjects through specific inhalation challenges to a paint system component containing polymethylene polyphenyl isocyanate (9).

Other comments

Not known to occur naturally.
Toxicology, industrial hygiene and medical control of TDI, MDI and polymeric-MDI reviewed (10).

References

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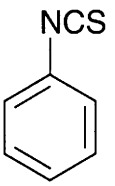
P115 phenyl isothiocyanate



C_7H_5NS **Mol. Wt.** 135.19 **CAS Registry No.** 103-72-0

Synonyms isothiocyanatobenzene; isothiocyanic acid, phenyl ester; phenyl thioisocyanate; thiocarbanil; phenyl mustard oil

EINECS No. 203-138-1 **RTECS No.** NX 9275000

Uses In preparation of derivatives of primary and secondary amines; in sequencing peptides by Edman degradation; in amino acid analysis by HPLC.

Physical properties

M. Pt. –21°C **B. Pt.** 221°C **Flash point** 87°C **Specific gravity** 1.1288 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.28 (1)
Solubility Water: insoluble. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 2.09 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 87 mg kg^{-1} (2).
LD_{50} intraperitoneal, subcutaneous mouse 100, 250 mg kg^{-1}, respectively (3,4).

Teratogenicity and reproductive effects
Teratogenic effects reported in mice given 225 mg kg^{-1} (total dose) by subcutaneous injection on days 6-14 of pregnancy (5).

Other effects

Any other adverse effects
Inhibits the phosphate carrier protein of bovine heart mitochondria on incubation (6).

Legislation

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

Other comments

Degradation product of diphenylthiourea.
Found not to migrate to food from a diphenylthiourea-stabilised hard PVC film (8).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. *Agents Actions* 1978, **8**, 610.
3. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
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6. Genchi, G. et al *Biochem. Biophys. Acta* 1988, **936**(3), 413-420.
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.
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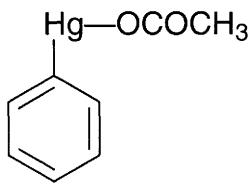
P116 phenylmercuric acetate



$C_8H_8HgO_2$ **Mol. Wt.** 336.74 **CAS Registry No.** 62-38-4

Synonyms phenylmercury acetate; (acetato-*O*)phenylmercury; acetoxyphenylmercury; Algimycin 200; Ruberon; Ziarnik

EINECS No. 200-532-5 **RTECS No.** OV 6475000

Uses Fungicide. Herbicide.

Physical properties

M. Pt. 149°C **Volatility** v.p. 9×10^{-6} mmHg at 35°C
Solubility Water: 4.37 g l^{-1} at 15°C. Organic solvents: acetone, benzene, ethanol

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)
US-TWA 0.1 mg m^{-3} (as Hg)

UN No. 1674 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic if swallowed – Causes burns – Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed (R25, R34, R48/24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe fumes – Avoid contact with skin and eyes – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S24/25, S37, S45)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) rainbow trout 0.004 mg l^{-1} (1).
LC_{50} (48 hr) goldfish 0.07 mg l^{-1} (2).
LC_{50} (48 hr) carp 0.08 mg l^{-1} (3).
Brachydanio rerio frequency of eggs hatching were higher at 10 μg kg^{-1} and 20 μg kg^{-1} than in controls, but at 50 μg kg^{-1} no eggs hatched (4).

Invertebrate toxicity

LC_{50} *Westiellopsis prolifica* slight enhancement in oxygen evolution rate, at LC_{50} (5).

Environmental fate

Degradation studies

Quickly degraded by soil and aquatic microorganisms with diphenylmercury as one of the major metabolites (6).
Mercury resistant *Penicillium* sp. MR-Z, *P. frequentans* and *P. werchlosam* reductively decomposed phenylmercuric acetate tó metallic mercury and benzene, mediated by organomercury lyase and mercuric reductase activities (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken, quail 60, 71 mg kg^{-1}, respectively (8).
LD_{50} oral mouse, rat 13, 22 mg kg^{-1}, respectively (9,10).
LD_{50} intravenous mouse 18, 20 mg kg^{-1} (11).
LD_{50} subcutaneous mouse 12 mg kg^{-1} (12).

Sub-acute and sub-chronic data

Rat (40 day) (route unspecified) 0.5, 1.5, 3.0, 7.5 or 15.0 mg kg^{-1}. Only unbound mercury was accumulated in the kidney and the structural and functional damage was severe. Repeated application increased renal damage but adaption occurred with high doses (13).
Oral rabbit 5 mg kg^{-1} reduced albumin:globulin ratio to 0.95:1 compared with 1.31:1 for controls (duration unspecified) (14).
Inhalation rat (5.5 month) 0.1 mg m^{-3} lesions in the central nervous system were observed (15).

Teratogenicity and reproductive effects

Oral ♀ pheasants (duration unspecified) administered either as capsules (20 mg kg^{-1}) or in feed (14.18 g bushel of seed $wheat^{-1}$). The birds given capsules showed a reduction in egg hatchability, eggshell thickness, chick weight and survival, but no effect on egg production, egg volume, fertility or chick behaviour. Birds dosed through feed showed none of these effects (15).
Intraperitoneal ♀ prairie vole (gestation days 8, 9, 10) 0.06-5 mg kg^{-1}. Resorptions occurred at doses >0.25 mg kg^{-1} on each day of gestation tested (16).
In vitro chick limb bud ≥10μM reduced cartilage formation in 4-day cultures (17).

Genotoxicity

In vitro human lymphocytes, sister chromatid exchange and endoreduplication positive (18).

Other effects

Any other adverse effects

Intragastric rat 1/5 and 1/10 of LD_{50} (duration unspecified) gave accumulation factors of 9.2 and 7.1, respectively (14).
Oral rabbit (3.5 month) 5 mg kg^{-1} caused a noticeable reduction in sulfhydryl groups, total amines and carboxyl groups in the blood serum (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentrations 1 $\mu g\ l^{-1}$ (19).
Included in Schedules 4, 5 and 6 (Release into Air, Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (20).
Quality objectives under EC Directives 82/176/EEC and 84/156/EEC 0.3 mg kg^{-1} (wet weight) in a representative sample of fish flesh; 1 $\mu g\ l^{-1}$ (annual mean) total mercury in inland surface waters; 0.5 $\mu g\ l^{-1}$ (annual mean) dissolved mercury in estuarine waters; 0.3 $\mu g\ l^{-1}$ (annual mean) dissolved mercury in marine waters. A 'standstill' provision applies to concentrations in shellfish or sediments. Limit values under EC Directive 84/156/EEC 0.05 mg l^{-1} effluent and 0.1 g l^{-1} vinyl chloride production capacity for chemical industries using mercury catalysts in vinyl chloride production; 0.05 mg l^{-1} effluent and 5 g kg^{-1} mercury processed for chemical industries using mercury catalysts in other processes; 0.05 mg l^{-1} effluent and 0.7 g kg^{-1} mercury processed for manufacture of mercury catalysts used in vinyl chloride production; 0.05 mg l^{-1} effluent and 0.05 g kg^{-1} mercury processed for manufacture of organic and non-organic mercury compounds (other than mercury catalysts for vinyl chloride production); 0.05 mg l^{-1} effluent and 0.03 g kg^{-1} mercury processed for manufacture of primary batteries containing mercury; 0.05 mg l^{-1} effluent for mercury recovery plants and extraction and refining of non-ferrous metals; 0.05 mg l^{-1} effluent for plants treating toxic wastes containing mercury (21).
WHO Toxicity Class Ia (22).
EPA Toxicity Class I (formulation) (23).

Other comments

Can enter the soil and water systems from treated seeds. Pretreatment of *Bacillus pasteurii* DR_2 with phenylmercuric acetate improved its oxygen consumption, induced superoxide dismutase, increased its catalase level and enhanced its resistance to exogenous hydrogen peroxide (24).
It is decomposed in the presence of intestinal contents (species unspecified) to yield elemental mercury (25).
Inhibits the degradation of cellulose ether-thickened acrylic emulsion paints (26).
The major mercury species are elemental mercury (Hg^0), inorganic mercury (Hg^{2+}) and methylmercury (CH_3Hg^+); the last is the most toxic and most bioaccumulated form of mercury (27).
Extensively reviewed (28).

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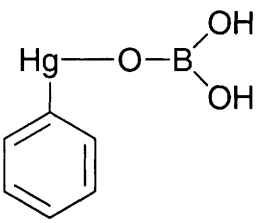
P117 phenylmercuric borate



$C_6H_7BHgO_3$ **Mol. Wt.** 338.52 **CAS Registry No.** 102-98-7

Synonyms phenylmercury(II) borate; [orthoborato(3–)-*O*]phenylmercurate(2–), dihydrogen; Exomycol gel; Famosept; Merfen; PMB; Spidoxol

EINECS No. 203-068-1 **RTECS No.** ED 4680000

Uses Topical antiseptic.

Physical properties

M. Pt. 112-113°C
Solubility Water: soluble in water. Organic solvents: ethanol, glycerol

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)
US-TWA 0.1 mg m^{-3} (as Hg)

UN No. 2026 **HAZCHEM Code** 2X **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)

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Rats were administered 0.45 mg kg^{-1} day^{-1} for 45 days. Body weight was not affected by changes in the activity of liver enzymes and slight hepatorenal lesions were seen (1).

Irritancy

Eye rabbit (duration unspecified) 150 mg caused moderate irritation (2).
Installation into eye of guinea pig (duration unspecified) 500 mg caused severe irritation (2).
No irritation was seen in rabbit eyes 1-48 hr after a single exposure (100 drops in 5 min) to 0.001% in 0.9% NaCl solution (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Boron: guide level 1000 μg l^{-1}. Mercury: maximum admissible concentration 1 μg l^{-1} (4).
Included in Schedules 4, 5 and 6 (Release into Air, Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
Quality objectives under EC Directives 82/176/EEC and 84/156/EEC 0.3 mg kg^{-1} (wet weight) in a representative sample of fish flesh; 1 μg l^{-1} (annual mean) total mercury in inland surface waters; 0.5 μg l^{-1} (annual mean) dissolved mercury in estuarine waters; 0.3 μg l^{-1} (annual mean) dissolved mercury in marine waters. A 'standstill' provision applies to concentrations in shellfish or sediments. Limit values under EC Directive 84/156/EEC 0.05 mg l^{-1} effluent and 0.1 g l^{-1} vinyl chloride production capacity for chemical industries using mercury catalysts in vinyl chloride production; 0.05 mg l^{-1} effluent and 5 g kg^{-1} mercury processed for chemical industries using mercury catalysts in other processes; 0.05 mg l^{-1} effluent and 0.7 g kg^{-1} mercury processed for manufacture of mercury catalysts used in vinyl chloride production; 0.05 mg l^{-1} effluent and 0.05 g kg^{-1} mercury processed for manufacture of organic and non-organic mercury compounds (other than mercury catalysts for vinyl chloride production); 0.05 mg l^{-1} effluent and 0.03 g kg^{-1} mercury processed for manufacture of primary batteries containing mercury; 0.05 mg l^{-1} effluent for mercury recovery plants and extraction and refining of non-ferrous metals; 0.05 mg l^{-1} effluent for plants treating toxic wastes containing mercury (6).

Other comments

It has the best preservation properties for ointments and hydrogels containing methyl cellulose, Na CM-cellulose, polyvinyl alcohol, Na alginate, and bentonite (7).

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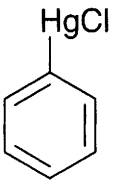
P118 phenylmercuric chloride



C_6H_5ClHg **Mol. Wt.** 313.15 **CAS Registry No.** 100-56-1

Synonyms phenylmercury(II) chloride; phenyl chloromercury; PMC; Argenal; Hexason; Mersolite 2

EINECS No. 202-865-1 **RTECS No.** OW 1400000

Uses Agricultural fungicide. Antibacterial agent in pharmaceuticals.

Physical properties

M. Pt. 250-252°C

Solubility Organic solvents: benzene, diethyl ether, pyridine

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)

US-TWA 0.1 mg m^{-3} (as Hg)

UN No. 2026 **HAZCHEM Code** 2X **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

BG/F epitheloid cells from bluegill sunfish phenylmercuric chloride had the greatest cytotoxic effects compared with other organomercury chlorides (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 60 mg kg^{-1} (2).

LD_{Lo} intraperitoneal rat 50 mg kg^{-1} (3).

LD_{50} subcutaneous rat 47 mg kg^{-1} (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 μg l^{-1} (5).

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

Quality objectives under EC Directives 82/176/EEC and 84/156/EEC 0.3 mg kg^{-1} (wet weight) in a representative sample of fish flesh; 1 μg l^{-1} (annual mean) total mercury in inland surface waters; 0.5 μg l^{-1} (annual mean) dissolved mercury in estuarine waters; 0.3 μg l^{-1} (annual mean) dissolved mercury in marine waters. A 'standstill' provision applies to concentrations in shellfish or sediments. Limit values under EC Directive 84/156/EEC 0.05 mg l^{-1} effluent and 0.1 g l^{-1} vinyl chloride production capacity for chemical industries using mercury catalysts in vinyl chloride production; 0.05 mg l^{-1} effluent and 5 g kg^{-1} mercury processed for chemical industries using mercury catalysts in other processes; 0.05 mg l^{-1} effluent and 0.7 g kg^{-1} mercury processed for manufacture of mercury catalysts used in vinyl chloride production; 0.05 mg l^{-1} effluent and 0.05 g kg^{-1} mercury processed for manufacture of organic and non-organic mercury compounds (other than mercury catalysts for vinyl chloride production); 0.05 mg l^{-1} effluent and 0.03 g kg^{-1} mercury processed for manufacture of primary batteries containing mercury; 0.05 mg l^{-1} effluent for mercury recovery plants and extraction and refining of non-ferrous metals; 0.05 mg l^{-1} effluent for plants treating toxic wastes containing mercury (7).

Other comments

Extensively reviewed (8).

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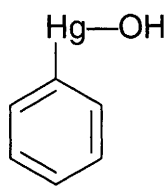
P119 phenylmercuric hydroxide



C_6H_6HgO **Mol. Wt.** 294.70 **CAS Registry No.** 100-57-2

Synonyms phenylmercury(II) hydroxide; hydroxyphenylmercury; Mersolite 1; phenylhydroxymercury

EINECS No. 202-866-7 **RTECS No.** OW 4940000

Physical properties

M. Pt. 190°C (decomp.)

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)
US-TWA 0.1 mg m^{-3} (as Hg)

UN No. 1894 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic if swallowed – Causes burns – Irritating to the respiratory system – Risk of explosion if heated under confinement – Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed (R25, R34, R37, R44, R48/24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe fumes – Avoid contact with skin and eyes – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S24/25, S37, S45)

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. Mercury: maximum admissible concentration 1 μg l^{-1} (2).
Included in Schedules 4, 5 and 6 (Release into Air, Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
Quality objectives under EC Directives 82/176/EEC and 84/156/EEC 0.3 mg kg^{-1} (wet weight) in a representative sample of fish flesh; 1 μg l^{-1} (annual mean) total mercury in inland surface waters; 0.5 μg l^{-1} (annual mean) dissolved mercury in estuarine waters; 0.3 μg l^{-1} (annual mean) dissolved mercury in marine waters. A 'standstill' provision applies to concentrations in shellfish or sediments. Limit values under EC Directive 84/156/EEC 0.05 mg l^{-1} effluent and 0.1 g l^{-1} vinyl chloride production capacity for chemical industries using mercury catalysts in vinyl chloride production; 0.05 mg l^{-1} effluent and 5 g kg^{-1} mercury processed for chemical industries using mercury catalysts in other processes; 0.05 mg l^{-1} effluent and 0.7 g kg^{-1} mercury processed for manufacture of mercury catalysts used in vinyl chloride production; 0.05 mg l^{-1} effluent and 0.05 g kg^{-1} mercury processed for manufacture of organic and non-organic mercury compounds (other than mercury catalysts for vinyl chloride production); 0.05 mg l^{-1} effluent and 0.03 g kg^{-1} mercury processed for manufacture of primary batteries containing mercury; 0.05 mg l^{-1} effluent for mercury recovery plants and extraction and refining of non-ferrous metals; 0.05 mg l^{-1} effluent for plants treating toxic wastes containing mercury (4).

References

1. *U.S. Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals* NX 03648, Aberdeen Proving Ground, MD, USA.
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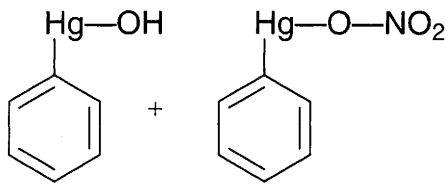
4. *DoE Circular 7/89: Water and the environment. The implementation of EC Directive on pollution caused by certain dangerous substances discharged into the aquatic environment* 1989, HMSO, London, UK

P120 phenylmercuric nitrate, basic



$C_{12}H_{11}Hg_2NO_4$ **Mol. Wt.** 586.41 **CAS Registry No.** 8003-05-2

Synonyms phenylmercury(II) nitrate; hydroxyphenylmercury mixture with (*nitrato-O*)phenylmercury; basic phenylmercuric nitrate; DZ; Gyne-merfen; Merfen-styli

RTECS No. OW 8575000

Uses Pharmaceutical aid. Antiseptic, germicide. Superseded fungicide.

Physical properties

M. Pt. 187-190°C (decomp.)
Solubility Water: 1 in 1250 parts water. Organic solvents: glycerol

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)
US-TWA 0.1 mg m^{-3} (as Hg)

UN No. 1895 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic if swallowed – Causes burns – Irritating to the respiratory system – Risk of explosion if heated under confinement – Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed (R25, R34, R37, R44, R48/24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe fumes – Avoid contact with skin and eyes – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S24/25, S37, S45)

Mammalian & avian toxicity

Acute data
LD_{50} subcutaneous rat 63 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 μg l^{-1}. Nitrates: guide level 25 mg l^{-1}; maximum admissible concentration 50 mg l^{-1} (2). Included in Schedules 4, 5 and 6 (Release into Air, Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
Quality objectives under EC Directives 82/176/EEC and 84/156/EEC 0.3 mg kg^{-1} (wet weight) in a representative sample of fish flesh; 1 μg l^{-1} (annual mean) total mercury in inland surface waters; 0.5 μg l^{-1} (annual mean) dissolved mercury in estuarine waters; 0.3 μg l^{-1} (annual mean) dissolved mercury in marine waters. A 'standstill' provision applies to concentrations in shellfish or sediments. Limit values under EC Directive 84/156/EEC 0.05 mg l^{-1} effluent and 0.1 g l^{-1} vinyl chloride production capacity for chemical industries using mercury catalysts in vinyl chloride production; 0.05 mg l^{-1} effluent and 5 g kg^{-1} mercury processed for chemical industries using mercury catalysts in other processes; 0.05 mg l^{-1} effluent and 0.7 g kg^{-1} mercury

processed for manufacture of mercury catalysts used in vinyl chloride production 0.05 mg l^{-1} effluent and 0.05 g kg^{-1} mercury processed for manufacture of organic and non-organic mercury compounds (other than mercury catalysts for vinyl chloride production); 0.05 mg l^{-1} effluent and 0.03 g kg^{-1} mercury processed for manufacture of primary batteries containing mercury; 0.05 mg l^{-1} effluent for mercury recovery plants and extraction and refining of non-ferrous metals; 0.05 mg l^{-1} effluent for plants treating toxic wastes containing mercury (4).

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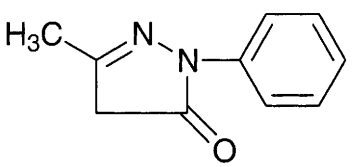
4. *DoE Circular 7/89: Water and the environment. The implementation of EC Directives on pollution caused by certain dangerous substances discharged into the aquatic environment* 1989, HMSO, London, UK

P121 1-phenyl-3-methyl-5-pyrazolone



$C_{10}H_{10}N_2O$ **Mol. Wt.** 174.20 **CAS Registry No.** 89-25-8

Synonyms 2,4-dihydro-5-methyl-2-phenyl-3*H*-pyrazol-3-one; 3-methyl-1-phenyl-2-pyrazolin-5-one; C.I. Developer 1; Developer Z; Norphenazone; Norantipyrine

EINECS No. 201-891-0 **RTECS No.** UQ 9625000

Uses Dye intermediate.

Physical properties

M. Pt. 129-130°C **B. Pt.** 191°C at 7 mmHg

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >96.0 mg kg^{-1} (1).
LD_{50} oral rat 3500 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 2012 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Oral (2 yr) rat 2500 or 5000 ppm in diet and mouse 7500 or 15,000 ppm. Mice showed a compound-related mean body weight reduction, rats did not. In both species no toxic effects or increased incidences of tumours were recorded compared with the controls (4).

Irritancy

500 mg instilled into rabbit eye (24 hr) caused moderate irritation (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6). CASE study predicted it to be equivocal for the induction of sister chromatid exchanges and chromosomal aberrations (7).

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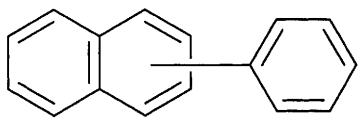
P122 phenylnaphthalene



$C_{16}H_{12}$ **Mol. Wt.** 204.27 **CAS Registry No.** 35465-71-5

Occurrence Has been detected in river sediments (1).

Ecotoxicity

Bioaccumulation

It has been detected in tissues of the blue crab which live in Chesapeake Bay, USA (2).

Sub-adult rainbow trout exposed to 10 mg (total dose) over 5 days, $t_{1/2}$ 24 days for accumulation in the fish body; this is longer than for other polycyclic aromatic hydrocarbons tested (3).

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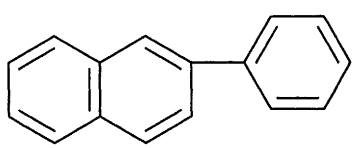
P123 2-phenylnaphthalene



$C_{16}H_{12}$ **Mol. Wt.** 204.27 **CAS Registry No.** 612-94-2

Synonyms (β-naphthyl)benzene; β-phenylnaphthalene

EINECS No. 210-324-6

Occurrence Has been detected in sediments, from polycyclic aromatic hydrocarbon areas of the Great Lakes, at levels of 0.67-2.0 μg g^{-1} dry sediments (1).

Physical properties

M. Pt. 103-104°C **B. Pt.** 357-358°C

Ecotoxicity

Bioaccumulation

Analysis of sediments contaminated with polycyclic aromatic compounds found it present at 1.3×10^{-3} ng g^{-1} dry sediment, it was not detected in water or fish from the same area (2).

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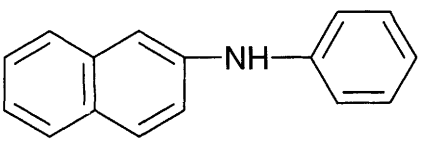
P124 *N*-phenyl-2-naphthylamine



$C_{16}H_{13}N$ **Mol. Wt.** 219.29 **CAS Registry No.** 135-88-6

Synonyms *N*-phenyl-β-naphthylamine; *N*-phenyl-2-naphthalenamine; Aceto PBN; Age Rite Powder; 2-anilinonaphthalene; Antioxidant 116; *N*-(2-naphthyl)aniline; Neozone; Nonox D; Vulkanox PBN

EINECS No. 205-223-9 **RTECS No.** QM 4550000

Uses Rubber, grease and oil antioxidant. Stabiliser during synthetic rubber manufacture. Intermediate in dye synthesis.

Physical properties

M. Pt. 107-108°C **B. Pt.** 395.5°C **Specific gravity** 1.24

Solubility Organic solvents: hot benzene, hot diethyl ether, hot ethanol

Occupational exposure

Supply classification harmful, dangerous for the environment

Risk phrases Irritating to eyes and skin – Possible risk of irreversible effects – May cause sensitisation by skin contact – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R36/38, R40, R43, R51/53)

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 – Wear suitable protective clothing and gloves – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S26, S36/37, S61)

Ecotoxicity

Bioaccumulation

Confirmed to be non- or low accumulative (1).

Environmental fate

Degradation studies

Confirmed to be non-biodegradable (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1450 mg kg^{-1} (2).

LD_{50} oral rat 8730 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral (14 day) rat ≤50,000 ppm in feed. 3/5 ♂ and 4/5 ♀ receiving 50,000 ppm died before 14 day. 12,5000 ppm caused a significant decrease in final mean body weight, lower by 18-57% than controls. ♂ receiving 12,500 ppm and ♀ receiving 25,000 or 50,000 ppm had arched backs and diarrhoea (3).

Oral (14 day) mouse ≤20,000 ppm in feed no toxic effects (3).

Oral (13 wk) rat ≤40,000 ppm in diet. 9/10 ♀ and 4/10 ♂ receiving 40,000 ppm died before 13 wk. 5000-40,000 ppm caused a 9-60% decrease in final mean body weight compared with the controls. Liver weight to body weight ratios increased with dose. Nephropathy characterised by renal tubular epithelial degeneration and hyperplasia occurred. Other compound-related adverse effects included atrophy of the femoral bone marrow lymphoid degeneration of the thymus, haematopoietic hypoplasia, lymphoid depletion of the spleen and testicular hypospermatogenesis (3).

Inhalation (14 day) rat 900 mg m^{-3} suffered from weight loss, slight erythrocytopenia and pulmonary emphysema (4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (5).

Oral (2 yr) rat 2500 or 5000 ppm in feed (calculated to be equivalent to 100 or 225 mg kg^{-1} day^{-1} for ♂ and 120 or 260 mg kg^{-1} day^{-1} for ♀). The mean body weights of the treated rats were lower than the controls throughout the study. The main target for toxic effects was the kidney in both sexes. Necrosis of the renal papilla, mineralisation of the kidney and epithelial hyperplasia and calculi of the kidney pelvis were observed in the high dose ♀ group; this group also developed atrophy, hydronephrosis, chronic focal inflammation and fibrosis of the kidney. Both sexes suffered from cysts and acute suppurative inflammation of the kidney. No compound-related renal neoplasms were observed (3).

Oral (2 yr) mouse 2500 or 5000 ppm in feed (calculated to be equivalent to 500 or 1000 mg kg^{-1} day^{-1} for ♂ and 450 or 900 mg kg^{-1} day^{-1} for ♀). Mean body weight was decreased in the high-dose groups compared with controls. High dose ♀ developed nuclear enlargement of the renal tubular epithelial cells and nephropathy. Two high-dose ♀ also developed atypical tubular cell hyperplasia, 1 tubular cell adenoma and 1 tubular cell adenocarcinoma, and were observed in 2 other high dose ♀. No renal neoplasms were observed in dosed ♂ mice (3).

♂, ♀ mice (strains (C57BL/6xC3H/Anf)F_1 and (C57BL/6xAKR)F_1, 18 in each group, were given 464 mg kg^{-1} body weight in 0.5% aqueous gelatin via gavage on day 7 of age and the same amount (not adjusted for increased body weight) daily for up to 28 days. Subsequently they were given 1206 mg kg^{-1} in diet for 78 wk. By 78 wk 13 ♂, 18♀ of the 1st strain and 18♂, 17♀ of the 2nd strain were alive. The total numbers with tumours among those necropsied were 7/17, 1/18, 7/18 and 3/18, respectively. ♂ of the 1st strain had a significant increase in tumours, mainly hepatomas, compared with the controls (6,7).

Oral (4.5 yr) dog 540 mg day^{-1} no bladder tumours were observed (3 dogs tested) (8).

Subcutaneous (80 wk) ♂, ♀ mice (strains C57BL/xC3H/Anf)F_1 and 464 mg kg^{-1}(C57BL/xADR)F_1 single injection of 464 mg kg^{-1} on day 28 of life followed by observation. By wk 80 16 ♂, 17 ♀ of the 1st strain and 16 ♂, 18♀ of the

2nd strain were still alive. The total number of tumours amongst those necropsied were 4/17, 5/18, 3/18 and 1/18 respectively. ♀ of the 1st strain and ♂ of the 2nd strain had a significant increase in tumour (mainly hepatomas) incidence (6,7).
Intragastric (18 month) rat 20 or 100 mg kg^{-1}. 20 mg kg^{-1} caused no significant toxic effects. 100 mg kg^{-1} caused an increase in urinary protein and lung weight after ~1 month, a decrease in urinary hippuric acid and adrenal ascorbic acid, gastro-intestinal tract changes and impairment of reproductive function within 6 month, increase in liver weight by 12 months, and a drop in urinary function after 18 months (9).

Metabolism and toxicokinetics
Metabolised to β-naphthylamine in humans and dogs (details unspecified) (10).
In dogs given [^{14}C]-*N*-phenyl-2-naphthylamine, more than 90% of the administered radiolabel was excreted over 3 days, mainly in faeces, only 2.5% was found in urine (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (3,11).
In vitro mouse lymphoma cell mutation assay without metabolic activation equivocal, with metabolic activation positive (12).
In vitro Chinese hamster ovary cells with or without metabolic activation chromosomal aberrations negative; sister chromatid exchanges without metabolic activation negative, with metabolic activation equivocal (3,13).
In vitro Chinese hamster lung cells chromosomal aberrations without metabolic activation negative, with metabolic activation weakly positive (14).
In vitro Chinese hamster ovary cells with and without metabolic activation chromosomal aberrations negative (14).

Other effects

Other adverse effects (human)
Occupationally exposed workers have developed acne, leucoplakia and hypersensitivity to light (15).

Any other adverse effects
Rats given unspecified-repeated intragastric doses had a reduction in body weight, disturbance of liver function and nervous system depression (2).

Other comments

Use, manufacture, toxicity reviewed (16).
Commercial *N*-phenyl-2-naphthylamine is frequently contaminated with the known carcinogen 2-naphthylamine (16).
Toxicity reviewed (17).

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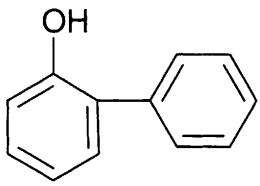
P125 2-phenylphenol



$C_{12}H_{10}O$ **Mol. Wt.** 170.21 **CAS Registry No.** 90-43-7

Synonyms [1,1'-biphenyl]-2-ol; 2-biphenylol; *o*-diphenylol; 2-hydroxydiphenol; *o*-phenylphenol; *o*-xenol

EINECS No. 201-993-5 **RTECS No.** DV 5775000

Uses In the rubber industry. Fungicide. Disinfectant.

Physical properties

M. Pt. 57-59°C (99+% pure) **B. Pt.** 282°C **Flash point** 123°C **Specific gravity** 1.217 at 25°C with respect to water at 25°C **Volatility** v.p. 20 mmHg at 163°C

Solubility Water: 0.7 g l^{-1} at 25°C. Organic solvents: ethanol, ethylene glycol, glycol ethers, isopropanol

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) – Do not breathe dust (S2, S22)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 6 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (2 day) *Tetrahymena pyriformis* 13.7 mg l^{-1} (2).

EC_{50} (5 min) *Photobacterium phosphoreum* 2.05 ppm Microtox test (3).

Environmental fate

Nitrification inhibition

Inhibition of nitrification on agar occurred at 25 mg l^{-1} (4).

Degradation studies

In a mixed culture for the degradation of 2-phenylphenol only acetate was found as an intermediate (dose and duration unspecified) (5).

Strain B10 (species unspecified) slowly degraded 2-phenylphenol if supplied as the only carbon source (6). After 3 wk of adaption at 10-40 mg l^{-1} and 22°C, 100% degradation under aerobic conditions, as sole carbon source or with synthetic sewage (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1050, 2000 mg kg^{-1}, respectively (8,9).
LD_{50} intraperitoneal mouse 50 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Gavage ♀ B6C3F1 rat (10 day) 0, 10 or 200 mg kg^{-1} day^{-1}, no evidence of altered immune function or host susceptibility (11).
Oral rat 1.5 mg kg^{-1} for 3 successive days. A marked change in the kidney was the detachment of brush border accompanied by the dilation of tubular lumen. The swelling of mitochondria, the disruption of cristae in mitochondria and the small vacuolation of rough endoplasmic reticulum were also observed in the cytoplasm (12).
Dermal 10 ♂ and 10 ♀ Swiss Webster mice (4 wk) 0, 6, 11, 21, 36 or 56 mg in 0.1 ml of acetone. Dose-related ulcerative lesions were caused at the site of application It was judged not to be life-threatening (13).
Oral rat (32 day) 200 mg kg^{-1} day^{-1}, no effects on growth rate and blood haemoglobin, total white cell count or differential white cell count were observed (14).

Carcinogenicity and chronic effects

Oral mouse (52 wk) 0.0, 0.65, 1.3 or 2.6%. No dose-related effects on clinical signs or urinary pH. Serum urea nitrogen in the 2.6% group was significantly higher than in the controls. The incidence and severity of necrosis in liver cells and tubular epithelium of the kidney showed a dose-related increase in the treated group (15).
Gavage 18 ♂ and 18 ♀ 7-day-old mice (18 month) single dose of 100 mg kg^{-1}. After 4 wk until the end of the study, they were fed 280 mg kg^{-1}. No differences were observed in the tumour incidences between test and control animals (16).
Oral ♂ rat (26 wk) 1.25%. Urinary bladder tumours, papillomas and carcinomas occurred in 12/31 (39%) (17).
Dermal Swiss CD-1 ♂, ♀ mice (104 wk) 55.5 mg in 0.1 ml acetone 3 day wk^{-1}. Non-neoplastic lesions consisting of inflammation, ulceration, hyperkeratosis and acanthosis were induced at the site of application. No skin neoplasms were observed in the ♂ and ♀ mice (15).
Oral ♂ Fischer 344 rats 8-11 wk old (90 day) 2% diet. No neoplastic lesion of the urinary tract was reported (18).
Subcutaneous ♂, ♀ mice (78 wk) 1000 mg kg^{-1} in corn oil from 28th day of life. No increase in the incidence of tumours was observed in treated mice compared with control mice (19).

Teratogenicity and reproductive effects

Gavage Sprague-Dawley rats (6-15 day of gestation) 0, 100, 300 or 700 mg kg^{-1} day^{-1}. No apparent teratogenic or embryotoxic effects were observed (20).

Metabolism and toxicokinetics

Excreted in mammals principally as the parent compound and as the glucuronide and sulfate conjugates (21).
Oral rat 100 mg kg^{-1} the cumulative biliary excretion of the conjugates was about 4% in 6 hr (22).
In vitro it was converted into 2,5-dihydroxybiphenyl by microsomal cytochrome P_{450} (species unspecified) (23).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation, eye rabbit (24 hr) 50 µg caused severe irritation (24).
Dermal application of 5.0% solution in sesame oil and as a 0.1% aqueous solution as the sodium salt did not cause primary skin irritation or sensitisation in humans (25).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation weakly mutagenic; TA98, TA100 and TA1537 without metabolic activation negative (13).
Drosophila melanogaster no induction of sex linked recessive lethal mutations (13).

In vitro Chinese hamster ovary cells with metabolic activation induced chromosomal aberrations and sister chromatid exchanges (26).
In vitro mouse lymphoma L5178 tk^+/tk^- with and without metabolic activation positive (13).
Oral ♂ CD-1 mice 2000 mg kg^{-1} induced DNA damage in the stomach, liver, kidney, bladder and lung. Increased DNA damage peaked at 3-8 hr after administration and tended to decrease at 24 hr (27).

Other effects

Other adverse effects (human)
Biphenyls and phenylphenols show a dose-dependent inhibitory effect on human cutaneous cell respiration with IC_{50} values of 100-250 μmol l^{-1} and may cause skin damage. Of 800 garments tested, 24 contained 109-250 ppm 2-phenylphenol: the highest content was in a cotton/viscose scarf (28).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phenols: maximum admissible concentration 0.5 μg l^{-1} (29).

Other comments

Xenoestrogen and possible environmental endocrine disruptor (30).
Toxicity reviewed (31).
Reviews on human health effects and experimental toxicity listed (32).

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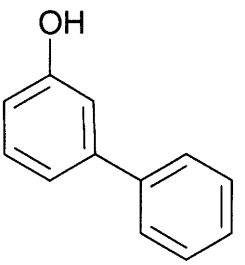
P126 3-phenylphenol



$C_{12}H_{10}O$ **Mol. Wt.** 170.21 **CAS Registry No.** 580-51-8

Synonyms [1,1'-biphenyl]-3-ol; *m*-biphenylol; 3-hydroxybiphenyl

Physical properties

M. Pt. 76-78°C **B. Pt.** 120-130°C at 0.01 Torr

Solubility Water: slightly soluble in water. Organic solvents: benzene, chloroform, diethyl ether, ethanol, petroleum ether, pyridine

Environmental fate

Degradation studies

Pseudomonas testosteroni B-356 can utilise 3-phenylphenol as a carbon source (1).

Genotoxicity

Salmonella typhimurium G46, TA1535, TA100, C3076, TA1537, D3052, TA1538, TA98 negative (metabolic activation not specified) (2).

Escherichia coli WP2, WP2 *UVRA*⁻ negative (metabolic activation not specified) (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phenols: maximum admissible concentration 0.5 μg l^{-1} (3).

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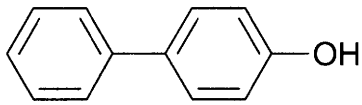
P127 4-phenylphenol



$C_{12}H_{10}O$ **Mol. Wt.** 170.21 **CAS Registry No.** 92-69-3

Synonyms [1,1'-biphenyl]-4-ol; 4-biphenylol; 4-diphenylol; *p*-hydroxybiphenyl; paraxenol; *p*-phenylphenol; tetrosin P300

EINECS No. 202-179-2 **RTECS No.** DV 5850000

Uses Intermediate in resin manufacture. In the rubber industry. In the printing industry.

Physical properties

M. Pt. 165-167°C (99% pure) **B. Pt.** 321°C **Flash point** 165°C **Partition coefficient** log P_{ow} 3.20 (1)

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 2.35 ppm Microtox test (2).

Bioaccumulation

Confirmed to be non- or low accumulative (3).

Environmental fate

Degradation studies

Metabolised by *Pseudomonas testosteroni* B-356 isolated from sewage sludge and *Pseudomonas putida* KT2440, DA1 and DA2 carrying cloned biphenyl/chlorobiphenyl degrading genes from strain B-356 to produce 2-hydroxy-6-oxo-6-(2'-hydroxyphenyl)hex-4-enoic acid, 2-hydroxy-6-oxo-6-(2'-hydroxyphenyl)-hexanoic acid and 2-hydroxybenzoic acid in varying amounts (4).

Mammalian & avian toxicity

Acute data

TD_{Lo} oral mouse 153 g kg^{-1} (5).

TD_{Lo} subcutaneous mouse 1000 mg kg^{-1} (5).

LD_{50} intraperitoneal mouse 150 mg kg^{-1} (6).

Legislation

Included in Schedule 4 (Release into Air: 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).

Other comments

Xenoestrogen and possible environmental endocrine disruptor (9).

References

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2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
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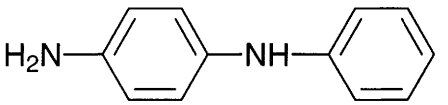
6. *NTIS Report* No. AD 691-490, Natl. Tech. Inf. Ser., Springfield, VA, USA.
7. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
9. Soto, A. M. et al in *Proc. Conf. Endocrine Disrupters in the Environment, 20-21 May, 1997* 1997, IBC UK Conferences Limited, 57-61 Mortimer Street, London W1N 8JX, UK

P128 *N*-phenyl-*p*-phenylenediamine



$C_{12}H_{12}N_2$ **Mol. Wt.** 184.24 **CAS Registry No.** 101-54-2

Synonyms *N*-phenyl-1,4-benzenediamine; 4-aminodiphenylamine; C.I. Developer 15; Pelton BR II; 4-(phenylamino)aniline; semidine

EINECS No. 202-951-9 **RTECS No.** ST 3150000

Uses Intermediate for photographic chemicals, microbiocides, dyes and pharmaceuticals.

Physical properties

M. Pt. 73-75°C

Environmental fate

Degradation studies

Model wastewater containing 15 mg l^{-1} *N*-phenyl-*p*-phenylenediamine together with peptone, starch, and inorganic salts was treated by a 2-step method; the 1st step involved activated sludge and the 2nd using spent catalyst from vinyl acetate production. The *N*-phenyl-*p*-phenylenediamine content and COD after the 1st step were 10 mg l^{-1} and 120 mg O_2 l^{-1}, respectively, and after the 2nd step 4 mg l^{-1} and 80 mg O_2 l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 464 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Oral (2 yr) rat 600 or 1200 ppm in diet for 78 wk followed by observation for 26 wk. The mean body weights of dosed rats were slightly lower than that of the controls. The incidences of neoplasms (details unspecified) of the treated rats was not significantly higher than the controls (3).

Oral (91 wk) ♂ mouse 2500 or 5000 ppm in diet, ♀ mouse 5000 or 10,000 ppm in diet both for 31 wk. These doses were toxic and were lowered at 31 wk, treatment continued until wk 43, the mice were then observed until wk 91. The time-weighted average doses over the treatment period were 2057 or 4114 ppm for ♂, and 3672 or 8170 for ♀. The mean body weights of treated mice were considerably less than those of the controls, and the doses were toxic prior to reduction. Extensive hepatic inflammation occurred in large numbers of the ♂ and to a lesser extent ♀. There was not a significant increase in the incidence of neoplasms (3).

Irritancy

100 mg instilled into rabbit eye (24 hr) caused severe irritation (4).

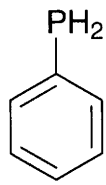
Other comments

Acute toxicity reviewed (5).

References

1. Buday, M. et al *Biological treatment of wastewater with activated sludge – Patent Application* Czech. CS 230, 872 (CI. CO2F3/12), 15 Nov. 1986, Appl. 82/5,385, 14 Jul. 1982 (*Chem. Abstr.* **106**, 182103y).
2. Lewis, R. C. *Sax's Dangerous Properties of Industrial Materials* 8th ed., 1992, 2768, Van Nostrand Reinhold, New York, NY, USA.
3. *NTIS Report* No. TR-082, Natl. Tech. Inf. Ser., Springfield, VA, USA.
4. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, 70, Prague, Czechoslovakia.
5. Randall, D. J. et al *Acute Toxic. Data* 1990, **1**(1), 63-64

P129 phenylphosphine



C_6H_7P **Mol. Wt.** 110.10 **CAS Registry No.** 638-21-1

EINECS No. 211-325-4 **RTECS No.** SZ 2100000

Physical properties

M. Pt. 164-165°C **B. Pt.** 305-308°C **Flash point** 73°C **Specific gravity** 1.001
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VLE 0.05 ppm (0.25 mg m^{-3})
US-STEL ceiling limit 0.05 ppm (0.23 mg m^{-3})

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) inhalation rat 38 ppm (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

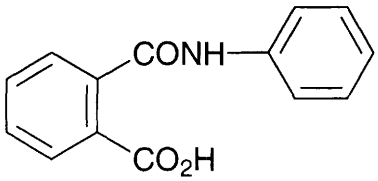
Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (3).

References

1. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 154.
2. *S. I. 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

P130 *N*-phenylphthalamic acid



$C_{14}H_{11}NO_3$ **Mol. Wt.** 241.25 **CAS Registry No.** 4727-29-1

Synonyms Nevirol; 2-[(phenylamino)carbonyl]benzoic acid; phthalanilic acid; 2-carboxybenzanilide; Lemax; phthalic monoanilide

RTECS No. DH 6298150

Uses Plant growth regulator.
Fruit tree and vegetable growth stimulant, used in Bulgaria and Hungary (1).

Physical properties

M. Pt. 163-170 °C
Solubility Water: 20 mg l^{-1} at 20°C. Organic solvents: acetone, acetonitrile, ethanol, methanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat and mice >5000 mg kg^{-1} (2,3).

Sub-acute and sub-chronic data
Daily administration to rats (route unspecified) of 210-840 mg kg^{-1} for 15 days caused a dose-dependent effect on serum leucine aminopeptidase, glutamate dehydrogenase and ceruloplasmin; liver morphology was affected (lesions) at the high dose (4).

Teratogenicity and reproductive effects
Chronic long-term exposure (dose and duration unspecified) increased body, liver and kidney weight in rats but caused no foetal malformations; fertility was slightly increased in a two-generation study but live births and neonatal survival were unaffected (5).

Genotoxicity

Salmonella typhimurium TA98, TA100 (activation unspecified) negative (6).
Mouse bone marrow micronucleus test negative (7).

Other effects

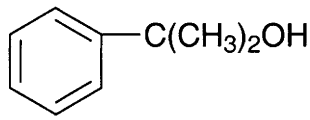
Other adverse effects (human)
Peak leucine aminopeptidase activity occurred 24 hr after oral administration of 2000 mg kg^{-1} to rats; peak glutamate dehydrogenase activity occurred at 48 hr (8,9).

References

1. *European Directory of Agrochemical Products* 4th ed., 1990, The Royal Society of Chemistry, London, UK.
2. *Pesticides Dictionary* 1983.
3. Filipescu, G. et al *Rev. Roum. Morphol. Embryol.* 1991, **27**, 49.
4. Kretzschmar, M. et al *J. Exp. Anim. Sci.* 1991, **34**, 132.
5. Filipescu, G. et al *Proc. Int. Symp. Contam. in Central and Eastern Europe* 1992.

6. Maron, D. et al *Mutat. Res.* 1983, **113**, 173.
7. Garriott, M. J. et al *J. Appl. Toxicol.* 1988, **8**, 141.
8. *Diagnosis of hepatic diseases* 1980, Verlag Giebeler, Darmstadt, Germany.
9. Codorean, E. et al *Rev. Roum. Morphol. Embryol.* 1991, **27**, 143

P131 2-phenyl-2-propanol



$C_9H_{12}O$ **Mol. Wt.** 136.19 **CAS Registry No.** 617-94-7

Synonyms α,α-dimethylbenzenemethanol; α,α-dimethylbenzyl alcohol; α-cumyl alcohol; dimethylphenylcarbinol; α-hydroxycumene; 2-phenylisopropanol; dimethylphenylmethanol

EINECS No. 210-539-5 **RTECS No.** DO 4562000

Uses Fragrances. Catalyst. Solvent.

Physical properties

M. Pt. 35-37°C **B. Pt.** 202°C **Flash point** 87°C **Specific gravity** 0.973

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1300, 1950 mg kg^{-1}, respectively (1,2).

Threshold concentration inhalation rats, mice 360 mg m^{-3}. Acute inhalation caused a steady decrease in peroxidase activity and increase in blood cholinesterase activity in rats (3).

LD_{50} dermal rabbit 4300 mg kg^{-1} (2).

Metabolism and toxicokinetics

When administered at 0.5 g kg^{-1} to rabbits (route unspecified), 85% excreted in urine as a conjugated glucuronide (4).

Irritancy

Dermal rabbit (24 hr) 500 mg caused severe irritation. No irritation in 48 hr closed-patch test on humans (2).

Genotoxicity

Saccharomyces cerevisiae sake induced respiratory-deficient mutants (5,6).

Other effects

Any other adverse effects

Adverse effects in acute studies in mammals included central nervous system depression, damage to liver and kidneys, and steady decrease in peroxidase activity and increase in blood cholinesterase activity, increased number of leukocytes, increased activity of amino transferases and an increase in blood haemoglobin (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Detected in river and tap water, effluents (8-11).
Impurity in hydroxyethyl starch plasma expander (12).

References

1. Bukhalorskii, A. A. et al *Promst. Sint. Kauch.* 1976, **2**, 4 (*Chem. Abstr.* **85**, 88130).
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3. Lopatneua, Z. Ye. *Kauch. Rezina* 1981, **6**, 55 (*Chem. Abstr.* **95**, 55852w).
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6. Kojima, M. et al *Hakko Kogaku Zasshi* 1979, **57**, 315 (Japan.) (*Chem. Abstr.* **91**, 187268n).
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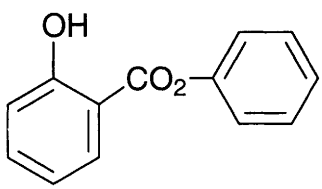
12. De Belder, A. M. et al *IRCS Med. Sci.: Libr. Compend.* 1976, **4**, 457 (*Chem. Abstr.* **85**, 198134)

P132 phenyl salicylate



$C_{13}H_{10}O_3$ **Mol. Wt.** 214.22 **CAS Registry No.** 118-55-8

Synonyms 2-hydroxybenzoic acid, phenyl ester; salicylic acid, phenyl ester; 2-phenoxycarbonylphenol; phenyl 2-hydroxybenzoate; Salphenyl; salol; Musol

EINECS No. 204-259-2 **RTECS No.** VO 6125000

Uses Sunscreening agent; in polymer manufacture; in lacquers, adhesives, waxes and polishes; anti-inflammatory analgesic.

Physical properties

M. Pt. 41-43°C **B. Pt.** 172-173°C at 12 mmHg **Flash point** >110°C **Specific gravity** 1.25 at 20°C with respect to water at 4°C
Solubility Water: 0.81 mg ml^{-1}. Organic solvents: benzene, diethyl ether, hot ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3 g kg^{-1} (1).
LD_{Lo} oral rabbit 3 g kg^{-1} (2).

Teratogenicity and reproductive effects
Teratogenic and reproductive effects reported in rats following oral administration of 600 mg kg^{-1} (total dose) on days 7-12 of pregnancy (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, with and without metabolic activation negative (4).

Other comments

Poor spectral stability, reflecting photochemical stability, exhibited in simulated solar irradation study (5).

References

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2. *Rev. Med. Suisse Romande* 1895, **15**, 561.
3. *Osaka City Med. J.* 1966, **12**, 23.
4. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
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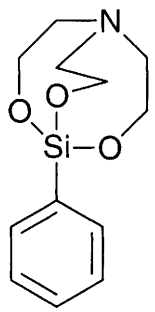
P133 phenylsilatrane



$C_{12}H_{17}NO_3Si$ **Mol. Wt.** 251.36 **CAS Registry No.** 2097-19-0

Synonyms 1-phenyl-2,8,9-trioxa-5-aza-1-silabicyclo[3.3.3]undecane; 1-phenylsilatrane

EINECS No. 218-263-7 **RTECS No.** YJ 9050000

Mammalian & avian toxicity

Acute data

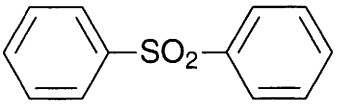
LD_{Lo} oral rat 1 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 330 μg kg^{-1} (2).

References

1. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
2. *Russ. Chem. Rev. (Engl. Transl.)* 1969, **38**(12), 975

P134 phenyl sulfone



$C_{12}H_{10}O_2S$ **Mol. Wt.** 218.28 **CAS Registry No.** 127-63-9

Synonyms 1,1'-sulfonylbisbenzene; diphenyl sulfone; sulfobenzide; DPS

EINECS No. 204-853-1 **RTECS No.** SX 2400000

Uses Ovicide used to control eggs and larval stages of mites.

Physical properties

M. Pt. 128-129°C **B. Pt.** 378-379°C **Partition coefficient** log P_{ow} 2.40 (1)

Solubility Organic solvents: benzene, hot ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 15.8 ppm Microtox test (1).

Environmental fate

Abiotic removal

>90% removal by passing over a vanadium pentoxide catalyst at 600°C (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1390 mg kg^{-1} (2).

LD_{50} intravenous mouse 320 mg kg^{-1} (3).

Genotoxicity

Salmonella typhimurium positive (strain and metabolic activation unspecified) (4).

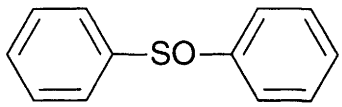
Other comments

US EPA recommended testing phenyl sulfone's chemical fate, health effects and ecological effects (5).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Kazimierczak, Z. et al *Stud. Environ. Sci.* 1986, **29**(Chem. Prot. Environ. 1985), 103-111.
3. *Sax's Dangerous Properties of Industrial Materials* 8th ed, 1992, Van Nostrand Reinhold, New York, NY, USA.
4. *US Army Armament Research and Development Command, Chemical Systems Lab., NIOSH Exchange Chemicals* NX 01761, Aberdeen Proving Ground, MD, USA.
5. Grifoll, M. et al *Arch. Environ. Contam. Toxicol.* 1990, **19**(2), 175-184

P135 phenyl sulfoxide



$C_{12}H_{10}OS$ **Mol. Wt.** 202.28 **CAS Registry No.** 945-51-7

Synonyms 1,1'-sulfinylbisbenzene; diphenyl sulfoxide

EINECS No. 213-415-9 **RTECS No.** DA 9185000

Physical properties

M. Pt. 69-71°C **B. Pt.** 206-208°C at 13 mmHg **Volatility** v.den. 7.0

Environmental fate

Abiotic removal

Adsorbed onto silicon dioxide (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 750 mg kg^{-1} (2).

Metabolism and toxicokinetics

Metabolised to diphenyl sulfone by intact guinea pig liver under normoxia, in the nonrecirculating perfusion method *in situ*; only under hypoxia does the reductive, rather than the oxidative pathway become the major route (3).

Genotoxicity

Salmonella typhimurium TA1535 *umu* test with and without metabolic activation negative (4).

References

1. Curtis, C. W. et al *Fuel Sci. Technol. Int.* 1989, **7**(9), 1225-1268.
2. *Int. J. Radiat. Biol. Relat. Stud. Phys., Chem. Med.* 1961, **3**, 41.
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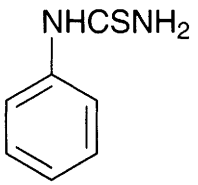
4. Nakamura, S. et al *Mutat. Res.* 1987, **192**(4), 239-246

P136 phenylthiourea



$C_7H_8N_2S$ **Mol. Wt.** 152.22 **CAS Registry No.** 103-85-5

Synonyms 1-phenyl-2-thiourea; phenylthiocarbamide; *N*-phenylthiourea; α-phenylthiourea; 1-phenylthiourea; PTU; U 6324

EINECS No. 203-151-2 **RTECS No.** YU 1400000

Uses In medical genetics. Corrosion inhibitor.

Physical properties

M. Pt. 148-150°C **Specific gravity** 1.3 **Partition coefficient** log P_{ow} 0.73 (1)
Solubility Water: soluble in 400 parts cold water, 17 parts boiling water. Organic solvents: ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 3.49 ppm Microtox test (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit 3, 10, 40 mg kg^{-1}, respectively (3,4).
LD_{50} intraperitoneal rat, mouse 5, 25 mg kg^{-1}, respectively (5,6).

Carcinogenicity and chronic effects
National Toxicology Program investigated 1-phenyl-2-thiourea in rat, mouse. Designated non-carcinogen in rat and mouse (7).

Teratogenicity and reproductive effects
JCR mice were given drinking water containing 40 mg l^{-1} throughout pregnancy. Newborn mice had reduced brain weight and nitrogen content. The impaired brain development was possibly due to inhibition of thyroxine synthesis (8).

References

1. Kaiser, K. L. E. *QSAR Environ. Toxicol., Proc. Int. Workshop, 2nd* 1986, 153-168.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
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4. Litton Biotechnics Inc. *Progess Report for Contract No. NIH-NCI-E-C-72-3252* Natl. Cancer Inst., Bethesda, MD, USA.
5. *J. Pharmacol. Exp. Ther.* 1947, **89**, 186.
6. *NTIS Report* AD 277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
7. *National Toxicology Program Research and Testing Division* 1992, Report No. PB 287357, NIEHS, Research Triangle Park, NC, USA.
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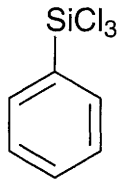
P137 phenyltrichlorosilane



$C_6H_5Cl_3Si$ **Mol. Wt.** 211.55 **CAS Registry No.** 98-13-5

Synonyms trichlorophenylsilane; phenylsilicon trichloride

EINECS No. 202-640-8 **RTECS No.** VV 6650000

Physical properties

B. Pt. 201°C **Flash point** 91°C **Specific gravity** 1.321

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2390 mg kg^{-1} (1).

LC_{50} (2 hr) inhalation mouse 330 mg m^{-3} (2).

LD_{50} intravenous mouse 100 mg kg^{-1} (3).

LD_{50} dermal rabbit 890 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation and 5 mg instilled into rabbit eye (24 hr) caused severe irritation (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 μg l^{-1} (5).

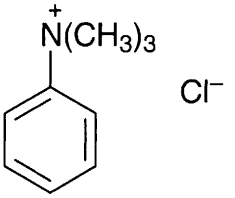
Other comments

Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicology, exposure levels, workplace experience listed (6).

References

1. *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
2. *Toksikol. Nov. Prom. Khim. Veshchestv.* 1961, (3), 23.
3. *U.S. Army Armament Research and Development Command* Exchange Chemicals, Aberdeen Proving Ground, MD 21010, USA.
4. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
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. *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

P138 phenyltrimethylammonium chloride



$C_9H_{14}ClN$ **Mol. Wt.** 171.67 **CAS Registry No.** 138-24-9

Synonyms trimethylphenylammonium chloride; trimethylanilinium chloride; *N,N,N*-trimethylanilinium chloride

EINECS No. 205-319-0 **RTECS No.** BT 2190000

Physical properties

M. Pt. 237°C (sublimes)

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) – 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 (S1/2, S25, S39, S45, S53)

Mammalian & avian toxicity

Acute data

LD_{Lo} oral mouse 200 mg kg^{-1} (1).

LD_{Lo} intravenous mouse 15 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chloride: 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).

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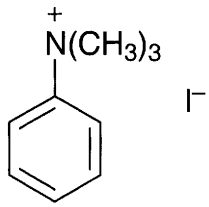
P139 phenyltrimethylammonium iodide



$C_9H_{14}NI$ **Mol. Wt.** 263.12 **CAS Registry No.** 98-04-4

Synonyms *N,N,N*-trimethylbenzenaminium iodide; *N,N*-dimethylaniline methiodide; PHT; trimethylanilinium iodide; *N,N,N*-trimethylanilinium iodide; trimethylphenylammonium iodide

EINECS No. 202-630-3 **RTECS No.** BT 2450000

Uses Used in the detection and determination of cadmium.

Physical properties

M. Pt. 227°C (sublimes)
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 55 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 85 mg kg^{-1} (2).
LD_{50} intravenous mouse 5620 μg kg^{-1} (3).

Legislation

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

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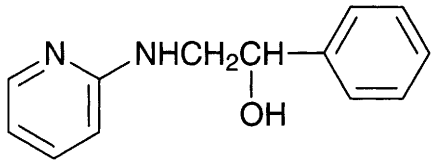
P140 phenyramidol



$C_{13}H_{14}N_2O$ **Mol. Wt.** 214.27 **CAS Registry No.** 553-69-5

Synonyms α-[(2-pyridinylamino)methyl]benzenemethanol; α-[(2-pyridylamino)methyl]benzyl alcohol; Analexin; Cabral; Evasprin; Fenyramidol; IN 511; MJ 505

EINECS No. 209-044-7 **RTECS No.** DP 1050000

Uses Hydrochloride used as analgesic, relaxant (skeletal muscle).

Physical properties

M. Pt. 82-85°C (crystals from dilute methanol)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 756, 1850 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal mouse 355 mg kg^{-1} (3).
LD_{50} subcutaneous mouse 405 mg kg^{-1} (4).
LD_{50} intravenous mouse 124 mg kg^{-1} (3).

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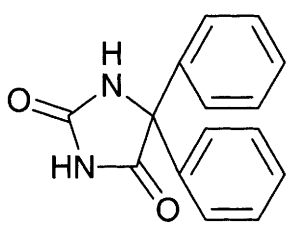
P141 phenytoin



$C_{15}H_{12}N_2O_2$ **Mol. Wt.** 252.27 **CAS Registry No.** 57-41-0

Synonyms 5,5-diphenyl-2,4-imidazolidinedione; 5,5-diphenylhydantoin; 5,5'-diphenylimidazolidin-2,4-dione; DPH; Phenytoin

EINECS No. 200-328-6 **RTECS No.** MU 1050000

Uses Anticonvulsant, anti-epileptic drug and in treatment of Parkinson's syndrome.

Physical properties

M. Pt. 294.5-298°C
Solubility Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 150 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 100 mg kg^{-1} (2).
TD_{Lo} intravenous child 15 mg kg^{-1} (3,4).

Sub-acute and sub-chronic data
Oral rat (90 day) 0.2, 0.1, 0.05, 0.025, 0.012 or 0% in diet caused inhibition of body weight gain at high-dose levels with an increase in circulating alkaline phosphatase activity, triglycerides and total proteins (5).

Carcinogenicity and chronic effects
Limited evidence for carcinogenicity to humans and animals, IARC classification group 2B (6).
The National Toxicology Program tested rats and mice via feed. No evidence of carcinogenicity in ♀ rats and ♂ mice, equivocal evidence in ♂ rat and clear evidence of carcinogenicity in ♀ mice (7).
Intraperitoneal mouse (11 month) 0.6 mg kg^{-1} day^{-1}. No weight gain observed, but thymic and mesenteric lymphomas and leukaemias induced (8).
Oral rat (2 yr) 0, 0.025, 0.05% in diet showed no carcinogenic potential (9).
Oral mice (78 wk) 0.006, 0.012% in diet induced a non-significant number of hepatocellular tumours. No significant increase of any particular tumour type in other organs (10).

Teratogenicity and reproductive effects
Oral rat (7-18 day gestation) 200 mg kg^{-1}. Maternal serum concentrations 1 hr after dosing on day 18 were 16%. Pre-weaning mortality was 25%. Offspring showed increased early locomotor activity, exhibiting abnormal circling behaviour. These abnormal-circling rats accounted for higher levels of activity in an open-field test and for longer surviving times (11).
Oral mice (8-16 day gestation) 50, 75, 125 mg kg^{-1}. Reduced foetal weight and retarded long bone ossification demonstrated at highest dose, indicating 59-66 % weight variability predictable by bone measurements (12).
Oral rat (7-16 day gestation) 200 mg kg^{-1} caused reduced weight gain and survival of pups (13).

Metabolism and toxicokinetics
Intravenous administration in the rat led to accumulation in the liver, kidneys and salivary glands, with the liver the principal site of metabolism (14).
Metabolites identified include: 5-(3,4-dihydroxy-1,5-cyclohexadienyl-1-yl)-5-phenylhydantoin and glucoronide conjugates of 5-(3,4-dihydroxyphenyl)-5-phenylhydantoin and 5-(4-hydroxy-3-methoxyphenyl)-5-phenylhydantoin (15-18).
Diphenylhydantoin *p*-hydroxylation was determined in 24 patients with Parkinson's disease. Different function of the cytochrome P_{450} subsystem was found in 6 patients, but not in controls (19).

Genotoxicity

Salmonella typhimurium TA100, TA1535, TA1537, TA98 with and without metabolic activation negative (20).
In vitro human peripheral leukocytes 50-100 μg ml^{-1} induced chromosome abnormalities (21).
In vitro human lymphocyte cells induced chromosomal aberrations (22).
Micronucleus test *in vivo* mice bone marrow cells dose-dependent increase in micronucleated polychromatic erythrocytes (23).
Induced sperm abnormalities and micronuclei but not dominant lethal mutations in mice *in vivo* or chromosomal aberrations in rat bone marrow cells or cultured human lymphocytes (20).
Enhanced virus-induced transformation of Syrian hamster embryo cells and weakly inhibited intercellular communication in Chinese hamster V79 cells (20).

Sister chromatid exchanges positive following intraperitoneal mice dosed with 1, 10, 20 mg kg^{-1} (24).
In vivo mice bone marrow cells dose-dependent increase in chromosome aberrations, structural anomalies and mitotic index frequencies (25).

Other effects

Other adverse effects (human)

6% of births to 98 epileptic mothers taking diphenylhydantoin during first 4 months of pregnancy had malformations, including cleft lip and cleft palate (26).
Numerous case reports have described lymphomas and leukaemias occurring in patients treated with diphenylhydantoin (8).
A review of 516 cases of malignant lymphomas revealed 8 patients who had prolonged treatment with diphenylhydantoin. The authors conclude the excess risk of malignant lymphoma to be 2- to 3-fold (27).

Any other adverse effects

IC_{50} 2.52 mg l^{-1} reported for effect of diphenylhydantoin on aldose reductase from human, rat and bovine lens (28).
In vitro dog hepatocytes (2, 24 hr) 230-920 mg l^{-1} increased alkaline phosphatase activity (29).

Other comments

Teratogenic effects reviewed (30).
Human health effects and experimental toxicology reviewed (31,32).
The metabolism and pharmacokinetics reviewed (33).
Possible mechanisms of embryotoxicity reviewed (34).

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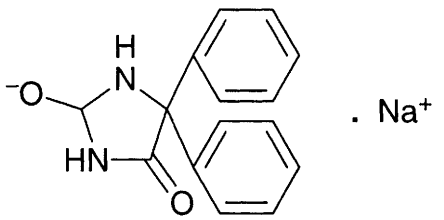
P142 phenytoin sodium



$C_{15}H_{11}N_2NaO_2$ **Mol. Wt.** 274.25 **CAS Registry No.** 630-93-3

Synonyms diphenylhydantoin sodium; sodium 5,5-diphenylhydantoinate; soluble phenytoin; sodium phenytoin; 5,5-diphenylhydantoin sodium; sodium 5,5-diphenyl-2,4-imidazolidinedione; Diphenin; Hydantoin

EINECS No. 211-148-2 **RTECS No.** MU 1400000

Uses Anticonvulsant. Anti-epileptic drug.

Physical properties

M. Pt. 292-299°C
Solubility Water: soluble at pH >11.7. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral mice 165 mg kg^{-1} (1).
LD_{50} intravenous rabbit 125 mg kg^{-1} (2).
Intraperitoneal rat 20 mg kg^{-1} increased motor activity and decreased rigidity (3).

Carcinogenicity and chronic effects
Limited evidence for carcinogenicity to humans and animals, IARC classification group 2B (4).
Oral mice (168 day) 60 mg kg^{-1} day^{-1} in liquid diet induced thymic lymphomas (5).

Teratogenicity and reproductive effects
Subcutaneous mice (7-15 day gestation) 12.5, 25 or 50 mg kg^{-1} produced 15-43% cleft palates at the highest dose (6,7).
Oral ♀ mice (15 day gestation) 0.48 mg kg^{-1} 3 × wk^{-1} for 2 months induced teratogenesis in 41% of foetuses but had no effect on bone marrow cells. 50, 100 mg kg^{-1} on days 11, 12, 13 of pregnancy induced teratogenesis and increased frequency of aneuploid metaphases in bone marrow cells (8).

Metabolism and toxicokinetics
Metabolised in liver by hydroxylation and excreted in bile and urine (9,10).
Metabolites identified include: 5-(3,4-dihydroxy-1,5-cyclohexadienyl-1-yl)-5- phenylhydantoin and glucuronide conjugates of 5-(3,4-dihydroxyphenyl)-5-phenylhydantoin and 5-(4-hydroxy-3-methoxyphenyl)-5- phenylhydantoin (10-13).

Genotoxicity

Salmonella typhimurium TA100, TA1535, TA1537, TA98 with and without metabolic activation negative (14).
Induced sperm abnormalities and micronuclei but not dominant lethal mutations in mice *in vivo* or chromosomal aberrations in rat bone marrow cells or cultured human lymphocytes. Enhanced virus-induced transformation of Syrian hamster embryo cells and a weak inhibitor of intercellular communication in Chinese hamster V79 cells (14).
Intraperitoneal mice 115, 145 mg kg^{-1} dominant lethal test negative (15).

Other effects

Other adverse effects (human)

Side effects include nausea, vomiting, constipation, ataxia, slurred speech, mental confusion together with headache, dizziness and insomnia. Skin rashes, especially in children, are common (16).

Any other adverse effects

Antiarrhythmic activity maintained in ouabain-induced dogs (17).

Other comments

Hypersensitivity in 38 patients undergoing therapy with diphenylhydantoin reviewed (18).
Adverse effects of phenytoin sodium reviewed (16).

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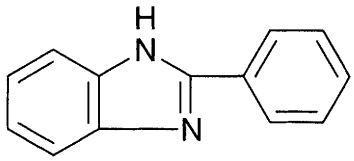
P143 phenzidole



$C_{13}H_{10}N_2$ **Mol. Wt.** 194.24 **CAS Registry No.** 716-79-0

Synonyms 2-phenyl-1*H*-benzimidazole; G 570; phenzidol; Gainex

EINECS No. 211-939-2 **RTECS No.** DE 0360000

Uses Anthelmintic

Physical properties

M. Pt. 291-299°C

Solubility Organic solvents: benzene, chloroform, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 167 mg kg^{-1} (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

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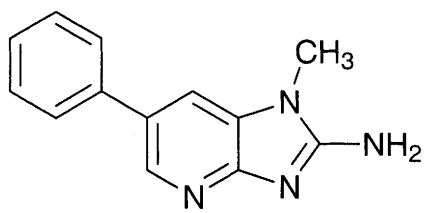
P144 PhIP



$C_{13}H_{12}N_4$ **Mol. Wt.** 224.27 **CAS Registry No.** 105650-23-5

Synonyms 2-amino-1-methyl-6-phenylimidazole[4,5-*b*]pyridine; 1-methyl-6-phenyl-1*H*-imidazo[4,5-*b*]pyridin-2-amine

Uses Not used commercially.

Physical properties

M. Pt. 327-328°C
Solubility Organic solvents: dimethyl sulfoxide, methanol

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Administration of total doses of 50 and 150 mg kg^{-1} orally over 5 days to B6C3F1 mice caused a dose-dependent suppression of the humoral immune response of spleen cells to sheep red blood cells (1).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).
Oral rats (52 wk) 400 mg kg^{-1} in diet. Colon adenocarcinomas were found in 16/29 treated ♂s and 2/30 treated ♀s. Mammary adenocarcinomas were found in 14/30 treated ♀s. No adenocarcinomas were observed in 40♂ and 40♀ controls (3).
Oral F344 rats (6-wk-old) administered 0, 25, 100 or 400 ppm in diet for up to 104 wk. (Rats administered 400 ppm were killed at 52 wk owing to marked retardation in body weight gain.) Clear evidence of dose-dependent carcinogenicity to colon in ♂s and mammary glands in ♀s. The virtually safe dose was calculated to be 0.023-0.52 ppm in diet (4).
Oral ♂ F344 rats (52 wk) 400 ppm in diet. Prostate carcinomas occurred in 18/27 treated animals and 0/37 controls. Atypical hyperplasias were seen in the prostate and the seminal vesicles (5).
Oral mice 400 ppm in diet 579 days. The incidence of lymphomas was higher in treated animals than in controls. Lung tumours were observed in two controls and nine treated mice (6).
Oral mice 300 ppm in diet for 28 wk followed by standard diet for 78 wk. Results showed that although PhIP is a potent lymphomagen, it caused very few and sporadic tumours in other tissues (7).
Intraperitoneal neonatal ♂ mice, PhIP administered at 2 dose levels (5-10,000-fold less than used in standard chronic bioassays) on days 1, 8, and 15 after birth. Mice were examined at 8 and 12 months after treatment and the incidence of hepatic adenomas was found to be significantly higher than for DMSO-treated controls (8).

Metabolism and toxicokinetics
C57BL/6 mice administered a single dose of 100 mg kg^{-1} via gavage or intraperitoneal injection excreted 39% of the dose of the 24-hr urine and 12% in the 24 hr-faeces when dosed via the intrapertioneal route and 31% in the 24-hr urine and 30% in the 24-hr faeces when dosed via gavage (9).
Two-generation exposure (transplacental and trans-breast milk) experiments on Sprague-Dawley rats showed that PhIP was excreted into milk and transferred to foetuses and neonates where PhIP-DNA adduct formation occurred. An increased risk of the development of mammary adenocarcinoma also occurred (10).
Rats administered [^{3}H]PhIP-dG or [^{3}H]PhIP-DNA intraperitoneally excreted 15-20% of the dose in the urine and 80-85% in the faeces. Urinary excretion was maximum to 24 hr (90%) with a rapid decline, 10% to 48 hr and 0% to 72 hr. Faecal excretion was maximum to 24 hr (60%) with a slower decline, 30% to 48 hr and 10% to 72 hr. PhIP was excreted mainly unmetabolised. PhIP-DNA was mainly excreted as nucleoside adducts (11).
Urine samples (24 hr) of 10 subjects on a normal diet contained 0.12-1.97 mg PhIP; no PhIP could be detected in 24 hr urine samples of 3 patients who were receiving parenteral alimentation (12).
Lactating ♀ rats, with suckling pups, were administered 50, 500 and 1000 ng of [^{14}C]PhIP kg^{-1}. PhIP, PhIP-4'-sulfate, 4'-hydroxy-PhIP, and *N*2-hydroxy-PhIP-glucuronide were found in the milk at all doses. PhIP was also found in the blood and mammary tissue of dams and the liver tissues of pups (13).

Genotoxicity

Salmonella typhimurium TA98 and TA100 with metabolic activation positive, 1800 revertants μg^{-1} (14).
Mutagenicity in Chinese hamster V79 cells (using 6-thioguanine resistance as the marker of mutagenicity) with metabolic activation positive (15).
Cooking fumes generated by frying strips of bacon and hamburgers were mutagenic in a microsuspension Ames *Salmonella* test (TA98 with metabolic activation). PhIP was the most abundant heterocyclic amine (HCA) present

in both cooked meats. The total amounts of HCAs in the smoke condensates were 3 ng g^{-1} from fried bacon and 0.37 ng g^{-1} from fried beef (16).
In vitro human mammary epithelial cells were treated with 500 μM PhIP or *N*-hydroxy-PhIP. Mean DNA adducts per 108 nucleotides were 0.96 and 176 for PhIP and *N*-hydroxy-PhIP, respectively, confirming that *N*-hydroxylation by cytochrome P450 is needed for metabolic activation of PhIP (17).

Other effects

Any other adverse effects

PhIP fed in the diet to F344 rats caused *in vivo* DNA adduct formation in the liver and pancreas. The level of DNA adducts found in the pancreas was high – 36 × higher than that in the liver – but no pancreatic lesions were observed. The N^2-(deoxyguanin-8-yl)-derivative as the major adduct formed, comprising > 90% of the DNA adducts detected. PhIP also cause dose-dependent DNA modification *in vitro* in primary rat hepatocytes that was correlated with the cytotoxicity in these cells (18).
Shown by the Dlb-1 assay to be a potent intestinal mutagen in the mouse when administered either intraperitoneally or orally (19).

Other comments

Carcinogenic heterocyclic amine found in cooked foods.
Black and green tea extracts inhibit PhIP mutagenicity in *Salmonella typhimurium* TA98 assay with metabolic activation (20).
Isolated from a complete human diet cooked simulating household conditions (21).
Carcinogenic heterocyclic amines reviewed (14).

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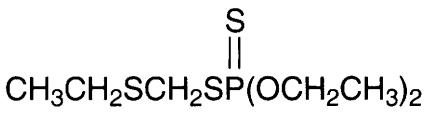
P145 phorate



$C_7H_{17}O_2PS_3$ **Mol. Wt.** 260.38 **CAS Registry No.** 298-02-2

Synonyms *O,O*-diethyl *S*-[(ethylthio)methyl]phosphorodithioate; phosphorodithioic acid, *O,O*-diethyl *S*-[(ethylthio)methyl] ester; Granutox; Thimet; Agrimet; Chim; Darlem; Forate

EINECS No. 206-052-2 **RTECS No.** TD 9450000

Uses Insecticide. Acaricide. Nematocide.

Physical properties

M. Pt. –15°C (technical grade) **B. Pt.** 118-120°C at 0.8 mmHg **Specific gravity** 1.167 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.92 (1) **Volatility** v.p. 8.4×10^{-4} mmHg at 20°C
Solubility Water: 50 mg l^{-1}. Organic solvents: miscible in carbon tetrachloride, dibutyl phthalate, 1,4-dioxane, methyl cellosolve, vegetable oils, xylene

Occupational exposure

FR-VME 0.05 mg m^{-3}
UK-LTEL 0.05 mg m^{-3} **UK-STEL** 0.2 mg m^{-3}
US-TWA 0.05 mg m^{-3} **US-STEL** 0.2 mg m^{-3}
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)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 0.013 mg l^{-1} (1).
LC_{50} (96 hr) channel catfish 0.28 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) >50 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) >50 mg l^{-1} (2).
Growth of the protozoan *Tetrahymena pyriformis* was retarded at concentrations of 1-20 ppm. At 50 ppm the organism lysed in 6 hr (3).
LC_{50} (96 hr) *Gammarus fasciatus* 0.6 μg l^{-1} (4).
LC_{50} (96 hr) *Orconectes nais* 50 μg l^{-1} (4).
LD_{50} topical bee 10 μg^{-1} (5).

Environmental fate

Nitrification inhibition
Some evidence of effect on growth rate and nitrogen fixation on *Westiellopsis prolifica* and *Scytonema schmidlei* (6).

Degradation studies
Can be effectively removed from wastewater by PACT (bench-scale powdered carbon activated sludge treatment) (7).

Metabolised by *Pseudomonas* in soil, the major metabolite was phorate sulfoxide. Concentrations of 100 ppm completely degraded in various soils in 25-40 days (8).
$t_{1/2}$ in soils 2-14 day (1).

Abiotic removal
$t_{1/2}$ for photolytic degradation under daylight ~1 day (9).
$t_{1/2}$ for hydrolysis 3.2 at pH 7, 3.9 day at pH 9 (9).

Adsorption and retention
Soil K_{oc} 543 (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, starling, mallard duck, pheasant 0.6-7.5 mg kg^{-1} (9,10).
LD_{50} oral mallard duck 0.62 mg kg^{-1} (1).
LD_{50} oral common grackle 1.33 mg kg^{-1} (11).
LD_{50} oral rat, mouse 1.1, 6.6 mg kg^{-1}, respectively (12,13).
LC_{50} (1 hr) inhalation rat 11 mg m^{-3} (14).
LD_{50} dermal rat 2.5-6.2 mg kg^{-1} (12).
LD_{50} dermal rabbit 99 mg kg^{-1} (15).
LD_{50} intravenous rat 1.2 mg kg^{-1} (16).

Sub-acute and sub-chronic data
Rats receiving 6 mg kg^{-1} in diet for 90 days showed no adverse effects other than reduced level of cholinesterase activity (9).
LC_{50} (8 day) oral Japanese, bobwhite quail, ring-necked pheasant, mallard duck 200-440 mg kg^{-1} diet (17).
Inhalation mouse (12 weeks) 6728.5 mg m^{-3}. A significant increase in aspartate aminotransferase and alanine aminotransferase activities was observed throughout. Alkaline phosphatase activity showed an increase in the fourth week. The increased activity of these three enzymes suggested hepatocellular necroinflammatory disease. Increases in bilirubin levels (direct and indirect) suggested both prehepatic and hepatocellular hyperbilirubinaemia. Liver lesions were present throughout (18).

Metabolism and toxicokinetics
Undergoes sulfoxidation in mouse liver, lung and kidney microsomes *in vitro*. Phorate sulfone and phorate oxon sulfoxide were also yielded in liver microsomes, and phorate oxon and phorate oxon sulfoxide in lung microsomes but not in kidney microsomes (19).

Sensitisation
Did not cause a significant reaction in skin patch tests in humans (20).

Other effects

Any other adverse effects
Oral buffalo calves, single dose of 1 mg kg^{-1} induced moderate cholinergic symptoms. Erythrocyte and serum cholinesterase and carboxylesterase activity were inhibited. The serum levels of transferases and phosphatases increased significantly. A marked hyperglycaemia and increased total plasma protein were also induced (21).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (22).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (24).
WHO Toxicity Class Ia (25).
EPA Toxicity Class 1 (5).
ADI (JMPR) 0.0005 mg kg^{-1} body weight (5).

Other comments

Environmental pollutant and food contaminant.

Application of phorate to soil at 1 kg ha^{-1} stimulated the population growth of bacteria, actinomycetes, fungi and *Azotobacter* in calcareous soils (26).

The compound is an inhibitor of acetylcholinesterase (true) and cholinesterase (pseudo) and affects the central, autonomic and voluntary nervous systems (12).

In plants phorate is oxidised to the sulfoxide and sulfone and other phosphorothioate analogues, followed by hydrolysis to dithio-, thio- and orthophosphoric acids (1).

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24. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/321/EEC* 1991, HMSO, London, UK.
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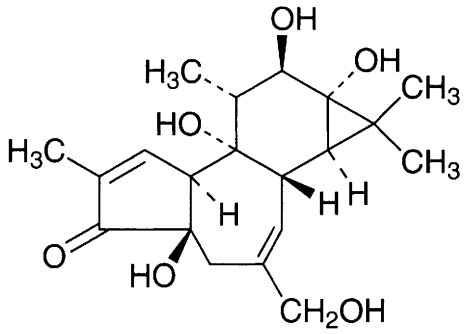
P146 phorbol



$C_{20}H_{28}O_6$ **Mol. Wt.** 364.44 **CAS Registry No.** 17673-25-5

Synonyms 4β-phorbol

RTECS No. GZ 0600000

Occurrence Parent alcohol in croton oil, expressed from *Croton tiglium*

Physical properties

M. Pt. 162-163°C and 233-234°C (2 forms) **B. Pt.** 250-251°C (decomp.)

Mammalian & avian toxicity

Carcinogenicity and chronic effects

♀ SWR mice were injected intraperitoneally with 0.2 mg for 20-30 wk with or without prior dermal treatment with 0.25 mg 7,12-dimethylbenz[*a*]anthracene. No skin tumour promotion effect was seen but both groups showed a high incidence of leukaemias compared with controls (1).

Teratogenicity and reproductive effects

C3H/He lactating ♀ mice received 400 and 100 μg subcutaneous injections 2 × day^{-1} on days 12 and 13 of lactation and 1 × day^{-1} on day 14. Reduced litter growth, decreased anterior pituitary weights and increased DNA and RNA synthesis were seen on *in vitro* analysis of the mammary gland at 400 μg but not at 100 μg (2).

Irritancy

Dermal mouse 36 mg caused mild irritation (3).

References

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P147 phorone

$$(CH_3)_2C{=}CHC(O)CH{=}C(CH_3)_2$$

$C_9H_{14}O$ **Mol. Wt.** 138.21 **CAS Registry No.** 504-20-1

Synonyms 2,6-dimethyl-2,5-heptadien-4-one; diisobutenyl ketone; diisopropylidene acetone; *sym*-diisopropylidene acetone; Foron

EINECS No. 207-986-3 **RTECS No.** MI 5500000

Physical properties

M. Pt. 28°C **B. Pt.** 198-199°C **Flash point** 85°C (open cup) **Specific gravity** 0.885 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.26 (1) **Volatility** v.p. 1 mmHg at 42°C
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 60 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{Lo} subcutaneous rabbit 700 mg kg^{-1} (3).

References

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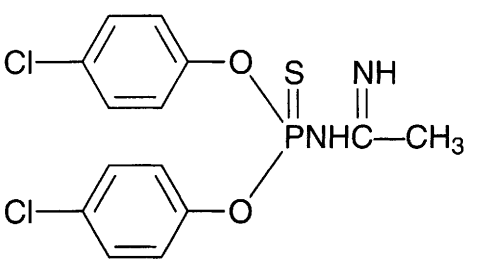
P148 phosacetim



$C_{14}H_{13}Cl_2N_2O_2PS$ **Mol. Wt.** 375.21 **CAS Registry No.** 4104-14-7

Synonyms (1-iminoethyl)-phosphoramidothioic acid, *O,O*-bis(4-chlorophenyl)ester; acetimidoylphosphoramidothioic acid, *O,O*-bis(*p*-chlorophenyl)ester; BAY 38819; Bayer 38819; DRC 714; Gophacide

EINECS No. 223-874-7 **RTECS No.** TB 4725000

Uses Superseded rodenticide.

Physical properties

M. Pt. 104-106°C
Solubility Organic solvents: benzene, diethyl ether, ethanol, methylene chloride

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, 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)

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, starling 4.22-4.46, 17.8 mg kg^{-1}, respectively (1).
LD_{50} oral rat 37 mg kg^{-1} (2).
LD_{50} oral mouse, guinea pig, dog, 12, 20, 23 mg kg^{-1}, respectively (3-5).
LD_{50} dermal rat 25 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse 3.5, 5.5 mg kg^{-1}, respectively (4).
LD_{50} intraperitoneal guinea pig 14 mg kg^{-1} (4).

Sub-acute and sub-chronic data
In three-day feeding trials, 74.1 mg kg^{-1} day^{-1} killed 50% of deer mouse population (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
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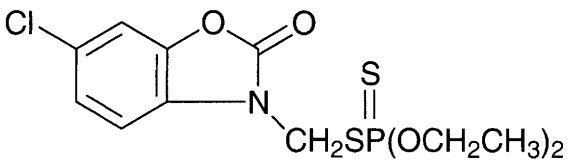
P149 phosalone



$C_{12}H_{15}ClNO_4PS_2$ **Mol. Wt.** 367.81 **CAS Registry No.** 2310-17-0

Synonyms phosphorodithioic acid, *S*-[(6-chloro-2-oxo-3(2*H*)-benzoxazolyl)methyl]*O*,*O*-diethyl ester; phosphorodithioic acid, *O*,*O*-diethyl ester, *S*-ester with 6-chloro-3-(mercaptomethyl)-2-benzoxazolinone; benzofos; benzophosphate; Agria 1060; Rubitox; Zolone

EINECS No. 218-996-2 **RTECS No.** TD 5175000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 45-48°C **Partition coefficient** log P_{ow} 4.01 at 20°C (1) **Volatility** v.p. $<5.18 \times 10^{-7}$ mmHg at 25°C
Solubility Water: 3.5 mg l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, benzene, chloroform, dichloromethane, 1,4-dioxane, ethyl acetate, methyl ethyl ketone, toluene, xylene

Occupational exposure

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} bluegill sunfish, rainbow trout, 0.11 and 0.30-0.63 mg l^{-1}, respectively (1).
LC_{50} *Saccobranchus fossilis* 0.083 mg l^{-1} at 18°C (2).

Environmental fate

Degradation studies
Soil $t_{1/2}$ 7 days. Degraded in plants to chlorobenzoxazolone, formaldehyde and diethyl phosphorodithioate in ~14 hr (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken 661 mg kg^{-1} (3).
LD_{50} oral pheasant, mallard duck 290, >2150 mg kg^{-1}, respectively (1).
LD_{50} oral mouse, rat, guinea pig 73, 85, 150 mg kg^{-1}, respectively (4,5,6).
LD_{50} dermal rat, rabbit 390, 1000 mg kg^{-1}, respectively (7,8).

Sub-acute and sub-chronic data
♂ Wistar rats received 12.7 mg kg^{-1} day^{-1} for 1, 3, 7, 15, 30, 60 days. A duration-dependent increase in red blood cells, haemoglobin concentration and white blood cells and decrease in whole body and kidney oxygen consumption was seen (9).

Carcinogenicity and chronic effects

In 2-year feeding trials, rats receiving 250 mg kg^{-1} diet and dogs receiving 290 mg kg^{-1} diet suffered no ill-effects (1).

Metabolism and toxicokinetics

Oxidised in mammals to phosphorothioate which is rapidly hydrolysed to water-soluble metabolites (1).

Legislation

WHO Toxicity Class II (10).

ADI 0.001 mg kg^{-1} body weight (11).

EC maximum residue levels: citrus fruit, strawberries 1 ppm; stone fruit, peaches 2 ppm; root vegetables, olives 0.1 ppm; other fruit and vegetables 1 ppm (1).

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).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (14).

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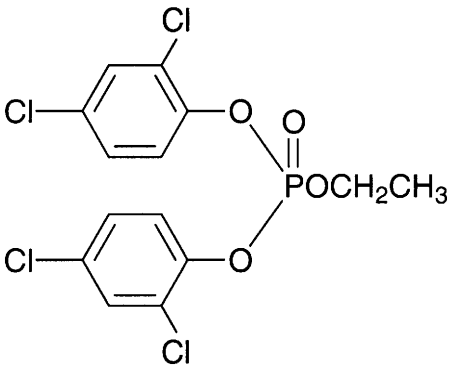
P150 phosdiphen



$C_{14}H_{11}Cl_4O_4P$ **Mol. Wt.** 416.02 **CAS Registry No.** 36519-00-3

Synonyms phosphoric acid, bis(2,4-dichlorophenyl)ethyl ester; EDP; MTO-460

RTECS No. TB 7500000

Uses Superseded fungicide.

Physical properties

B. Pt. 175°C at 0.2 mmHg **Specific gravity** 1.405 at 25°C **Volatility** v.p. 4.95×10^{-4} mmHg at 20°C
Solubility Water: 0.7 mg l^{-1} at 20°C. Organic solvents: acetone, hexane, xylene

Occupational exposure

UN No. 3018

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 1.7 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, ♂ rat 5300, 6200 mg kg^{-1}, respectively (1).
LD_{50} dermal rat, mouse, >5000 and 9000-9600 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials, no-effect level for rats and mice 30 mg kg^{-1} diet. No reproductive, teratogenic or mutagenic effects observed in rats (1).

Legislation

WHO Toxicity Class Table 5 (2).
EPA Toxicity Class III (3).
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

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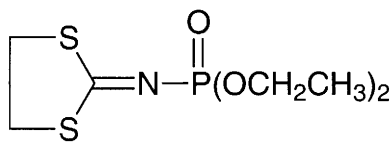
P151 phosfolan



$C_7H_{14}NO_3PS_2$ **Mol. Wt.** 255.30 **CAS Registry No.** 947-02-4

Synonyms 1,3-dithiolan-2-ylidene-phosphoramidic acid, diethyl ester; imidocarbonic acid, phosphonodithio-, cyclic ethylene *P,P*-diethyl ester; American Cyanamid 47031; Cyolane; EI 47031; ENT 25830; phospholan

EINECS No. 213-423-2 **RTECS No.** NJ 6475000

Uses Superseded insecticide.

Physical properties

M. Pt. 36.5°C **B. Pt.** 115-118°C at 0.001 mmHg

Solubility Water: 650 g l^{-1}. Organic solvents: acetone, benzene, cyclohexane, ethanol, 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) – 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)

Environmental fate

Degradation studies

Loamy sand soil $t_{1/2}$ 3.5 day (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral pigeon, quail 2.4, 24 mg kg^{-1}, respectively (2).

LD_{50} oral redwing blackbird, starling 2.37, 5.62 mg kg^{-1}, respectively (3).

LD_{50} oral rat, mouse 9, 12 mg kg^{-1}, respectively (4,5).

LD_{50} dermal guinea pig 54 mg kg^{-1} (6).

Sub-acute and sub-chronic data

In 90-day feeding trials no clinical symptoms were seen in dogs receiving 1 mg kg^{-1} day^{-1} (6).

Metabolism and toxicokinetics
Oral rat 2 mg kg^{-1} [^{14}C]phosfolan, 58% of radioactivity was excreted in 192 hr, 32.2% in urine, 15.5% in faeces and 3.1% recovered from cage washings (7).
Oral rat 1 mg kg^{-1} [^{14}C]phosfolan, 98% of radioactivity was recovered: 20% as respired gases; 48% in excreta; 1% in cage wash; 29% in carcass. Major metabolite was thiocyanate ion (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).

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P152 phosgene

$$C(O)Cl_2$$

CCl_2O **Mol. Wt.** 98.92 **CAS Registry No.** 75-44-5

Synonyms carbonic dichloride; carbon dichloride oxide; carbon oxychloride; carbonyl chloride; carbonyl dichloride; chloroformyl chloride; phosgen

EINECS No. 200-870-3 **RTECS No.** SY 5600000

Uses For the preparation of many organic chemicals. As a war gas. Cross-linking agent. Used in methyl isocyanate production.
Occurrence Photodecomposition product of chlorinated organics in air.

Physical properties

M. Pt. −118°C **B. Pt.** 8.2°C **Specific gravity** 1.432 at 0°C with respect to water at 4°C
Volatility v.p. 1.2×10^{-3} mmHg at 20°C ; v.den. 3.4
Solubility Water: slightly soluble. Organic solvents: benzene, glacial acetic acid, toluene, most liquid hydrocarbons

Occupational exposure

DE-MAK 0.02 ppm (0.082 mg m^{-3})
FR-VLE 0.1 ppm (0.4 mg m^{-3})
JP-OEL 0.1 ppm (0.4 mg m^{-3})
SE-CEIL 0.05 ppm (0.2 mg m^{-3})
UK-LTEL 0.02 ppm (0.08 mg m^{-3}) **UK-STEL** 0.06 ppm (0.25 mg m^{-3})
US-TWA 0.1 ppm (0.40 mg m^{-3})

UN No. 1076 **HAZCHEM Code** 2XE **Conveyance classification** toxic gas, corrosive
Supply classification very toxic
Risk phrases Very toxic by inhalation – Causes burns (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 – 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)

Mammalian & avian toxicity

Acute data
LC_{Lo} inhalation man (duration unspecified) 3200 mg m^{-3} (1).
LC_{Lo} (30 min) inhalation man 360 mg m^{-3} (2).
LC_{Lo} (15 min) inhalation cat 190 mg m^{-3} (2).
LC_{50} (20 min) inhalation rat 25 ppm (3).

Sub-acute and sub-chronic data
♂ Fischer 344 rats (60-days-old) were exposed either to clean air or phosgene (0.1-1.0 ppm) 6 hr day^{-1} 1-5 days wk^{-1}. A group of rats was allowed clean air recovery for 4 wk after 12 wk of phosgene exposure. The exposure scenario was designed to provide equal concentration × time (C×T) product for all concentrations at one particular time point except for 0.1 ppm (50% C×T). Phosgene exposure for 4 or 12 wk increased lung to body weight ratio and lung displacement volume in a concentration-dependent manner. Terminal bronchiolar and lung volume displacement changes occurred at very low phosgene concentrations (0.1 ppm). Phosgene concentration rather than C×T product appeared to drive toxic responses (4).
Inhalation rat (6 hr day^{-1} 5 days $week^{-1}$ or days 1 and 5 $week^{-1}$ for 4 or 12 weeks) 0.1 and 0.2 ppm or 0.5 ppm, respectively. After the final exposure the rats were infected, via aerosol, with *Streptococcus zooepidemicus*. All levels of exposure impaired bacterial clearance from the lungs and increased the formation of polymorphonuclear leukocytes (5).

Metabolism and toxicokinetics
In rabbits, which have a complex nasal structure, absorption occurs in the nasal passages but comparatively little reaches the lung compared with man. In man where the nasal structure is less complex, phosgene can reach deeper regions of the lung (6).
At doses of 200 ppm in man, phosgene passes through the blood-air barrier, reaches lung capillaries and reacts with blood constituents (7).

Irritancy
Vapours strongly irritating to human eyes (8).

Other effects

Other adverse effects (human)
Symptoms of poisoning include cough, burning of the eyes and throat, dyspnoea, cyanosis, pulmonary congestion and pulmonary oedema. Death may occur from anoxia. Intravascular haemolysis, thrombus formation, and immediate death can result from massive exposure (9).

Any other adverse effects
Rats exposed to 5 ppm for 10 minutes showed pulmonary oedema after 48 hr with widening of pulmonary interstices at a lowest dose rate of 25 ppm min^{-1} (10).
Pathological changes in rat lungs were seen 96 hr after exposure to 0.5 ppm for 2 hr. Some abnormalities were seen in rats exposed to 2 ppm for 80 min after 3 months (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (11).

Other comments

Maximum allowable concentration will turn paper soaked in an alcoholic or carbon tetrachloride solution containing equal parts of *p*-dimethylaminobenzaldehyde and colourless diphenylamine, then dried, from yellow to deep orange (12).

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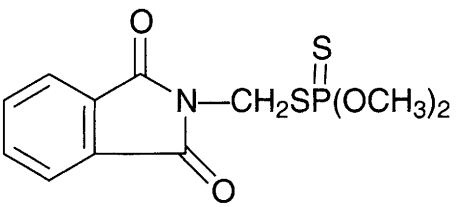
P153 phosmet



$C_{11}H_{12}NO_4PS_2$ **Mol. Wt.** 317.33 **CAS Registry No.** 732-11-6

Synonyms *S*-[(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl] *O*,*O*-dimethyl phosphorodithioate; phosphorodithioic acid, *O*,*O*-dimethyl ester, *S*-ester with *N*-(mercaptomethyl)phthalimide; *O*,*O*-dimethyl *S*-phthalimidomethyl phosphorodithioate; phosphorodiethioic acid, *S*-[(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)methyl] *O*,*O*-dimethyl; Decemthion; Phtalophos; Imidan; Imidathion; PMP; Prolate; Safidon; Simidan

EINECS No. 211-987-4 **RTECS No.** TE 2275000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 72-72.7°C **Flash point** > 106°C **Partition coefficient** log P_{ow} 2.83 (1)
Volatility v.p. 0.001 mmHg at 50°C
Solubility Water: 25 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, methyl isobutyl ketone, toluene, 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) – Do not breathe dust – Wear suitable protective clothing and gloves (S2, S22, S36/37)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) chinook salmon, bluegill sunfish, small mouth bass, rainbow trout 70-560 μg l^{-1} static bioassay (2).
LC_{50} (96 hr) fathead minnow, channel catfish 7.3-11 mg l^{-1} static bioassay (2).

Invertebrate toxicity

LC_{50} (24, 48 hr) *Daphnia magna* 2.75, 0.84 mg l^{-1}, respectively (3).
LC_{50} (48 hr) *Gammarus pseudolimnaeus* 2.4 μg l^{-1} (2).
LC_{50} contact bee 0.001 mg bee^{-1} (3).

Bioaccumulation

Bioconcentration factor for fathead minnow, channel catfish, bluegill sunfish and damselfly 2-11 (2).

Environmental fate

Abiotic removal

$t_{1/2}$ on exposure of aqueous solution on glass plates to sunlight 2.5-3.0 hr (3).
$t_{1/2}$ for hydrolysis at 20°C 13 days at pH 4.5; <12 hr at pH 7.0; <4 hr at pH 8.3 (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 17.8, >100 mg kg^{-1}, respectively (4).
LD_{50} oral Japanese quail, ringnecked pheasant, mallard duck 2000-4500 mg kg^{-1} diet (5).
LD_{50} oral rat, mouse 26, 160 mg kg^{-1}, respectively (6,7).
LC_{50} (4 hr) inhalation rat 54 mg m^{-3} (8).
LD_{50} dermal rat 1330 mg kg^{-1} (8).

Carcinogenicity and chronic effects

Oral dog (2 yr) 20, 40, 400 mg kg^{-1} diet resulted in decreased red cell count and plasma cholinesterase activity and lachrymation (9).
In 2-yr feeding trials, the no-effect level for rats was 40 mg kg^{-1} (10).

Teratogenicity and reproductive effects

Oral rat, 30 mg kg^{-1} on day 9 of gestation and 1.5 mg kg^{-1} throughout the period of pregnancy increased post-implantation mortality. The single dose of 30 mg kg^{-1} caused developmental abnormalities including hypognathia and hydrocephaly (11).

Metabolism and toxicokinetics

In mammals rapidly metabolised to phthalamic acid, phthalic acid and phthalic acid derivatives which are eliminated in the urine (12).

Irritancy

100 mg instilled into rabbit eye caused irritation that persisted for more than 21 days after treatment (13).

Other effects

Any other adverse effects

Cholinesterase activity inhibitor (3).
Intragastric rat, single dose of 145 mg kg^{-1} caused an increase in liver concentrations of glycogen and proteins and blood triglycerides and a decrease in blood sugar concentration and liver triglycerides and cholesterol concentrations. These effects were moderated by oral administration of 200 mg kg^{-1} silymarin (14).
Intragastric mouse single dose 1.1-5.6 mg kg^{-1} caused increased number of abnormal sperm (15).

Legislation

EEC maxiumum residue levels: kiwi fruit 10 ppm; pome fruit 2 ppm (10).
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 II (18).
EPA Toxicity Class II (formulation) (3).
ADI 0.01 mg kg^{-1} body weight (10).

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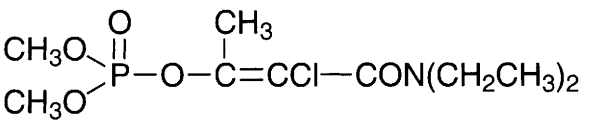
P154 phosphamidon



$C_{10}H_{19}ClNO_5P$ **Mol. Wt.** 299.69 **CAS Registry No.** 13171-21-6

Synonyms phosphoric acid, 2-chloro-3-(diethylamino)-1-methyl-3-oxo-1-propenyl dimethyl ester; phosphoric acid, dimethyl ester, ester with 2-chloro-*N*,*N*-diethyl-3-hydroxycrotonamide; phosphamidone; Dimecron; Merkon; Sundaram 1975

EINECS No. 236-116-5 **RTECS No.** TC 2800000

Uses Insecticide.

Physical properties

M. Pt. –45°C **B. Pt.** 162°C at 1.5 mmHg **Specific gravity** 1.213 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.79 **Volatility** v.p. 2.5×10^{-5} mmHg at 20°C
Solubility Water: miscible. Organic solvents: acetone, dichloromethane, toluene

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Toxic in contact with skin – Very toxic if swallowed – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24, R28, R40, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – 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, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) rainbow trout 5 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish, snakehead fish 4.5, 10.5 mg l^{-1}, respectively (2,3).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia pulex* 0.0088 mg l^{-1} (4).
LC_{50} (96 hr) *Gammarus lacustris* 2.8 μg l^{-1} (5).
LC_{50} (96 hr) *Pteronarcys californica* 150 μg l^{-1} (6).

Environmental fate

Degradation studies
In plants, the ethyl group is split off from the amide group and the ester bond between the side chain and the phosphorus atom is hydrolytically cleaved. Dechlorination also occurs, as does further degradation to smaller fragments. (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral duck 3.1 mg kg^{-1} (8).
LD_{50} oral mouse, rat, rabbit 6, 8, 70 mg kg^{-1}, respectively (9-11).
LC_{50} (4 hr) inhalation rat, guinea pig 135, 1300 mg m^{-3}, respectively (12,13).
LD_{50} dermal duck, rabbit, rat 26, 80, 125 mg kg^{-1}, respectively (10,14,15).
LD_{50} intraperitoneal mouse, rat 5800, 8700 μg kg^{-1}, respectively (16,17).

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice via feed. Designated equivocal carcinogen in ♂, ♀ rats and non-carcinogen in ♂, ♀ mice (17).

Metabolism and toxicokinetics
85-90% of oral dose (unspecified) excreted in mammals, almost entirely in the urine. Complete metabolism occurs by oxidative dealkylation of the amide group and hydrolysis of the phosphorus-ester bond (18).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (19).
Drosophila melanogaster wing spot test positive for single *mwh* spots, negative or weak for twin spots (20).

Other effects

Any other adverse effects

♂ Swiss mice, Wistar rats treated intraperitoneally with 1.4 mg kg^{-1} and 1.5 mg kg^{-1}, respectively, had stimulated autonomic parameters (diarrhoea, urination, piloerection, lachrymation, salivation and ear skin colour) and depressed behavioural parameters (spontaneous motor activity, exploratory behaviour and conditional avoidance response) peaking after 15 minutes (21).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (22).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).
WHO Toxicity Class Ia (24) EPA Toxicity Class I (formulation) (25).
ADI 0.0005 mg kg^{-1} body weight (25).

Other comments

The commerical compound contains 70% *m/m* (*Z*)-isomer (β-isomer), which has the greater insecticidal activity, and 30% *E*-isomer (α-isomer) (25).

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P155 phosphine

PH_3

H_3P **Mol. Wt.** 34.00 **CAS Registry No.** 7803-51-2

Synonyms hydrogen phosphide; phosphorus trihydride

EINECS No. 232-260-8 **RTECS No.** SY 7525000

Uses Fumigant. Doping agent for electronic components. Used in chemical synthesis.

Occurrence Occurs transiently at sites of anaerobic degradation of phosphorous-containing organic matter and in marsh gas.

Physical properties

M. Pt. –133.5°C **B. Pt.** –87.4°C **Volatility** v.den. 1.17

Solubility Water: 0.26 vol. at 20°C. Organic solvents: cyclohexanol, ethanol, ether, oil of turpentine

Occupational exposure

DE-MAK 0.1 ppm (0.14 mg m^{-3})

FR-VME 0.1 ppm (0.13 mg m^{-3}) **FR-VLE** 0.3 ppm (0.4 mg m^{-3})

SE-LEVL 0.3 ppm (0.4 mg m^{-3}) **SE-STEL** 1 ppm (1.4 mg m^{-3})

UK-STEL 0.3 ppm (0.42 mg m^{-3})

US-TWA 0.3 ppm (0.42 mg m^{-3}) **US-STEL** 1 ppm (1.4 mg m^{-3})

UN No. 2199 **Conveyance classification** toxic gas, danger of fire (flammable gas)

Supply classification very toxic

Ecotoxicity

Invertebrate toxicity

Toxicity of phosphine to one and two day old pupae of *Tribolium castaneum* was increased by atmospheric CO_2 concentrations up to 40% in air. A maximum pupal mortality of 11% was observed for CO_2 levels at 10-70% for 24 hr (1).

Toxicity to other species

LC_{50} (30 min) frog 0.56 mg l^{-1} (2).

Bioaccumulation

Oxidation to phosphate is likely in biological systems, with no suggestion of bioaccumulation or biomagnification (3).

Environmental fate

Degradation studies

Phosphine introduced in the headspace of tubes containing 3 types of soil at 0, 25, 50, 75 and 100% moisture saturation disappeared within 18 days in air dried soils, but took up to 40 days from moisture saturated soils. Phosphate recovery depended on soil acidity, soil matrix, moisture content and organic matter (4).

Abiotic removal

Oxidised to phosphoric acid by oxidising agents and atmospheric oxygen (5).

Mammalian & avian toxicity

Acute data

Inhalation CD rats (4 hr) 0-40 ppm. No phosphine-related neuropathological changes were seen (0-14 days post-exposure) (6).

LC_{Lo} inhalation human 1000 ppm (duration unspecified) (7).
Three turkeys exposed to 211 mg m^{-3} exhibited apathy, restlessness, dyspnoea, and tonic-clonic convulsions and died after 68, 74 and 80 min, respectively. Six hens exposed to 224 mg m^{-3} exhibited tonic-clonic convulsions and died after an average of 59 min. Both species showed organs congested with oxygenated blood on examination. Similar effects were seen in cats, rabbits, rats and guinea pigs treated with 35-564 mg m^{-3} and death was attributed to respiratory paralysis followed by cardiac arrest (8).
Rabbits exposed to 70 mg m^{-3} for 10 minutes showed no symptoms, but exposure to 140 mg m^{-3} was fatal in 2.5-3 hr and to 700 mg m^{-3} was fatal in 25-30 min (9).

Sub-acute and sub-chronic data
Albino rats fed fumigated diet for 12 wk showed slight increase in liver and kidney weights (concentration in diet unspecified) (10).
♂ and ♀ Wistar rats were fed food treated with phostoxin to give 1 mg kg^{-1} phosphine for 16 wk. No differences in behaviour, development, body weight, food consumption or blood and urine composition were seen compared with controls (11).
Inhalation CD rats (13 wk) 0-3 ppm 6 hr day^{-1} 5 days wk^{-1} followed by recovery for 2 wk. No phosphine-related changes were seen, suggesting that phosphine was not neurotoxic at these concentrations (6).

Carcinogenicity and chronic effects
♂ and ♀ Sprague-Dawley rats fed for 2 yr a diet with phosphine residue level of 5 mg kg^{-1} after fumigation, for 6 months, showed no differences in weight gain, food consumption, plasma chemistry, haematology, urinalysis, behaviour, growth, survival, organ weights, histopathology or tumour incidence compared with controls (12).

Metabolism and toxicokinetics
Readily absorbed through the lungs (species unspecified) (13).
In rats, expired in air or oxidised to hypophosphite and phosphite and excreted in urine (14,13).
Oxyhaemoglobin in mammals is converted into a verdichromogen-like material through Fe^{3+}-containing compounds (15).

Genotoxicity

Drosophila melanogaster 0.8 mg l^{-1} for 10, 30, 60 min caused sex-linked recessive lethal mutations (16).
Neurospora sitophila (concentration unspecified) induced forward mutation characterised by resistance to surfactants (17).
Fumigant applicators exposed to phosphine at above national standards had chromosome deletions and gaps during the application season and significantly increased stable chromosome rearrangements, primarily translocations in G-banded lymphocytes, 6 wk to 3 months after (18).

Other effects

Other adverse effects (human)
Twelve people developed nausea and one died when phosphine was emitted from a warehouse adjacent to their apartment house (19).
Metalworkers at a Norwegian shipyard exposed to phosphine at ~1 ppm reported symptoms of nausea, dizziness, chest tightness, dyspepsia and disturbance of smell and taste. The symptoms were no longer seen when local exhaust ventilation was installed (20).
Fumigant workers with a mean exposure to 11.1 yr reported cough, dyspnoea, chest tightness, headache, giddiness, numbness, lethargy, anorexia and epigastric pain (21).

Any other adverse effects
Cats, guinea pigs and rats were exposed to 5 ppm for 6-8 hr day^{-1}. Cats showed apathy, anorexia, unsteadiness, vomiting, agitation, dyspnoea, and apnoea before cardiac arrest after 35.5-45.5 hr. Guinea pigs and rats had similar effects and died after 24-32 hr and 27-36 hr, respectively. Postmortem examinations showed proteinuria, pulmonary oedema and congestion of other organs (8).
Produces neurological and hepatic symptoms, suggesting it reaches the nervous system and liver, (species unspecified) (22).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).

Other comments

Reviews on human health effects, experimental toxicology, environmental effects, exposure levels, ecotoxicology, workplace experience and epidemiology listed (24).

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P156 phosphoric acid

$$H_3PO_4$$

H_3O_4P **Mol. Wt.** 98.00 **CAS Registry No.** 7664-38-2

Synonyms orthophosphoric acid; Sonac; WC-Reiniger; EVITS

EINECS No. 231-633-2 **RTECS No.** TB 6300000

Uses In manufacture of superphosphates for fertilisers, phosphate salts, polyphosphates, detergents. Catalyst in ethylene manufacture, hydrogen peroxide purification. Flavour, acidulant, synergistic antioxidant and sequestrant in food. Pharmaceutic acid. In dental cements. Used in process engraving, metal rustproofing, latex coagulation, analytical reagent. Used in veterinary lead poisoning.

Physical properties

M. Pt. 42.35°C (crystals) **Specific gravity** 1.864 at 20°C **Volatility** v.p. 2.85×10^{-2} mmHg at 20°C
Solubility Water: miscible. Organic solvents: ethanol, soluble in 8 vols of a 3:1 ether:ethanol mixture.

Occupational exposure

FR-VME 1 mg m^{-3} **FR-VLE** 3 mg m^{-3}
JP-OEL 1 mg m^{-3}
SE-LEVL 1 mg m^{-3} (mist) **SE-STEL** 3 mg m^{-3} (mist)
UK-STEL 2 mg m^{-3}
US-TWA 1 mg m^{-3} **US-STEL** 3 mg m^{-3}

UN No. 1805 **HAZCHEM Code** 2R **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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1530 mg kg^{-1} (1).
LC_{50} (duration unspecified) inhalation mouse 25.5 mg m^{-3} (2).
LD_{50} dermal rabbit 2740 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Rats chronically (duration unspecified) exposed to aerosols equivalent to 14.6 mg H_3PO_4 m^{-3} resulted in progressive bronchitis and bronchiectasis development, altered liver function and histological changes in liver, spleen and kidney (2).
No adverse effects on body weight, blood chemistry, or substance related abnormalities in the liver, spleen, adrenals, testicles, skeletal muscles and femur were seen in rats fed 0, 4000 or 7500 ppm in diet from weaning to 15 months or their offspring fed similarly for 6 months (3).

Teratogenicity and reproductive effects
No adverse reproductive effects were seen in rats fed 0, 4000 ppm in diet since weaning and mated at 32 wk and 43 wk or offspring fed the same diet after weaning (3).

Metabolism and toxicokinetics
Rats administered phosphoric acid in diet (dose and duration unspecified) showed increased inorganic phosphate levels in urine indicating some oral absorption and subsequent elimination in urine (3).

Irritancy
Dermal rabbit (24 hr) 595 mg caused severe irritation and 119 mg instilled into rabbit eye (72 hr) caused severe irritation (1).
In vivo rabbit eyes exposed to 100 µl of 17% aqueous solution showed mild irritation (duration unspecified) (4).
Irritating to the eyes, respiratory tract and mucous membranes (species unspecified) (5).
Irritating to the upper respiratory tract and may cause pulmonary oedema (6).
1 ppm phosphoric acid mist is irritating to unacclimatised workers but tolerated by the acclimatised (7).
A 75% solution will cause serious skin burns in humans (8).
The dust is more irritating in the presence of water to humans and prolonged or repeated exposure may result in permament damage (8,9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA104 with and without metabolic activation negative (10).
Escherichia coli without metabolic activation negative (11).

Other effects

Other adverse effects (human)

The dental profession, which uses phosphoric acid as an etchant, reported that exposure of mouth soft tissues to 50% solutions for ≥5 min caused a mild chemical burn which healed within a few days (12).

Toxic symptoms following ingestion of large quantities included stomach pain, breathing difficulty, nausea, vomiting, diarrhoea, convulsions, collapse and death (13).

A patient who ingested a large single dose (concentration unstated) died after 19 days from widespread corrosion of the intestinal tract (14).

17 volunteers who consumed 200-400 mg (~40-80 mg kg^{-1}) day^{-1} in fruit juice for 10-14 days showed no change in urine composition (15).

Any other adverse effects

10% solution applied to rabbit skin caused body weight loss and leucocytosis (2).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).

Maximum tolerable daily intake (humans) of phosphates and polyphosphates in food, expressed as phosphorus is 70 mg kg^{-1} body weight for diets nutritionally adequate in calcium (17).

Other comments

LC_{50} (96 hr) "aquatic life" 100-1000 ppm (18).

Reviews on human health effects, experimental toxicology, physico-chemical properties, environmental effects listed (19).

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P157 phosphorous acid

H_3PO_3

H_3O_3P **Mol. Wt.** 82.00 **CAS Registry No.** 10294-56-1

Synonyms dihydrophosphine oxide

EINECS No. 233-663-1

Uses Catalyst.

Occurrence Degradation product of aluminium tris(ethylphosphonate).

Physical properties

M. Pt. 73.8°C **Specific gravity** 1.651

Solubility Water: 4250 g l^{-1} at 20°C. Organic solvents: ethanol

Occupational exposure

UN No. 2834 **HAZCHEM Code** 2R **Conveyance classification** corrosive substance

Other effects

Any other adverse effects

NOEL for oral administration to laboratory animals in chronic experiments 1.4 mg kg^{-1} and 1.0 mg l^{-1} to aquatic organisms (details for species and exposure not specified) (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. Phosphorous: guide level 400 μg l^{-1}; maximum admissible concentration 5000 μg l^{-1} (as P_2O_5) (3).

Other comments

Odour/taste threshold 86 mg l^{-1} (1).

Threshold concentration 85.7 mg l^{-1} according to the influence on organoleptic water properties and 1 mg l^{-1} according to the influence on the sanitary regimen of water reservoirs (1).

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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

P158 phosphorus

P

P **Mol. Wt.** 30.97 **CAS Registry No.** 7723-14-0

Synonyms Exolit 385; phosphorus, black; phosphorus, red; phosphorus, yellow; phosphorus, white

EINECS No. 231-768-7 **RTECS No.** TH 3495000

Uses In the manufacture of pesticides and fertilisers. Organic synthesis. Manufacture of inorganic phophorus compounds. Used in smoke screens and incendiary devices.

Occurrence In bones, teeth and in milk. Essential element in plant and animal metabolism. Occurs in chlorapatite, fluorapatite, vivianite, wavellite and phosphorite minerals. Exists in three main allotropic forms: white, black and red. White is sometimes called yellow phosphorus because of impurities.

Physical properties

M. Pt. 416°C (sublimes) (red); $^{0.1}$ 44.1°C (white) **B. Pt.** 280°C (white) **Specific gravity** 1.85 (white); 3.56 (black); 2.34 (red) **Volatility** v.p. 1 mmHg at 76.6°C (white)

Solubility Water: 3 mg l^{-1} (white). Organic solvents: white phosphorus is soluble in benzene, chloroform, carbon disulfide, diethyl ether, ethanol, olive oil, terpentine

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable fraction of aerosol)

JP-OEL 0.1 mg m^{-3}

UK-LTEL 0.1 mg m^{-3} (yellow) **UK-STEL** 0.3 mg m^{-3} (yellow)

US-TWA 0.02 ppm (0.1 mg m^{-3}) (yellow)

UN No. 1338 (amorphous)

UN No. 1381 (white or yellow, dry or under water, or in solution)

UN No. 2447 (white, molten) **HAZCHEM Code** 2WE **Conveyance classification** flammable solid (amorphous)

Conveyance classification spontaneously combustible substance, toxic substance (white, molten, white or yellow, dry or under water or in solution)

Supply classification highly flammable

Risk phrases Highly flammable – Explosive when mixed with oxidising substances (R11, R16)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container tightly closed – In case of fire, use sand and carbon dioxide – do not use water (S2, S7, S43)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 3.0-4.8 mg kg^{-1} (white in water) (1).

LD_{Lo} subcutaneous rabbit, dog 2, 10 mg kg^{-1}, respectively (white in water) (2,3).

Sub-acute and sub-chronic data

Gavage rat, 3 mg kg^{-1} day^{-1} yellow phosphorus for 4 days induced significant histopathological changes in the liver. Serum GPT and glutamate-oxalate transaminase activities were significantly elevated. Lipid peroxidases of serum and liver microsomes, serum IgM and complement C_3 contents were also significantly elevated (4).

Inhalation rat, exposure to concentrations >20 ppm for 7 hr day^{-1}, 5 days wk^{-1} (total exposure not specified) caused high mortality due to oedema of the lungs and bronchopneumonia (5).

Oral rat, single dose of 10 mg kg^{-1} (white phosphorus) caused toxic hepatitis within 140 hr (6).

Teratogenicity and reproductive effects

Oral rat, lowest toxic dose 11 μg kg^{-1} day^{-1} administered on days 1-22 of gestation caused post implantation mortalities (7).

Metabolism and toxicokinetics

In the dog, phosphorus is absorbed in the small intestine and the colon (8).

Irritancy

Inhalation human, 400 mg m^{-3} produces signs of irritation in 10-15 minutes (9).

Other effects

Other adverse effects (human)

Ingestion of white phosphorus may produce severe gastro-intestinal irritation, bloody diarrhoea, liver damage, skin eruptions, oliguria, circulatory collapse, coma and convulsions. Fatal dose ~50-100 mg. Chronic poisoning is characterised by bone necrosis, especially of the mandible (phossy jaw), spontaneous fractures, anaemia and weight loss. Red phosporus is relatively non-toxic (10).

Any other adverse effects

White phophorus has been reported to cause second and third degree burns on contact with the skin. The affected area turns greyish-white and infection follows. Dermal application has resulted in liver and kidney damage in laboratory animals (11,12).

Phosphorus levels as high as 3.5 mg have been found in the digestive tracts of dead ducks found near military artillery ranges (13).

Legislation

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

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phosphorous: guide level 400 $\mu g\ l^{-1}$; maximum admissible concentration 5000 $\mu g\ l^{-1}$ (as P_2O_5) (15).

Other comments

Reviews on physical properties, use, hazards, mammalian toxicity and safety precautions are listed (11,16).

Physiological role and requirements for phosphorus reviewed (17).

Exists in three main allotropic forms, white (or yellow), black and red phosphorus.

Autoignition temperature 30°C.

References

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P159 phosphorus oxychloride

$POCl_3$

Cl_3OP **Mol. Wt.** 153.33 **CAS Registry No.** 10025-87-3

Synonyms phosphoryl chloride; phosphoryl oxytrichloride; trichlorophosphine oxide

EINECS No. 233-046-7 **RTECS No.** TH 4897000

Uses Catalyst. Chlorinating agent. Dopant. Organic synthesis. Phosphorylating agent.

Physical properties

M. Pt. 1.25°C **B. Pt.** 105.8°C **Specific gravity** 1.645 at 25°C with respect to water at 4°C
Volatility v.p. 40 mmHg at 27.3°C ; v.den. 5.3

Occupational exposure

DE-MAK 0.2 ppm (1.3 mg m^{-3})
FR-VME 0.1 ppm (0.6 mg m^{-3})
UK-LTEL 0.2 ppm (1.3 mg m^{-3}) **UK-STEL** 0.6 ppm (3.8 mg m^{-3})
US-TWA 0.1 ppm (0.63 mg m^{-3})

UN No. 1810 **HAZCHEM Code** 4WE **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 dry – 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, S7/8, S26, S45)

Environmental fate

Abiotic removal
Reacts exothermically with water and ethanol (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 380 mg kg^{-1} (2).
LC_{50} (4 hr) inhalation rat, guinea pig 48-53 ppm (3).

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, inflamation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (4).

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. Phosphorous: guide level 400 µg l^{-1}; maximum admissible concentration 5000 µg l^{-1} (as P_2O_5) (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

References

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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. *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

P160 phosphorus pentachloride

$$PCl_5$$

Cl_5P **Mol. Wt.** 208.24 **CAS Registry No.** 10026-13-8

Synonyms pentachlorophosphorane; phosphoric chloride; phosphorus perchloride

EINECS No. 233-060-3 **RTECS No.** TB 6125000

Uses Catalyst. Chlorinating agent. Dehydrating agent. Phosphorylating agent.

Physical properties

M. Pt. 179-181°C (sublimes) **Specific gravity** 4.65 g l^{-1} (gas) at 296°C **Volatility** v.p. 1 mmHg at 55.5°C
Solubility Organic solvents: carbon disulfide, carbon tetrachloride

Occupational exposure

DE-MAK 1 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.1 ppm (1 mg m^{-3})
JP-OEL 0.1 ppm (0.85 mg m^{-3})
UK-LTEL 0.1 ppm (0.87 mg m^{-3})
US-TWA 0.1 ppm (0.85 mg m^{-3})

UN No. 1806 **HAZCHEM Code** 4WE **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 dry – 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, S7/8, S26, S45)

Environmental fate

Abiotic removal
Hydrolysed by water to form phosphoric acid and hydrogen chloride. Reacts with alcohols to give the corresponding chloride (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 660 mg kg^{-1} (2).

LC_{50} inhalation rat 200 mg m^{-3} (exposure not specified) (2).

Irritancy

Fumes are irritating to the eyes and respiratory passage (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4). Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phosphorous: guide level 400 μg l^{-1}; maximum admissible concentration 5000 μg l^{-1} (as P_2O_5) (5).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. *Toxicol. New Ind. Chem. Subst.* 1973, **13**, 104.
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4. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, 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. *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

P161 phosphorus pentafluoride

PF_5

F_5P **Mol. Wt.** 125.97 **CAS Registry No.** 7647-19-0

Synonyms pentafluorophosphorane

EINECS No. 231-602-3 **RTECS No.** TH 4070000

Uses Dopant. Catalyst.

Physical properties

M. Pt. –93.8°C **B. Pt.** –84.6°C **Specific gravity** 5.805 g l^{-1} (gas)

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)

UN No. 2198 **Conveyance classification** toxic gas, corrosive

Environmental fate

Abiotic removal

Hydrolysed by water to give phosphoric acid and hydrogen fluoride, via oxyfluorophosphate intermediates (1).

Mammalian & avian toxicity

Irritancy

Extremely irritating to the skin, eyes and mucous membranes (2).

Other effects

Other adverse effects (human)

Inhalation exposure may cause pulmonary oedema (2).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3). Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phosphorous: guide level 400 $\mu g\ l^{-1}$; maximum admissible concentration 5000 $\mu g\ l^{-1}$ (as P_2O_5) (4).

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P162 phosphorus pentasulfide

$$P_2S_5$$

P_2S_5 **Mol. Wt.** 222.28 **CAS Registry No.** 1314-80-3

Synonyms phosphoric sulfide; phosphorus persulfide; sulfur phosphide; thiophosphoric anhydride

EINECS No. 215-242-4 **RTECS No.** TH 4375000

Uses Organic synthesis. Manufacture of matches.

Physical properties

M. Pt. 286-290°C **B. Pt.** 513-515°C **Flash point** 137°C **Specific gravity** 2.090
Volatility v.p. 1 mmHg at 300°C
Solubility Organic solvents: carbon disulfide

Occupational exposure

DE-MAK 1 mg m^{-3} (inhalable fraction or aerosol)
FR-VME 1 mg m^{-3}
UK-LTEL 1 mg m^{-3} **UK-STEL** 3 mg m^{-3}
US-TWA 1 mg m^{-3} **US-STEL** 3 mg m^{-3}

UN No. 1340 (free from yellow and white phosphorus) **HAZCHEM Code** 4YE (free from yellow and white phosphorous) **Conveyance classification** substance which in contact with water emits flammable gas, danger of fire (flammable solid) (free from and white phosphorus)
Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful by inhalation and if swallowed – Contact with water liberates toxic gas (R11, R20/22, R29)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Environmental fate

Abiotic removal
Decomposes in water to give phosphoric acid and hydrogen sulfide (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 390 mg kg^{-1} (2).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation. 20 mg instilled into rabbit eye for 24 hr caused severe irritation (2).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phosphorous: guide level 400 $\mu g\ l^{-1}$; maximum admissible concentration 5000 $\mu g\ l^{-1}$ (as P_2O_5) (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).
Exists as P_4S_{10}.
Autoignition temperature 136°C.

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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. *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

P163 phosphorus pentoxide

$$P_2O_5$$

O_5P_2 **Mol. Wt.** 141.94 **CAS Registry No.** 1314-56-3

Synonyms diphosphorus pentoxide; phosphoric anhydride; phosphorus(v) oxide; POX

EINECS No. 215-236-1 **RTECS No.** TH 3945000

Uses In the preparation of bone cement. In ceramics. Drying and dehydrating agent.

Physical properties

M. Pt. 340°C **B. Pt.** 360°C (sublimes) **Specific gravity** 2.390 **Volatility** v.p. 1 mmHg at 384°C ; v.den. 4.9
Solubility Water: miscible

Occupational exposure

DE-MAK 1 mg m^{-3} (inhalable fraction or aerosol)
FR-VME 1 mg m^{-3}
UK-STEL 2 mg m^{-3}

UN No. 1807 **HAZCHEM Code** 4W **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 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, S22, S26, S45)

Environmental fate

Abiotic removal
Undergoes exothermic hydrolysis with water to give phosphoric acid (1).

Mammalian & avian toxicity

Acute data
LC_{50} (1 hr) inhalation guinea pig, mouse, rat, rabbit 61, 270, 1220, 1700 mg m^{-3}, respectively (2).

Other effects

Other adverse effects (human)
Extremely destructive to 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 (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phosphorous: guide level 400 μg l^{-1}; maximum admissible concentration 5000 μg l^{-1} (as P_2O_5) (5).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).
Exists as P_4O_{10}.

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
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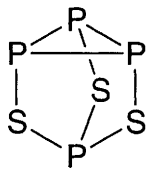
4. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *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

P164 phosphorus sesquisulfide



P_4S_3 **Mol. Wt.** 220.09 **CAS Registry No.** 1314-85-8

Synonyms phosphorus sulfide; tetraphosphorus trisulfide; trisulfurated phosphorus

EINECS No. 215-245-0 **RTECS No.** TH 4330000

Uses Used in the manufacture of match tips. Organic synthesis.

Physical properties

M. Pt. 172.5°C **B. Pt.** 407.5°C **Flash point** 100°C **Specific gravity** 2.03 at 20°C with respect to water at 4°C
Solubility Organic solvents: benzene, carbon disulfide

Occupational exposure

UN No. 1341 (free from yellow and white phosphorus) **HAZCHEM Code** 1Y (free from yellow and white phosphorus) **Conveyance classification** flammable solid (free from yellow and white phosphorus)
Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful if swallowed (R11, R22)
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 – Avoid contact with skin and eyes (S2, S7, S16, S24/25)

Environmental fate

Abiotic removal
Decomposes in hot water yielding hydrogen sulfide (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 100 mg kg^{-1} (2).

Irritancy
Dust and fumes extremely irritating to the eyes, respiratory tract and skin (3).

Sensitisation
Reported to cause allergic contact dermatitis among workers in a match factory. Skin tests showed an allergic reaction (4).

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. Phosphorous: guide level 400 μg l^{-1}; maximum admissible concentration 5000 μg l^{-1} (as P_2O_5) (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7). Autoignition temperature 100°C.

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. Spector, W. S. (Ed.) *Handbook of Toxicology* 1956, **1**, 236-237, Saunders, Philadelphia, PA, USA.
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4. Corde-Salazar, G. L. et al *Med. Seguridad Trob.* 1981, **29**(113), 27-30.
5. *S. I. 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. *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

P165 phosphorus tribromide

PBr_3

Br_3P **Mol. Wt.** 270.69 **CAS Registry No.** 7789-60-8

Synonyms phosphorus bromide; tribromophosphine

EINECS No. 232-178-2 **RTECS No.** TH 4460000

Uses Brominating agent. Catalyst.

Physical properties

M. Pt. –41.5°C **B. Pt.** 173.2°C **Specific gravity** 2.850 at 15°C **Volatility** v.p. 10 mmHg at 48°C
Solubility Organic solvents: acetone, carbon disulfide, carbon tetrachloride, chloroform, dichloromethane

Occupational exposure

UN No. 1808 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Reacts violently with water – Causes burns – Irritating to the respiratory system (R14, R34, R37)
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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

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 (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. Phosphorous: guide level 400 $\mu g\ l^{-1}$; maximum admissible concentration 5000 $\mu g\ l^{-1}$ (as P_2O_5) (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).
Decomposes in water (5).

References

1. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2824, Sigma-Aldrich, Milwaukee, WI, USA.
2. *S. I. 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. *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.
5. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

P166 phosphorus trichloride

PCl_3

Cl_3P **Mol. Wt.** 137.33 **CAS Registry No.** 7719-12-2

Synonyms phosphorus chloride; trichlorophosphine

EINECS No. 231-749-3 **RTECS No.** TH 3675000

Uses Catalyst. Chlorinating agent. Organic synthesis. Etchant. Phosphinylation agent.

Physical properties

M. Pt. –112°C **B. Pt.** 76°C **Flash point** none **Specific gravity** 1.574 at 21°C **Volatility** v.p. 100 mmHg at 21°C ; v.den. 4.75

Solubility Water: decomposes in water. Organic solvents: benzene, carbon disulfide, chloroform, ether

Occupational exposure

DE-MAK 0.5 ppm (2.8 mg m^{-3})
FR-VME 0.2 ppm (1.5 mg m^{-3})
JP-OEL 0.2 ppm (1.1 mg ml^{-3})
UK-LTEL 0.2 ppm (1.1 mg ml^{-3}) **UK-STEL** 0.5 ppm (2.9 mg m^{-3})
US-TWA 0.2 ppm (1.1 mg ml^{-3}) **US-STEL** 0.5 ppm (2.8 mg ml^{-3})

UN No. 1809 **HAZCHEM Code** 4WE **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 dry – 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, S7/8, S26, S45)

Environmental fate

Abiotic removal
Decomposes in water forming hydrochloric acid (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 550 mg kg^{-1} (2).
LC_{50} (4 hr) inhalation rat, guinea pig 50, 100 mg kg^{-1}, respectively (3).
LD_{50} dermal rabbit 1260 mg kg^{-1} (4).

Genotoxicity

In vivo rat bone marrow; human and mouse peripheral blood lymphocytes, chromosomal aberrations and induction of micronuclei negative (5).

Other effects

Other adverse effects (human)

Material is 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 (6).

Any other adverse effects

Reported to cause non-specific changes to the bones of foetal rats (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phosphorous: guide level 400 μg l^{-1}; maximum admissible concentration 5000 μg l^{-1} (as P_2O_5) (7).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. *Toxicol. New Ind. Chem. Subst.* 1973, **13**, 104.
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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. *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

P167 phosphorus trioxide

$$P_2O_3$$

O_3P_2 **Mol. Wt.** 109.95 **CAS Registry No.** 1314-24-5

Synonyms diphosphorus trioxide; phosphorus(III) oxide

Uses Catalyst.

Physical properties

M. Pt. 23.8°C **B. Pt.** 173.1°C in nitrogen atmosphere **Specific gravity** 2.135 at 21°C with respect to water at 4°C

Solubility Organic solvents: benzene, carbon disulfide

Occupational exposure

UN No. 2578 **HAZCHEM Code** 4X **Conveyance classification** corrosive substance

Environmental fate

Abiotic removal

In cold water phosphorous acid (H_3PO_3) is slowly formed.

Diproportionates into red phosphorus and P_2O_4 when heated >210°C (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. Phosphorous: guide level 400 μg l^{-1}; maximum admissible concentration 5000 μg l^{-1} (as P_2O_5) (3).

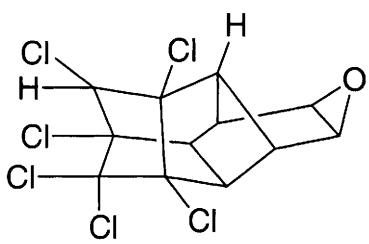
Other comments

Exists as P_4O_6; very poisonous (1).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. *S. I. 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

P168 photodieldrin



$C_{12}H_8Cl_6O$ **Mol. Wt.** 380.91 **CAS Registry No.** 13366-73-9

Synonyms 1,1,2,3,3a,7a-hexachloro-5,6-epoxydecahydro-2,4,7-methano-1*H*-cyclopenta[*a*]pentalene, stereoisomer

RTECS No. PC 8800000

Occurrence Photodegradation product of dieldrin, identified in liver and kidney of broiler fowl (1).

Physical properties

M. Pt. 194.5-197°C **Partition coefficient** log P_{ow} 6.91 (calc.) (2)

Solubility Water: <1 g l^{-1} at 20°C. Organic solvents: dimethyl sulfoxide, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) bluegill sunfish, minnow 10-30 μg l^{-1} (3).

Bioaccumulation
Bioconcentration factor for clam, crayfish, shrimp 3-30, and for bluegill sunfish, minnow, goldfish, guppy 60-820 (4).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
National Toxicology Program investigated photodieldrin in rat and mouse via oral administration. Negative results were reported (5).

Genotoxicity

Salmonella typhimurium TA97 with metabolic activation positive (6).

Legislation

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

References

1. Gallego-Iniesta, M. et al *Comp. Biochem. Physiol., C: Comp. Pharmacol. Toxicol.* 1987, **86C**(1), 121-124.
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5. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-017, NIEHS, Research Triangle Park, NC, USA.
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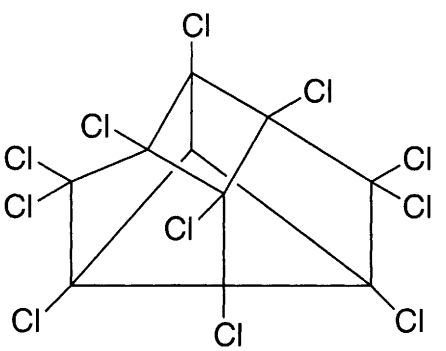
P169 photomirex



$C_{10}HCl_{11}$ **Mol. Wt.** 511.10 **CAS Registry No.** 39801-14-4

Synonyms 1,1a,2,2,3,3a,4,5,5,5a,5b-undecachlorooctahydro-1,3,4-metheno-1*H*-cyclobuta[*cd*]pentalene; 8-hydromirex; 8-monohydromirex

RTECS No. PC 8475000

Occurrence Photodegradation product of the insecticide mirex.

Ecotoxicity

Bioaccumulation

Found to be the 4th highest organochlorine contaminant of herring-gull eggs and body lipids (after PCBs, DDE and mirex). Also present at similar ratios in coho salmon muscle and liver, alewifes and smelt from Lake Ontario (1,2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 200 mg kg^{-1} (1).

Oral quail 1000 mg kg^{-1} caused moderate hepatic changes consisting of an increase in liver weight. No indication of severe liver damage (3).

Oral rat 100 or 200 mg kg^{-1} showed mottled and congested livers and kidneys. ♀ developed haemorrhagic ovaries (1).

Teratogenicity and reproductive effects

Designated positive for developmental toxicity in rats, negative in rabbits and predicted to be negative in humans (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (1).

References

1. Hallett, D. J. et al *J. Agric. Food Chem.* 1978, **26**, 388-391.
2. Hallet, D. J. et al *J. Agric. Food Chem.* 1976, **24**, 1189.
3. Strick, J. J. T. W. A. et al *Bull. Environ. Contam. Toxicol.* 1980, **24**, 350-355.
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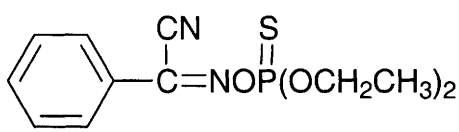
P170 phoxim



$C_{12}H_{15}N_2O_3PS$ **Mol. Wt.** 298.30 **CAS Registry No.** 14816-18-3

Synonyms *O,O*-diethyl *O*-(α-cyanobenzylideneamino)-phosphorothioate; 2-(diethoxylphosphino-thioyloxyamino)-2-phenylacetonitrile; 4-ethoxy-7-phenyl-3,5-dioxa-6-aza-4-phosphaoct-6-ene-8-nitrile 4-sulfide; phenylglyoxylonitrile oxime *O,O*-diethyl phosphorothioate; Sebacil; Volaton; Baythion

EINECS No. 238-887-3 **RTECS No.** MD 4740000

Uses Insecticide.

Physical properties

M. Pt. 5-6°C **B. Pt.** 102°C at 0.01 mmHg (decomp. on distillation) **Specific gravity** 1.176 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.38 **Volatility** v.p. ~7.5×10^{-4} mmHg at 20°C

Solubility Water: 1.5 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, propan-2-ol, toluene, vegetable and mineral oils

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)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) rainbow trout, minnow carp, goldfish 0.1-10 mg l^{-1} (1).

Environmental fate

Degradation studies
In the cotton plant, photochemical degradation and metabolism involve isomerisation to *O,O*-diethyl *S*-α-cyanobenzylideneaminothiophosphoroate and tetraethyl diphosphate (1).

Abiotic removal
In soil, undergoes photochemical isomerisation to diethyoxyphosphonylthioiminophenylacetonitrile. Tetraethyl diphosphate and tetraethyl phosphorodithioate are further metabolites (2).
Slowly degraded under UV irradiation. $t_{1/2}$ 700 hr at pH 7, 170 min at pH 11.6 in isopropanol/water mixture at 37°C (1).

Mammalian & avian toxicity

Acute data
LD_{50} redwinged blackbird, chicken, starling, quail 10-40 mg kg^{-1} (3).
LD_{50} oral rat, rabbit, cat, dog 300, 250, 250, 250 mg kg^{-1}, respectively (4-6).
LD_{50} oral mouse, guinea pig 600, 1050 mg kg^{-1}, respectively (1,7).
LC_{50} (1 hr) inhalation rat >3200 mg m^{-3} (1).
LD_{50} dermal ♂ rat >1000 mg kg^{-1} (1,5).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 15 kg^{-1} diet (1).

Teratogenicity and reproductive effects
Intragastric ♂ rat (10 wk) 0.7 mg kg^{-1} day^{-1}; gonadotoxic causing exfoliation of follicular epithelium from basal membrane and nuclear hypertrophy of testes (8).

Metabolism and toxicokinetics
In the mouse, rapidly metabolised to diethylphosphoric acid and desethyl phoxim. There is also rapid metabolism of the oxon. The nitrile group is also metabolised to yield phoxim carboxylic acid (1).
In rabbits and cattle phoxim is distributed to all tissues. Hydrolysis occurs more rapidly in animals exposed to UV irradiation (9).

Genotoxicity

In vitro human lymphocytes, sister chromatid exchanges positive (10).
Vicia faba root tips, sister chromatid exchanges positive (9).

Other effects

Any other adverse effects
Inhibits cholinesterase activities (11,12).

Legislation

EEC maximum residue level 0.1 ppm for cereals (1).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (13).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).
Log P_{ow} exceeds European Union recommended limit of 3.0 (15).
WHO Toxicity Class II (16).
EPA Toxicity Class III (formulation) (17).
ADI 0.001 mg kg^{-1} body weight (17).

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12. Zoun, P. E. F. et al *J. Chromatogr.* 1989, **462**, 448-453.
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.
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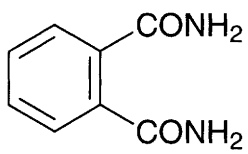
15. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
16. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
17. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

P171 phthalamide



$C_8H_8N_2O_2$ **Mol. Wt.** 164.16 **CAS Registry No.** 88-96-0

Synonyms 1,2-benzenedicarboxamide; *o*-carbamoylbenzamide; phthaldiamide; phthalic acid diamide

EINECS No. 201-870-6 **RTECS No.** CZ 2200000

Uses Organic synthesis. Analytical reagent. Paint ingredient.

Physical properties

M. Pt. 228°C (decomp.) **Partition coefficient** log P_{ow} –0.8045 (1)
Solubility Water: miscible. Organic solvents: benzene, diethyl ether, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat, mouse 4000-4100 mg kg^{-1} (2).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via feed. Negative results were reported in ♂ and ♀ rats and mice (3).

Teratogenicity and reproductive effects

Induced a low but significant incidence of specific malformations compared with controls after injection into fertile white leghorn eggs (dose not specified) (4).

Genotoxicity

In vitro mouse lymphoma L5178Y tk^+/tk^- forward mutation assay negative (5).

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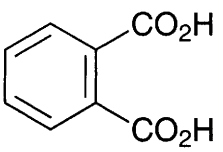
P172 phthalic acid



$C_8H_6O_4$ **Mol. Wt.** 166.13 **CAS Registry No.** 88-99-3

Synonyms 1,2-benzenecarboxylic acid; benzene-1,2-dicarboxylic acid; *o*-dicarboxybenzene; *o*-phthalic acid

EINECS No. 201-873-2 **RTECS No.** TH 9625000

Uses Organic synthesis. Analytical reagent.

Occurrence Isolated from the fungus *Gibberella fujikuroi*

Physical properties

M. Pt. 210°C (decomp.) **B. Pt.** 289°C **Specific gravity** 1.59 **Partition coefficient** log P_{ow} 0.10-0.41 (calc.) (1)

Volatility v.den. 5.7

Solubility Water: 5.4 g l^{-1} at 14°C. Organic solvents: diethyl ether, ethanol, methanol

Environmental fate

Degradation studies

>80% degradation by anaerobic sewage sludge, yielding methane and carbon dioxide (2).

97% removal (COD, 78 mg COD g^{-1} day inoculum hr^{-1}) adapted activated sludge at 20°C (3).

ThOD 1.44, BOD_5 0.85-1.44 COD 1.37 (4-6).

Metabolised by *Pseudomonas* sp. to yield 4,5-dihydroxyphthalic acid (7).

Mammalian & avian toxicity

Acute data

LD_{50} (unreported route) rat 1100 mg kg^{-1} (8).
LD_{50} oral mouse 2530 mg kg^{-1} (9).
LD_{50} intraperitoneal mouse 550 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Oral rat, 0.5 or 5.0% diet for 35 days caused no toxic effects (11).

Teratogenicity and reproductive effects

Oral pregnant rats (day 7 to day 16 of pregnancy) 0-2981 mg kg^{-1} average daily intake in feed. No deaths and no clinical signs of toxicity were seen in any animals but significant decreases in maternal body weight gain and food consumption occurred during the administration period in animals receiving more than 1763 mg kg^{-1} day^{-1}. Postimplantation loss and number and sex ratio of live foetuses were not significantly affected at any dose. Significant decreases in the weight of ♂ foetuses and the number of ossification centres of the caudal vertebrae were found in the rats receiving average daily intakes of 2981 mg kg^{-1}. Morphological examination of the foetuses revealed no evidence of teratogenesis (12).

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (14).

Other effects

Any other adverse effects

Intraperitoneal mouse, single dose of 100 mg kg^{-1} produced pulmonary damage within 24 hr. Pulmonary GSH was not depleted (15).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).

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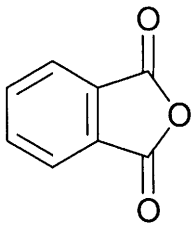
P173 phthalic anhydride



$C_8H_4O_3$ **Mol. Wt.** 148.12 **CAS Registry No.** 85-44-9

Synonyms 1,2-benzenedicarboxylic acid anhydride; 1,3-dioxonaphthalan; 1,3-isobenzofurandione; *o*-phthalic anhydride; 1,3-phthalandione; Retarder AK; Retarder ESEN; Retarder PD

EINECS No. 201-607-5 **RTECS No.** TI 3150000

Uses Acylating agent. Manufacture of polymers. Catalyst. Organic synthesis. Plasticiser.

Physical properties

M. Pt. 131-134°C **B. Pt.** 284°C **Flash point** 151°C (closed cup) **Specific gravity** 1.527 at 4°C
Partition coefficient log P_{ow} 1.5101 (1) **Volatility** v.p. 1 mmHg at 96.5°C ; v.den. 5.10
Solubility Water: 6.2 g l^{-1}. Organic solvents: hot benzene, carbon disulfide, diethyl ether, ethanol

Occupational exposure

DE-MAK 1 mg m^{-3} (inhalable fraction or aerosol)
FR-VLE 6 mg m^{-3}
SE-LEVL 2 mg m^{-3} **SE-CEIL** 3 mg m^{-3}
UK-LTEL MEL 4 mg m^{-3} **UK-STEL** MEL 12 mg m^{-3}
US-TWA 1 ppm (6.1 mg m^{-3})

UN No. 2214 (>0.05% maleic anhydride) **HAZCHEM Code** 2X (>0.05% maleic anhydride)
Conveyance classification corrosive substance (>0.05% maleic anhydride)
Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to respiratory system and skin – Risk of serious damage to eyes – May cause sensitisation by inhalation and skin contact (R22, R37/38, R41, R42/43)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour – Avoid contact with skin and eyes – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves and eye/face protection – If swallowed seek medical advice immediately and show this container or label (S2, S23, S24/25, S26, S37/39, S46)

Ecotoxicity

Fish toxicity
Not toxic to brown trout, bluegill sunfish, yellow perch and goldfish at 5 ppm for 24 hr. 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; temperature 12.8°C (2).

Bioaccumulation
Reported bioconcentration factor for the alga *Oedogenium* 4100. Phthalic anhydride did not bioconcentrate in *Daphnia, Physa* or mosquito fish (3).

Environmental fate

Degradation studies
BOD_5 0.72-1.26 (4,5).

2 ppm incubated with sewage 6.5 days (standard dilution method) 21% degradation; (seawater dilution method) 18% degradation. Results may report phthalic acid degradation because of rapid hydrolysis rate of the anhydride (6).

Abiotic removal

Hydrolysis $t_{1/2}$ ~1.5 min in water (7).
Reaction with photochemically produced hydroxyl radicals in the atmosphere $t_{1/2}$ 24 hr (8).
Susceptible to direct photolysis since it absorbs light >290 nm

Adsorption and retention

Estimated K_{oc} 36 indicates that phthalic anhydride would not adsorb to soil or sediments (9).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, cat 500-4000 mg kg^{-1} (10-12).
LD_{50} intraperitoneal guinea pig 100 mg kg^{-1} (13).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via feed. Negative results were reported in ♂ and ♀ rats and mice (14).

Teratogenicity and reproductive effects

Intraperitoneal mouse, lowest toxic dose 200 mg kg^{-1} day^{-1} on days 8-10 of gestation. Teratogenic effects (foetal malformations) were observed predominantly in the adult lethal range and the dose-response for teratogenicity may be complicated by adult toxicity (15).
Inhalation ♂ rat, lowest toxic dose 1 mg m^{-3} day^{-1} for 45 days, decreased seminiferous tubules acid and disrupted fertilisation ability (16).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation, 100 mg instilled into rabbit eye caused severe irritation (exposure unspecified) (10).
Inhalation human, 25 mg m^{-3} caused irritation of the mucous membranes; 30 mg m^{-3} caused conjunctival irritation (17).

Sensitisation

Repeated exposure has been reported to induce asthma (18).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (19).
In vitro Chinese hamster ovary cells sister chromatid exchanges and chromosomal aberrations negative (19).

Other comments

Contaminant in urban air, industrial effluents and in drinking water samples (20).
Environmental fate reviewed (20).
Physical properties, hazards, mammalian toxicity and safety precautions reviewed (21,22).
Autoignition temperature 570°C.

References

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21. *Chemical Safety Sheets* 1990, **3**, 202-205, The Royal Society of Chemistry, London, UK.
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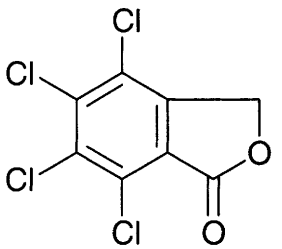
P174 phthalide



$C_8H_2Cl_4O_2$ **Mol. Wt.** 271.91 **CAS Registry No.** 27355-22-2

Synonyms fthalide; 4,5,6,7-tetrachlorophthalide; 4,5,6,7-tetrachloro-1(3*H*)-isobenzofuranone; Rabcide

EINECS No. 201-744-0 **RTECS No.** TI 3870000

Uses Insecticide and fungicide.

Physical properties

M. Pt. 209-210°C **B. Pt.** 290°C **Partition coefficient** log P_{ow} 3.01 **Volatility** v.p. 2.25×10^{-8} mmHg at 23 °C
Solubility Water: 2.5 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, dioxane, ethanol, tetrahydrofuran

Occupational exposure

JP-OEL 10 mg m^{-3}

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) young carp >320 mg l^{-1} (1).

Invertebrate toxicity
Non-toxic to bees; LD_{50} (contact) >0.4 mg bee^{-1} (1).

Environmental fate

Degradation studies

Principal metabolites in soil are 2-hydroxymethyl-3,4,5,6-tetrachlorobenzoic acid and its oxidation products (2).

Adsorption and retention

K_{oc} for various soils 130-950 (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse >10,000 mg kg^{-1} (1).
LD_{50} dermal rat, mouse >10,000 mg kg^{-1} (1).
LD_{50} intraperitoneal ♂, ♀ rat 9780, 15,000 kg^{-1} (1).
LD_{50} intraperitoneal mouse 10,000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral rat, mouse (2 yr) no-adverse-effect level for rats 2000 mg kg^{-1} diet and for mice 100 mg kg^{-1} diet (1).

Metabolism and toxicokinetics

In rats, the principal metabolites are 2-hydroxymethyl-3,4,5,6-tetrachlorobenzoic acid and its oxidation products (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 recommended limit of 3.0 (6).
WHO Toxicity Class Table 5 (7).
EPA Toxicity Class IV (formulation) (1).

References

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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. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
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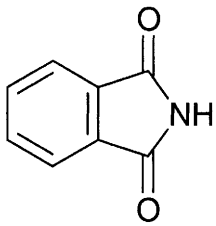
P175 phthalimide



$C_8H_5NO_2$ **Mol. Wt.** 147.13 **CAS Registry No.** 85-41-6

Synonyms 1,2-benzenedicarboximide; 2-diazoindan-1,3-dione; 1*H*-isoindole-1,3(2*H*)-dione; 1,3-isoindolinedione; phenylimide; *o*-phthalic imide

EINECS No. 201-603-3 **RTECS No.** TI 3920000

Uses Organic synthesis.

Physical properties

M. Pt. 234-238°C (sublimes) **Partition coefficient** log P_{ow} 1.15 (1)
Solubility Water: <1 g l^{-1}. Organic solvents: boiling acetic acid, acetone, dimethyl sulfoxide, hot diethyl ether, boiling ethanol

Ecotoxicity

Fish toxicity
Not toxic to brown trout, bluegill sunfish, yellow perch and goldfish at 5 ppm for 24 hr. Test conditions: pH 7.0; dissolved oxygen 7.5 ppm; total hardness (soap method) 300 ppm; free carbon dioxide 5 ppm; temperature 12.8°C (2).

Environmental fate

Degradation studies
96% removal as COD at 21 mg COD g^{-1} dry inoculum hr^{-1} in adapted activated sludge at 20°C (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 5000 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 1200 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Inhalation rat 50, 150 or 520 mg m^{-3} 5 days wk^{-1} for 4 wk caused no observable toxic effects except decreased lung weights in ♀ rats (6).

Teratogenicity and reproductive effects
Intraperitoneal mouse, lowest toxic dose simple administration of 6.2 mg on day 9 of gestation caused teratogenic effects including radius and tibia aplasia and occasional amelias (7).

Irritancy
Irritating to the skin, eyes, mucous membranes and respiratory tract (8).

Genotoxicity

Salmonella typhimurium TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (9).
Saccharomyces cerevisiae D4 with and without metabolic activation negative (9).

In vitro mouse lymphoma L5178Y cells, tk^+/tk^- forward mutation with and without metabolic activation negative (10).

Other comments

Detected in water samples after contact with medium density polyethylene pipes (11).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

References

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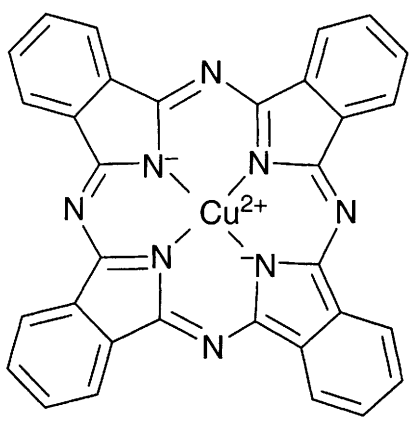
P176 phthalocyanine blue



$C_{32}H_{16}CuN_8$ **Mol. Wt.** 576.08 **CAS Registry No.** 147-14-8

Synonyms blue 15B; C.I. Pigment Blue 15; C.I. 74160; copper phthalocyanine; (*SP*-4-1)-[29*H*,31*H*-phthalocyaninato (2–)-N^{29},N^{30},N^{31},N^{32}]copper(II); Cyan Blue BNC; Duratint-1000; Fastogen Blue-5110; Graphtol Blue BL; Helio Fast Blue-BRN; Ingalite Fast Brilliant Blue-BL; Monastral Blue BF

EINECS No. 205-685-1 **RTECS No.** GL 8510000

Uses Catalyst. Charge-generating agent for electrophotographic photoreceptors and photoconductors. Pigment.

Physical properties

Solubility Water: < 1 g l^{-1} at 20°C. Organic solvents: dimethyl sulfoxide

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >15 g kg^{-1} (1).

LD_{50} intraperitoneal rat >3 g kg^{-1} (1).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (species unspecified) (2).

Legislation

Approved for use in polypropylene sutures by the Food and Drug Administration (3).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

Metal is firmly bound and not removed by strong acids (3).

Soluble in concentrated sulfuric acid.

References

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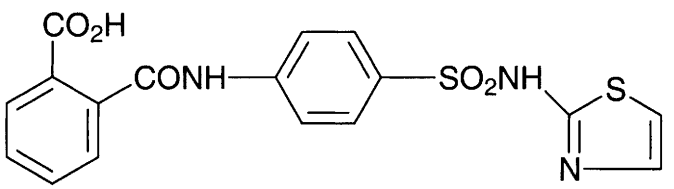
P177 phthalylsulfathiazole



$C_{17}H_{13}N_3O_5S_2$ **Mol. Wt.** 403.44 **CAS Registry No.** 85-73-4

Synonyms phthalylsulfonazole; 2-(N^4-phthalylaminobenzenesulfonamido)thiazole; Sulfathalidine; Sulfacetil; Talidene; 4′-(2-thiazolylsulfamyl)phthalanilic acid; 2-[[[4-[(2-thiazolylamino)sulfonyl]phenyl]amino]carbonyl]benzoic acid

EINECS No. 201-627-4 **RTECS No.** TH 8575000

Uses Intestinal antibacterial agent.

Physical properties

M. Pt. 272-277°C (dec.)

Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 920 mg kg^{-1} (1).

Metabolism and toxicokinetics

Poorly absorbed (in humans) after oral administration. ~95% remaining in the intestine and 5% being slowly hydrolysed to sulfathiazole, which is absorbed (2).

References

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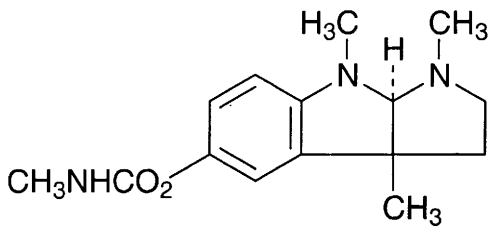
P178 physostigmine



$C_{15}H_{21}N_3O_2$ **Mol. Wt.** 275.35 **CAS Registry No.** 57-47-6

Synonyms (3a*S*-*cis*)-1,2,3,3a,8,8a-hexahydro-1,3a,8-trimethylpyrrolo[2,3-*b*]indol-5-ol methylcarbamate (ester); eserolein; methyl carbamate with eseroline; eserine; Physostol

EINECS No. 200-332-8 **RTECS No.** TJ 2100000

Uses Parasympathomimetic drug, used in the treatment of glaucoma and the atony of the gastro-intestinal tract.
Occurrence An alkaloid obtained from the Calabar bean.

Physical properties

M. Pt. 105-106°C
Solubility Water: slightly soluble. Organic solvents: benzene, chloroform, dichloromethane

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 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, rabbit 4.5, 11 mg kg^{-1}, respectively (1,2).
LD_{50} intramuscular rabbit 2.2 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse 0.6, 2.0 mg kg^{-1}, respectively (3,4).

LD_{50} intravenous mouse 0.4 mg kg^{-1} (5).
Intraperitoneal mouse, single injection of 0.5 mg kg^{-1} increased the steady-state concentration of brain acetylcholine by 84% within 1 min, while decreasing acetylcholine synthesis by 55% (6).

Teratogenicity and reproductive effects
Intraperitoneal mouse, lowest toxic dose single administration of 50 μg kg^{-1} on day 13 of gestation, teratogenic effects – biochemical and behavioural (7).

Metabolism and toxicokinetics
Following intramuscular administration to guinea pigs, plasma concentrations peaked in ~30 min and elimination $t_{1/2}$ was 40-50 min (8).
Readily absorbed through human skin and from the gastro-intestinal tract (9,10).
Crosses the blood-brain barrier (10).
Largely destroyed in human body by hydrolysis of the ester linkage by cholinesterases. Little is excreted in the urine (10).

Irritancy
No skin irritation was observed in rabbits using a modified Draize method (11).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA104, TA1535, TA1537 with and without metabolic activation negative (12).

Other comments

Used mainly in the form of the salicylate or sulfate (10).

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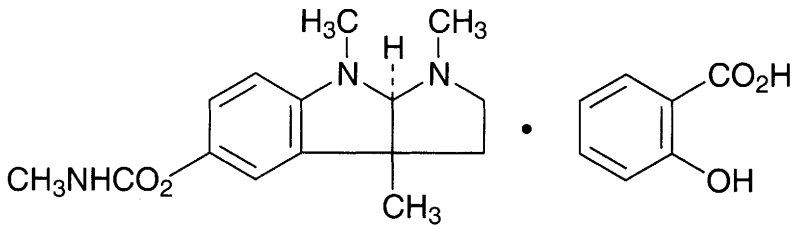
P179 physostigmine salicylate



$C_{22}H_{27}N_3O_5$ **Mol. Wt.** 413.47 **CAS Registry No.** 57-64-7

Synonyms eserine salicylate; physostal salicylate; salicylic acid with physostigmine (1:1); TL-1380

EINECS No. 200-343-8 **RTECS No.** TJ 2450000

Uses Protection against nerve agents; parasympathomimetic drug.

Physical properties

M. Pt. 185-187°C

Solubility Water: 1.3% at 25°C. Organic solvents: chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2.5 mg kg^{-1} (1).

LD_{50} intramuscular rabbit 1.6 mg kg^{-1} (1).

LD_{50} intravenous mouse 0.47 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 0.64 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 0.80 mg kg^{-1} (3).

Pigs were given pulmonary arterial infusion of 5 μg kg^{-1} min^{-1} for 2 hr. Red blood cell acetylcholinesterase was inhibited by 74% in 45 min. Minor changes were observed in the haematocrit, heart rate, body temperature, mean aortic pressure, pulmonary arterial wedge pressure and pulmonary artery pressure (4).

Irritancy

No skin irritation was observed in rabbits using a modified Draize method (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102, TA1535, TA1537, TA1538 with and without metabolic activation negative (6,7).

In vivo rat erythrocytes micronucleus assay negative (8).

Other effects

Other adverse effects (human)

Exposure may cause hyperaesthesia, vomiting, convulsions, diarrhoea, paralysis of the diaphragm, spasm of the glottis with transient dyspnoea, increased salivation, sweating, slowing of respiration and lowering of body temperature. Death usually occurs from respiratory paralysis (9).

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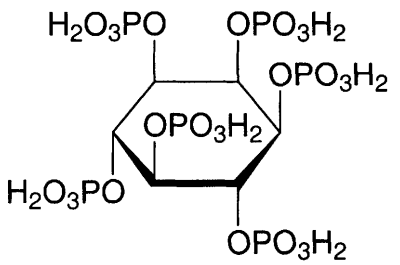
P180 phytic acid



$C_6H_{18}O_{24}P_6$ **Mol. Wt.** 660.04 **CAS Registry No.** 83-86-3

Synonyms cyclohexanehexyl hexaphosphate; 1,2,3,4,5,6-cyclohexanehexolphosphoric acid; *myo*-inositol hexakis(dihydrogen phosphate); inositolhexaphosphoric acid; *myo*-inositol hexaphosphate

EINECS No. 201-506-6 **RTECS No.** NM 7525000

Uses Chelating agent. Corrosion inhibitor. Scale inhibitor.
Occurrence In cereal grains.

Physical properties

Specific gravity 1.282
Solubility Water: miscible. Organic solvents: ethanol, glycerol, methanol

Environmental fate

Degradation studies
Hydrolysed by *Pisulithas tinctarius* and *Laccaria laccata in vitro* when utilised as sole phosphate source (1,2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 400, 1030 mg kg^{-1}, respectively (3,4).
LD_{50} intravenous mouse 500 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Oral germ-free rat, 2% diet as sodium phytate. 2/4 rats died and the remaining rats were dying with muscular paralysis after 1 wk. Haematological tests showed that the rats suffered from severe anaemia, with very low erythrocyte counts, haemoglobin concentration and haematoenic. Histopathological examination revealed that cardiac insufficiency with cardiac haemorrhage was the cause of death and that muscular paralysis was correlated with pressure on nerves caused by the lumbar or muscular haemorrhage. In addition, degeneration and necrosis of hepatocytes was observed. These toxic effects were not observed in normal rats in which the gastro-intestinal flora prevents phytate toxicity (6).

Metabolism and toxicokinetics

Undergoes hydrolysis, principally in the distal part of gastro-intestinal tract, following oral administration to rats. Bacterial phytases and alkaline phosphatase activities play a significant role in phytate hydrolysis (7).

Irritancy

Causes skin irritation (8).

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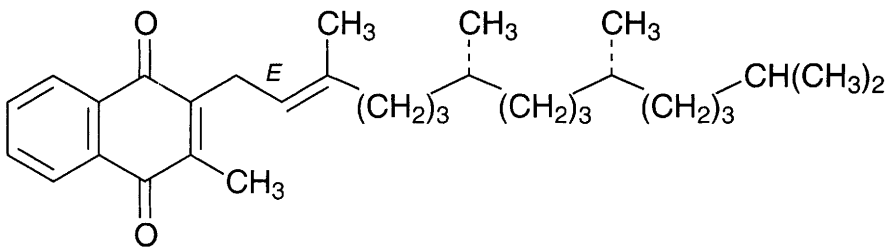
P181 phytomenadione



$C_{31}H_{46}O_2$ **Mol. Wt.** 450.71 **CAS Registry No.** 84-80-0

Synonyms phylloquinone; antihaemorrhagic vitamin; aqua mephyton; methylphytylnaphthochinonum; 2-methyl-3-phytyl-1,4-naphthoquinone; phytonadione; phytylmenaquinone; vitamin K_1; [*R*-[*R**,*R**-(*E*)]-2-methyl-3-(3,7,11,15-tetramethyl-2-hexadecenyl)-1,4-naphthalenedione

EINECS No. 201-564-2 **RTECS No.** QJ 5800000

Uses Treatment and prevention of haemorrhage associated with vitamin K deficiency. Antidote for dicoumarol poisoning.

Occurrence In leafy green vegetables, cows' milk, egg yolk and some cereals.

Physical properties

M. Pt. –20°C **B. Pt.** 140-145°C at 0.001 mmHg **Flash point** >110°C **Specific gravity** 0.967 at 25°C with respect to water at 25°C

Solubility Organic solvents: chloroform, diethyl ether, dioxane, ethanol, fixed oils, *n*-hexane

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 25,000 mg kg^{-1} (1).

LD_{50} subcutaneous mouse 1000 mg kg^{-1} (2).

LD_{50} intravenous mouse >6600 mg kg^{-1} (3).

Metabolism and toxicokinetics

In vitro studies demonstrated that transplacental transfer in humans is not significant (4).

Absorbed from the human gut only in the presence of bile. Poorly distributed into breast milk. Accumulates mainly in the liver, but is stored in the body only for short periods of time. Rapidly metabolised to more polar metabolites and excreted in the bile and urine as glucuronide and sulfate conjugates (5).

Metabolised in mouse fibroblasts *in vitro* to give the epoxide and γ-carboxyglutamic acid (6).

Other effects

Other adverse effects (human)

Administration has caused severe reactions resembling hypersensitivity or anaphylaxis. Such reactions have generally been associated with too rapid rate of infusion. Local skin reactions and pain have also been reported (5).

Administration to neonates, especially premature infants, has been associated with the development of haemolytic anaemia and hyperbilirubinaemia (5).

Other comments

In humans, phytomenadione is required for the maintenance of normal haemostatic function. Deficiency leads to the development of hypothrombinaemia in which the blood clotting time is prolonged and spontaneous bleeding can occur. Human dietary requirement ~1 μg kg^{-1} day^{-1} (6,7).

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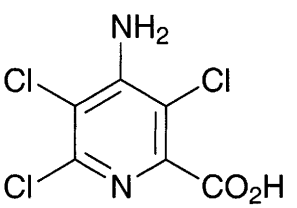
P182 picloram



$C_6H_3Cl_3N_2O_2$ **Mol. Wt.** 241.46 **CAS Registry No.** 1918-02-1

Synonyms 4-amino-3,5,6-trichloropicolinic acid; Tordon; 4-amino-3,5,6-trichloropyridine-2-carboxylic acid; Grazon; Spica 300

EINECS No. 217-636-1 **RTECS No.** TJ 7525000

Uses Herbicide.

Physical properties

M. Pt. 215°C (decomp.) **Volatility** v.p. 6.2×10^{-5} mmHg at 35°C

Solubility Water: 430 mg l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, dichloromethane, diethyl ether, ethanol, isopropanol

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}

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) cutthroat and lake trout 2050 to 8600 µg l^{-1}. Decreasing pH from 8.5 to 6.5 marginally decreased toxicity; increasing water temperature increased toxicity; alterations to water hardness had no effect on toxicity. Chronic toxicity on early life stages of lake trout was more significant than could be anticipated of only acute tests with fingerlings (1).

LC_{50} (96 hr) fathead minnow 55.3 mg l^{-1} (static bioassay) (2).

LC_{50} (96, 192 hr) rainbow trout 15.6 and 14.0 mg l^{-1}, respectively. In trout embryo-larvae studies concentration of 0.23-2.02 mg l^{-1} did not reduce the number of fertile eggs hatched, but survival weight and length of larvae were reduced in a dose-dependent manner (3).

Invertebrate toxicity

LC_{50} (96 hr) *Gammarus lacustris* 27 mg l^{-1} (4).

EC_{50} (48 hr) *Daphnia* sp. 50.7 mg l^{-1} (2).

LC_{50} honey bee >1000 mg kg^{-1} (2).

Toxicity to other species

Two submersed aquatic macrophytes, *Potamogeton pectinatus* and *Myriophyllum sibiricum Komarov*, were grown in the presence of 0.01 and 0.1 mg picloram l^{-1}. Picloram did not affect growth of either species, but injured *M. sibiricum* at both concentrations inhibited flowering at 0.1 mg l^{-1} (5).

Environmental fate

Degradation studies

Degraded slowly by soil microorganisms, $t_{1/2}$ 30-330 days. Degradation is assumed to occur via cleavage of the chlorine atom in the 3-position or its replacement by a hydroxy group, to form 4-amino-5,6-dichloro-2-picolinic acid and its 3-hydroxy derivative, respectively (6).

Major metabolite identified was decarboxypicloram (7).

Groundwater from four unspecified sites was incubated with 0.72 ppm and 10 ppm initial concentrations. After 15 wk ~30% degradation had occurred (8).

Abiotic removal

Application of 0.28 kg ha^{-1} sampled over 445 days at days 90, 365 and 445; persistence percentages were recorded as 36, 13 and 10.5%, respectively. Loss by photodegradation was important during the first 7 days after application (9).

In aqueous slurries of adsorbents (silt loam, calcareous silt loam and bentonite) at 85°C, hydrolytic $t_{1/2}$ >1000 hr. Adsorption for the three adsorbents at 20°C was 4%, 0% and 2%, respectively (10).

Direct photolysis by sunlight, $t_{1/2}$ 2-10 day (variable depending on depth in soil and time of year) (11).

In soil, photochemical isomerisation occurs to yield diethyoxyphosphorylthioiminophenylacetonitrile. Tetraethyl diphosphate (TEDP) and tetraethyl phosphorodithioate are additional metabolites (12).

Decomposed by UV irradiation DT_{50} 2.6 days (25°C (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1060 mg kg^{-1} (13).

LD_{50} oral guinea pig, rabbit 1920, 2000 mg kg^{-1}, respectively (13,14).

LD_{50} oral rat 2900 mg kg^{-1} (13).

LD_{50} oral chicken 4000 mg kg^{-1} (15).

LD_{50} dermal rabbit >4000 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rat (2 wk, 13 wk, 12 month) given 2000, 500 or 200 mg kg^{-1}, respectively, in diet. Only treatment-related effects regardless of duration of exposure were increase in liver to body weight ratio, slight hypertrophy and pallor of the centrilobular hepatocytes. No-observable-effect level was 20 mg kg^{-1} day^{-1} for 12-month study (16). LC_{50} (8 day) oral mallard duck, ring-necked pheasant, quail >5000 mg kg^{-1} in diet (6).

Carcinogenicity and chronic effects

Rats (2 yr) 0, 20, 60 or 200 mg kg^{-1} day^{-1} in feed. Primary treatment-related effects observed were hepatocellular swelling and altered tinctorial properties in the central regions of liver lobules and increased liver weight at high doses. No treatment-related increase in the incidence of tumours (17).

Metabolism and toxicokinetics

Intravenous ♂ Fischer 344 rats 10 mg kg^{-1} excreted unchanged in urine and faeces (18).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA97/TA1537 with and without metabolic activation negative (19).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticide: maximum admissible concentration 0.1 μg l^{-1} (20).
WHO Toxicity Class Table 5 (21).
EPA Toxicity Class IV (formulation) (2).
ADI 0.2 mg kg^{-1} (2).

Other comments

Toxicology and human health effects reviewed (22,23).
Metabolic pathways reviewed (24).

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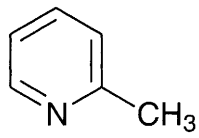
P183 2-picoline



C_6H_7N **Mol. Wt.** 93.13 **CAS Registry No.** 109-06-8

Synonyms 2-methylpyridine; α-methylpyridine; *o*-picoline; α-picoline

EINECS No. 203-643-7 **RTECS No.** TJ 4900000

Uses Solvent. Dye and resin intermediate.

Occurrence In coal tar and bone oil. Produced in coal and shale oil gasification. Identified in cigarette smoke (1).

Physical properties

M. Pt. -70°C **B. Pt.** 128-129°C **Specific gravity** 0.950 at 15°C with respect to water at 4°C

Partition coefficient log P_{ow} 1.06 (1) **Volatility** v.p. 8 mmHg at 20°C

Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2313 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Supply classification harmful

Risk phrases Flammable – Harmful by inhalation, in contact with skin and if swallowed – Irritating to eyes and respiratory system (R10, R20/21/22, R36/37)

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 – Wear suitable protective clothing (S2, S26, S36)

Ecotoxicity

Invertebrate toxicity

LC_{100} (24 hr) *Tetrahymena pyriformis* 6.0 g l^{-1} (2).

EC_{50} (30 min) *Photobacterium phosphoreum* 109 ppm Microtox test (3).

Toxic to *Nitzschia closterium* at 93.7 mg l^{-1}. Reported in oil shale waste waters at 3.7-46.8 mg l^{-1} (4).

Bioaccumulation

Bioconcentration factor of 4 predicted (5).

Bioconcentration not significant in organisms (6).

Environmental fate

Nitrification inhibition

100 mg l^{-1} (activated sludge) inhibited NH_3 oxidation by 40% (7).

Degradation studies

ThOD 2.75 mg l^{-1} O_2 (8).

Readily biodegradable (9).

Completely removed in 8 months under sulfate-reducing conditions in aquifer slurries (10).

93.7 mg with a fertile garden soil inoculum 100% degraded in 14-32 days (11).

187 μg g^{-1} incubated in silt loam soil, 2.7% remained after 16 days (12).

Abiotic removal

Reacts with hydroxyl radicals and scavenged by rain in the atmosphere $t_{1/2}$ 11.2 days (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling, quail >1000 mg kg^{-1} (13).
LD_{50} oral mouse, rat, guinea pig 674-900 mg kg^{-1} (14).
LC_{Lo} (4 hr) inhalation rat 4000 ppm (15).
LD_{50} dermal rabbit 410 mg kg^{-1} (5).
LD_{50} intraperitoneal rat 200 mg kg^{-1} (16).

Carcinogenicity and chronic effects

Carcinogenicity not determined, but expected to be non-carcinogenic from structure (17).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 with and without metabolic activation negative (18).

Legislation

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

Other comments

Reviews on human health effects, experimental toxicology, environmental effects and physico-chemical properties listed (20).
Characteristic sweet odour.

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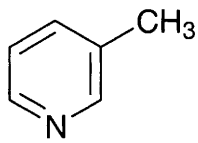
P184 3-picoline



C_6H_7N **Mol. Wt.** 93.13 **CAS Registry No.** 108-99-6

Synonyms 3-methylpyridine; β-methylpyridine; *m*-picoline; β-picoline

EINECS No. 203-636-9 **RTECS No.** TJ 5000000

Uses Solvent. Dye and resin intermediate. In manufacture of waterproofing agents, insecticides, niacin and niacinamide.

Physical properties

B. Pt. 143-144°C **Specific gravity** 0.9613 at 15°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.20
Solubility Water: miscible. Organic solvents: acetone, diethyl ether (miscible), ethanol

Occupational exposure

UN No. 2313 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 74.0 ppm Microtox test (1).
EC_{50} (2.5 day) *Tetrahymena pyriformis* 862.4 mg l^{-1} (2).

Environmental fate

Nitrification inhibition
100 mg l^{-1} (activated sludge) did not inhibit NH_3 oxidation (3).

Degradation studies
Only slightly degraded in methanogenic aquifer slurry (4).
Partially transformed (26%) in 8 months under sulfate-reducing conditions in aquifer slurries (4).
Adapted or fresh sludge is able to biodegrade wastewater containing ≥312 mg l^{-1} pyridine bases (5).
ThOD, 2.75 mg kg^{-1} O_2; COD, 4% ThOD (0.05 N $K_2Cr_2O_7$); $KMnO_4$, 2% ThOD (0.01 N $KMnO_4$) (6).
River water oxidation substrate, chemical analysis, 20% for 2 days. Observed feed, 1 mg l^{-1} 100% removed after 16 day acclimation (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, quail, starling >1000 mg kg^{-1} (8).
LD_{50} intraperitoneal rat, mouse 150, 596 mg kg^{-1}, respectively (9,10).
LD_{50} intravenous mouse 298 mg kg^{-1} (10).

Carcinogenicity and chronic effects
Carcinogenicity not determined, but from structure expected to be non-carcinogenic (11).

Irritancy
A man occupationally exposed to a number of chemicals, predominantly 3-picoline, developed skin eruptions on his face (12).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 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

Reviews on human health effects, experimental toxicology and environmental effects listed (15).

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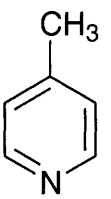
P185 4-picoline



C_6H_7N **Mol. Wt.** 93.13 **CAS Registry No.** 108-89-4

Synonyms 4-methylpyridine; Ba 35846; γ-methylpyridine; *p*-picoline; γ-picoline

EINECS No. 203-626-4 **RTECS No.** UT 5425000

Uses In manufacture of isonicotinic acid and derivatives. In waterproofing agents for fabrics. Solvent for resins.
Occurrence In coal tar, bone oil, urine of horses.

Physical properties

M. Pt. 2.4°C **B. Pt.** 145°C **Flash point** 57°C (open cup) **Specific gravity** 0.9571 at 15°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.22 **Volatility** v.p. 4 mm Hg at 20°C ; v.den. 3.21
Solubility Water: soluble. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

UN No. 2313 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid
Supply classification toxic
Risk phrases Flammable – Harmful by inhalation and if swallowed – Toxic in contact with skin – Irritating to eyes, respiratory system and skin (R10, R20/22, R24, R36/37/38)
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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 402.8 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 26.9 ppm Microtox test (2).
EC_{50} (60 hr) *Tetrahymena pyriformis* 730 mg l^{-1} (3).

Environmental fate

Nitrification inhibition
1.0 mg l^{-1} inhibited nitrification by 50% (4).
100 mg l^{-1} (activated sludge) inhibited NH_3 oxidation by 90% (5).

Degradation studies
In methanogenic incubations 47-84% of 4-picoline was recovered as CH_4 (6).
Biotransformed within 3 months under sulfate-reducing conditions in aquifer slurries (6).
Adapted or fresh sludge is able to biodegrade wastewater containing ≤312 mg l^{-1} pyridine bases (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, starling, quail 100-1000 mg kg^{-1} (8).
LD_{50} oral rat 1290 mg kg^{-1} (9).
LC_{Lo} (4 hr) inhalation rat 1000 ppm (10).
LD_{50} dermal rabbit 270 mg kg^{-1} (10).
LD_{50} intraperitoneal rat 163 mg kg^{-1} (11).

Carcinogenicity and chronic effects
Carcinogenicity not investigated, but expected to be negative (12).

Metabolism and toxicokinetics
Unmetabolised 4-picoline found in expired air and urine, for 24 hr following exposure, of rats treated with 300 mg kg^{-1} (13).

Irritancy
Dermal rabbit 10 mg applied for 24 hr (open) caused severe irritation (10).
750 μg instilled into rabbit eye caused severe irritation (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 with and without metabolic activation negative (14).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties and environmental effects listed (16).

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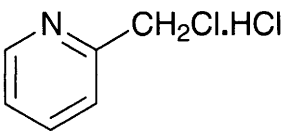
P186 2-picolyl chloride hydrochloride



$C_6H_7Cl_2N$ **Mol. Wt.** 164.03 **CAS Registry No.** 6959-47-3

Synonyms 2-chloromethylpyridine hydrochloride; 2-pyridylmethyl chloride hydrochloride

EINECS No. 230-149-9

Physical properties

M. Pt. 125-127°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 316 mg kg^{-1} (1).

Carcinogenicity and chronic effects

The National Toxicology Program tested rats and mice via gavage. No evidence of carcinogenic activity in ♂ or ♀ rats or mice (2).

In a 99-wk study with rats and mice, orally administered 2-picolyl chloride (dose unspecified) was not found to be carcinogenic (3).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (4).
The free base is mutagenic to *Salmonella typhimurium* TA97, TA98, TA100, TA102 with and without metabolic activation (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

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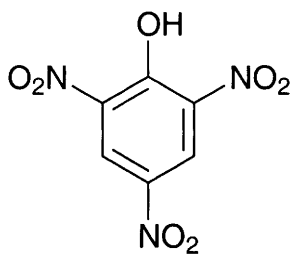
P187 picric acid



$C_6H_3N_3O_7$ **Mol. Wt.** 229.11 **CAS Registry No.** 88-89-1

Synonyms carbazotic acid; C.I. 10305; 2-hydroxy-1,3,5-trinitrobenzene; melinite; nitroxanthic acid; phenol trinitrate; picronitric acid; 2,4,6-trinitrophenol

EINECS No. 201-865-9 **RTECS No.** TJ 7875000

Uses Bacteriocide. Catalyst. Organic synthesis. Manufacture of explosives. Textile mordant.

Physical properties

M. Pt. 121-123°C **B. Pt.** >300°C (explodes) **Flash point** 150°C **Specific gravity** 1.763
Partition coefficient log P_{ow} 2.03 (1) **Volatility** v.p. <1 mmHg at 20°C ; v.den. 7.91
Solubility Water: 14 g l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

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 explosive, toxic
Risk phrases Risk of explosion by shock, friction, fire or other sources of ignition – Forms very sensitive explosive metallic compounds – Toxic by inhalation, in contact with skin and if swallowed (R2, R4, 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 followed by polyethylene glycol (mol. wt. 300) for at least 30 minutes – This material and its container must be disposed of in a safe way – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S35, S37, S45)

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 540 ppm, Microtox test (2).

Environmental fate

Degradation studies
2% removal after 48 hr at 220 mg l^{-1} in adapted culture (3).
ThOD 0.98 mg l^{-1} O_2; COD 0.92 mg l^{-1} O_2 (4).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral guinea pig, rabbit, cat 100, 120, 250 mg kg^{-1}, respectively (5,6).
LD_{Lo} subcutaneous dog, guinea pig, 60, 200 mg kg^{-1}, respectively (6).

Irritancy
Designated a mild eye irritant using modified Draize test (7).

Sensitisation
Local skin and generalised allergic reactions have been reported following dermal exposure (8).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (9,10).
Drosophila melanogaster sex-linked recessive lethal mutations and reciprocal translations negative (11).
In vivo mouse bone marrow cells, micronucleus assay negative (10).

Other effects

Other adverse effects (human)
Ingestion or dermal absorption may cause nausea, vomiting, diarrhoea, abdominal pain, oliguria, anuria, yellow staining of the skin (not icterus), pruritus, skin eruptions, stupor, convulsions and death (8).
High doses may cause destruction of red blood cells and damage to the kidney and liver (12).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).

Other comments

US EPA 1988 reference dose 0.00005 mg kg^{-1} day^{-1} for chronic toxicity. US Army Center for Health Promotion and Preventive Medicine reference dose 0.03 mg kg^{-1} day^{-1} based on the chronic toxic effects on haematological and histopathological changes in mammalian testes and kidney (14).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (15).
Autoignition temperature 250°C.

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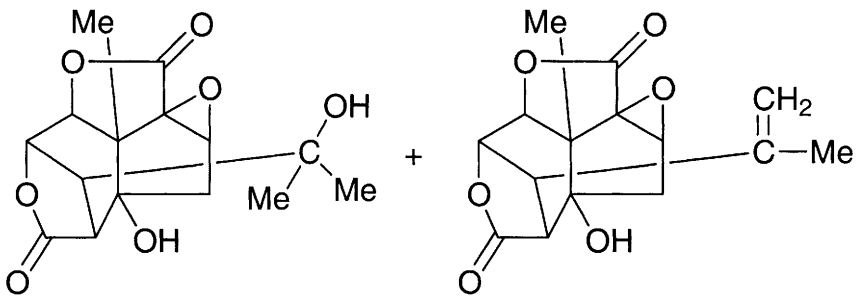
P188 picrotoxin



$C_{30}H_{34}O_{13}$ **Mol. Wt.** 602.59 **CAS Registry No.** 124-87-8

Synonyms Cocculin

EINECS No. 204-716-6 **RTECS No.** TJ 9100000

Uses Central nervous system stimulant. Antidote to barbiturates. Fish poison. Analeptic and respiratory stimulant. Memory enhancer and attention increasing drug.

Occurrence Isolated from the seed of *Anamirta cocculus* L., *Mensipermum cocculus*, and in *Tinomiscium philippinense* Diels.

Physical properties

M. Pt. 200-203°C

Solubility Water: 3 g l^{-1}. Organic solvents: chloroform, diethyl ether, ethanol, glacial acetic acid, pyridine

Occupational exposure

UN No. 3172

Ecotoxicity

Fish toxicity

Fatal to stickleback in 8-12 hr, and to brown trout and sockeye salmon in 4-6 hr at 10 mg l^{-1}. 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 (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral human 357 μg kg^{-1} (2).
LD_{50} oral mouse 15 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 7.2 mg kg^{-1} (3).
LD_{50} subcutaneous rat, mouse 2.9, 4.1 mg kg^{-1}, respectively (4,5).
LD_{50} intravenous rat, mouse 1.6, 2.4 mg kg^{-1}, respectively (6,7).

Other effects

Other adverse effects (human)

A case of poisoning was reported in a woman who ate a fish that has been killed with picrotoxin. She developed headache, chills, salivation and loss of vision with the pupils dilated and unreactive. Both retinas were observed to be oedematous (8).

Any other adverse effects

Single dose of 3 μg was injected into different brain areas of anaesthetised rabbits. Ventricular arrhythmia was most pronounced after a latency period of 5-8 min in posterior hypothalamus and medial part of the tuberal region (9).

Intraperitoneal rat single injection of 1.25-5.0 mg kg^{-1} induced dose-related effects from no effect at 1.25 mg kg^{-1} to generalised convulsions at the high dose. Chronic administration of 1.25 mg kg^{-1} day^{-1} induced convulsive, kinetic and emotional-behavioural disturbances with exaggerated defensive reflexes. These syndromes had a specific EEG pattern in the hippocampus, nucleus condatus, cortex and cerebellum (10).

Picrotoxin binds to allosterically coupled sites on the $GABA_A$ receptor complex, inhibiting the receptor currents (11).

Other comments

Picrotoxin comprises a 1:1 mixture of picrotoxinin (17617-45-7) and picrotin (21416-53-5).

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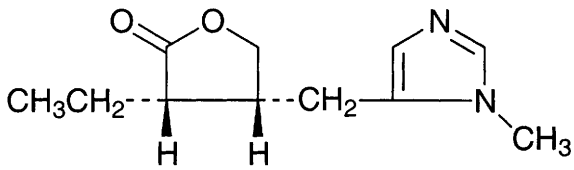
P189 pilocarpine



$C_{11}H_{16}N_2O_2$ **Mol. Wt.** 208.26 **CAS Registry No.** 92-13-7

Synonyms (3*S*-*cis*)-3-ethyldihydro-4-[(1-methyl-1*H*-imidazol-5-yl)methyl]-2(3*H*)-furanone; α-ethyl-β-(hydroxymethyl)-1-methylimidazole-5-butyric acid, γ-lactone; Ocusert Pilo; (+)-pilocarpine; pilocarpol

EINECS No. 202-128-4 **RTECS No.** TK 1400000

Uses Parasympathomimetic drug used in the treatment of glaucoma.
Occurrence In *Pilocarpus jaborandi* Holmes.

Physical properties

M. Pt. 34°C **B. Pt.** 260°C at 5 mmHg
Solubility Water: miscible. Organic solvents: benzene, chloroform, diethyl ether, ethanol, methanol

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 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 120, 400 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous rat, mouse 90, 370 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal rat 170 mg kg^{-1} (2).
LD_{50} intravenous mouse, rat 62, 89 mg kg^{-1}, respectively (2).

Sub-acute and sub-chronic data
In anaesthetised rats, intravenous administration (dose unspecified) produced dose-dependent increases in the frequency of hippocampal theta rhythm and blood pressure. The low response of theta wave frequency indicated that pilocarpine acted as a partial muscarinic antagonist (3).
Oral meadow vole, 0.001, 0.01 or 0.1% diet (duration unspecified) reduced the weight of the parotid gland by up to 31%. Serum transaminases and alkaline phosphatase activities were not affected. Histopathological examination showed liver and kidney damage at the high dose (4).

Other effects

Other adverse effects (human)
Following ocular administration may produce cilary spasm, ocular pain and irritation, blurred vision, myopia and browache. May also induce bronchospasm in susceptible patients and detached retina (5).

Any other adverse effects
EC_{50} *in vitro* stimulation of phosphoinositide turnover in the hippocampus (M_1/M_3 responses) 3700 mg l^{-1}, displaying 35% of the maximal carbachol response. Behaviourly pilocarpine restored deficits in a representational memory task (species unspecified) (6).

Inhibited lymphocyte basal DNA synthesis and proliferative responses to phytohaemaglutinin. The authors suggested that pilocarpine may be specific for the M_1 muscarinic receptor. Pilocarpine also inhibited the phytohaemaglutinin-induced production of γ-interferon, but was unable to reverse the pokeweed mitogen-induced DNA synthesis (7).

Other comments

Rapidly decomposed in eye drop solution to give isopilocarpine, pilocarpic acid and isopilocarpic acid (8). Used principally as the hydrochloride or nitrate (6).

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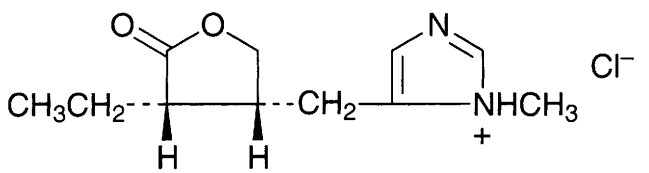
P190 pilocarpine hydrochloride



$C_{11}H_{17}ClN_2O_2$ **Mol. Wt.** 244.72 **CAS Registry No.** 54-71-7

Synonyms 3-ethyldihydro-4-[(1-methyl-*H*-imidazol-5-yl)methyl]-2(3*H*)-furanone, monohydrochloride; pilocarpine, monohydrochloride; pilocarpine muriate; pilocarpinium chloride; pilocarpine chloride

EINECS No. 200-212-5 **RTECS No.** TK 1450000

Uses Parasympathomimetic drug.

Physical properties

M. Pt. 204-205°C

Solubility Water: miscible. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 200 mg kg^{-1} (1).

LD_{50} subcutaneous rat, mouse 200-230 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 150-160 mg kg^{-1} (1,2).

Teratogenicity and reproductive effects

Subcutaneous rabbit, lowest toxic dose 20 mg kg^{-1} day^{-1} on days 24-27 of gestation, teratogenic effects (3).

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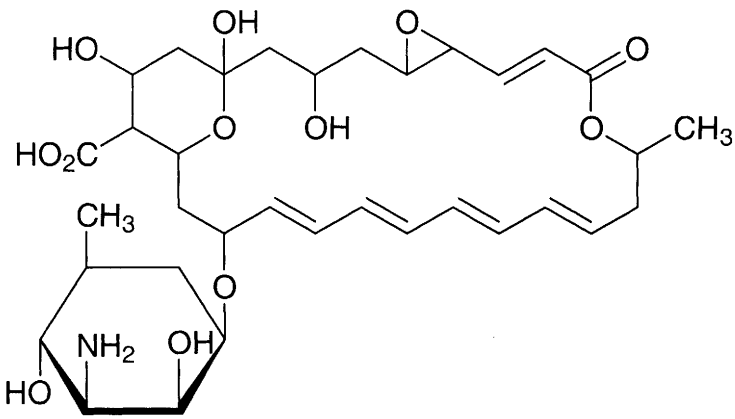
P191 pimaricin



$C_{33}H_{47}NO_{13}$ **Mol. Wt.** 665.74 **CAS Registry No.** 7681-93-8

Synonyms Tennecatin; Myprozine; Natamycin; Pimafucin

EINECS No. 231-683-5 **RTECS No.** TK 3325000

Uses Antibiotic. Fungicide.

Occurrence Isolated from *Streptomyces chattanoogenesis* and *Streptomyces natalensis*.

Physical properties

M. Pt. 200°C (decomp.) **Specific gravity** 1.020

Solubility Water: 4100 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, dimethyl sulfoxide, dioxane, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, mouse 2730, 1420, 1500 mg kg^{-1}, respectively (1,2).

LD_{50} intramuscular rat 130 mg kg^{-1} (3).

LD_{50} subcutaneous rat 190 mg kg^{-1} (3).

LD_{50} intravenous rat, dog 18, 36 mg kg^{-1}, respectively (3).

LD_{50} intraperitoneal rat, mouse 85, 96 mg kg^{-1}, respectively (3,4).

Genotoxicity

Aspergillus nidulans induction of mitotic non-disjunction positive (5).

Other effects

Other adverse effects (human)

May cause gastro-intestinal disturbance following oral administration of large doses. Topical application has caused irritation in some cases (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).

References

1. Levinskas, J. et al *Toxicol. Appl. Pharmacol.* 1966, **8**, 97.
2. *Index of Antibiotics from Actinomyces* 1967, 517, University of Tokyo Press, Tokyo, Japan.
3. *Antibiotics for Chemotherapy* 1959, **406**, 9.
4. *Drugs in Japan: Ethical Drugs* 6th ed., 1982, 639, Jakugyoc Jiho Co. Tokyo, Japan.
5. Bellincampi, D. et al *Mutat. Res.* 1980, **79**, 169-172.
6. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, 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 Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

P192 pinacolone

$$(CH_3)_3C(O)CH_3$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 75-97-8

Synonyms 3,3-dimethyl-2-butanone; *tert*-butyl methyl ketone; 2,2-dimethylbutanone; 3,3-dimethylbutanone; 1,1-dimethylethyl methyl ketone; pinacolin; 1,1,1-trimethylacetone

EINECS No. 200-920-4 **RTECS No.** EL 7700000

Uses Chemical intermediate.

Physical properties

M. Pt. –52.5°C **B. Pt.** 106.2°C **Flash point** 19°C **Specific gravity** 0.7250 at 25°C with respect to water at 25°C

Partition coefficient log P_{ow} 0.94 (1)

Solubility Water: 2.44% at 15°C. Organic solvents: acetone, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 87 mg l^{-1} flow-through bioassay (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, mouse 610-1625 mg kg^{-1} (3).

LD_{50} subcutaneous guinea pig 700 mg kg^{-1} (4).

References

1. Ahernethy, S. G. et al *Environ. Toxicol. Chem.* 1988, **7**(6), 469-481.
2. Veith, G. D. et al *Can. J. Fish Aquat. Sci.* 1983, **45**(1), 312.
3. *Gig. Sanit.* 1987, **52**(12), 91.
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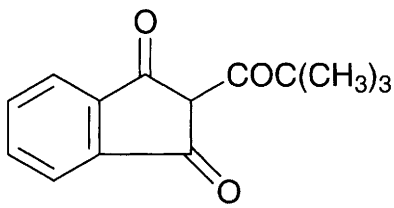
P193 pindone



$C_{14}H_{14}O_3$ **Mol. Wt.** 230.26 **CAS Registry No.** 83-26-1

Synonyms 2-(2,2-dimethyl-1-oxopropyl)-1*H*-indene-1,3(2*H*)-dione; 2-pivaloylindan-1,3-dione; 2-pivalyl-1,3-indandione; pivaldione; Pival; Pivacin; Pivalyl Valone; Tri-ban; Chemrat; Contrax-P; Parakakes

EINECS No. 201-462-8 **RTECS No.** NK 6300000

Uses Rodenticide. Rabbit poison. Organic synthesis.

Physical properties

M. Pt. 108.5-110.5°C **B. Pt.** 180°C at 1 mmHg **Specific gravity** 1.06
Solubility Water: 18 mg l^{-1} at 25°C. Organic solvents: acetone, ammonia, diethyl ether, ethanol

Occupational exposure

FR-VME 0.1 mg m^{-3}
US-TWA 0.1 mg m^{-3}

UN No. 2472
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)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout 0.21, 1.6 mg l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral dog, rabbit, rat 75-100, 150-170, 280 mg kg^{-1}, respectively (1,2).
LD_{50} intravenous rat 50 mg kg^{-1} (3).

Sub-acute and sub-chronic data

LC_{50} (8 day) mallard duck, bobwhite quail 250, 1560 mg kg^{-1}, respectively diet (4).

Oral dog, goat, cat, cattle, horse and chicken 0.3-2.5 mg kg^{-1} (duration unspecified) caused a significant extension of prothrombin time in all species except the horse. $t_{1/2}$ for elevated prothrombin time was 1.9-3.1 days (5).

Oral rabbit, 1 mg kg^{-1} day^{-1} gave average survival times of 7-10 days. Widespread haemorrhage occurred throughout the muscles and some organs in rabbits that died (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).

Other effects

Any other adverse effects

Inhibits blood coagulation by blocking prothrombin formation (1).

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 II (10).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (11).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Gaines, T. B. *Toxicol. Appl. Pharmacol.* 1969, **14**, 515.
3. *Yakkyoku* 1980, **31**, 1385.
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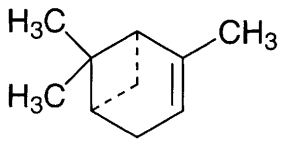
5. Martin, G. R. et al *Aust. Vet. J.* 1991, **68**(7), 241-243.
6. Oliver, A. J. et al *Aust. Wildl. Res.* 1978, **5**(1), 135-142.
7. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
8. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
9. *S. I. 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. *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

P194 (1*S*)-(–)-α-pinene



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 7785-26-4

Synonyms (–)-pinene; (1*S*,5*S*)-(–)-2-pinene; (1*S*)-2,6,6-trimethylbicyclo[3.3.1]hept-2-ene

EINECS No. 232-077-3

Uses Organic synthesis.

Occurrence In plant oils.

Physical properties

M. Pt. –64°C **B. Pt.** 155-156°C **Flash point** 32°C **Specific gravity** 0.8592 at 20°C with respect to water at 4°C

Solubility Organic solvents: vegetable oils

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

UN No. 2368 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

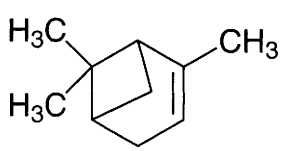
Metabolism and toxicokinetics

Following inhalation exposure in humans (2 hr on bicycle ergonometer) to 450 mg m^{-3}, the relative pulmonary uptake was ~60%. Total blood clearance was ~1.1 l hr^{-1} kg^{-1}. After exposure was terminated <0.001% of the total uptake was eliminated unchanged in the urine and ~8% in exhaled air. A high affinity for adipose tissue was indicated (1).

References

1. Falk, A. A. et al *Scand. J. Work, Environ. Health* 1990, **16**(5), 372-378

P195 α-pinene



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 80-56-8

Synonyms 2,6,6-trimethylbicyclo[3.1.1]hept-2-ene; 2-pinene

EINECS No. 201-291-9 **RTECS No.** DT 7000000

Uses Fragrance. Organic synthesis.

Occurrence In oil of turpentine (58-65%) and in many plant oils. Insect attractant. Residues are detectable in paper mill wastewater (1).

Physical properties

M. Pt. –55°C **B. Pt.** 155-156°C **Flash point** 33°C **Specific gravity** 0.859 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 4.12 (calc.) (2) **Volatility** v.p. 5 mmHg at 25°C ; v.den. 4.72
Solubility Organic solvents: vegetable oils

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

UN No. 2368 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity
Pinene, unspecified isomer, was reported to be non-toxic to brown trout, bluegill sunfish, yellow perch and goldfish at 5 ppm for 24 hr. 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; temperature 12.8°C (3).

Invertebrate toxicity
LD_{Lo} *Erwinia amylovora* 1500 mg l^{-1} (4).

Bioaccumulation
Calculated bioconcentration factor 800 (5).

Environmental fate

Degradation studies
No methanogenic biodegradation was observed at concentrations up to 200 mg l^{-1} in wastewater (1).

Abiotic removal
Calculated volatilisation $t_{1/2}$ 3.4 hr in model river water (5).
Reacts with photochemically produced hydroxyl radicals and ozone in the atmosphere, estimated $t_{1/2}$ 1.2-4.6 hr (6).

Adsorption and retention
Estimated K_{oc} 4200 indicates that α-pinene will adsorb to soil and sediments (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3700 mg kg^{-1} (7).
LC_{Lo} inhalation rat, mouse, guinea pig 360-625 μg m^{-3} (duration unspecified) (7).

Carcinogenicity and chronic effects
A CASE study reported a negative result for prediction of carcinogenicity (8).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (7).

Legislation

Log P_{ow} exceeds the European Union recommended limit of 3.0 (9).

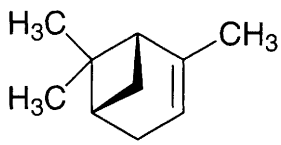
Other comments

α-pinene is dextrorotatory in most North American plant oils, and laevorotatory in most European plant oils (10).
Autoignition temperature 255°C.

References

1. Sierra-Alvarez, R. et al *Environ. Technol.* 1990, **11**(10), 891-898.
2. *GEMS: Graphic Exposure Modeling System: Fate of Atmospheric Pollutants* 1987, US EPA Washington, DC, USA.
3. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, PB 87-200-275, Washington, DC, USA.
4. Sartichini, M. et al *J. Appl. Microbiol.* 1991, **71**(2), 109-112.
5. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, NY, USA.
6. Winer, A. M. et al *Science (Washington, DC 1883-)* 1984, **224**, 156-159.
7. *Food Cosmet. Toxicol.* 1978, **16**, 637.
8. Rosenkranz, H. S. et al *Carcinogenesis (London)* 1990, **11**(2), 349-353.
9. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
10. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

P196 (1*R*)-(+)-α-pinene



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 7785-70-8

Synonyms (1*R*)-2,6,6-trimethylbicyclo[3.1.1]hept-2-ene; (+)-2-pinene; (+)-α-pinene; (1*R*,5*R*)-(+)-2-pinene

EINECS No. 232-087-8

Uses Organic synthesis.

Occurrence In plant oils.

Physical properties

M. Pt. –62°C **B. Pt.** 155-156°C **Flash point** 32°C **Specific gravity** 0.857

Solubility Organic solvents: vegetable oils

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

UN No. 2368 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

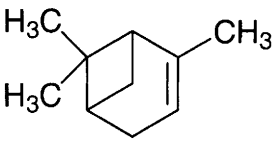
Metabolism and toxicokinetics

Following inhalation exposure in humans (2 hr on bicycle ergonometer) to 10, 225 or 450 mg m^{-3}, the relative pulmonary uptake was ~60%. Total blood clearance was ~1.1 l hr^{-1} kg^{-1}. After exposure as terminated < 0.001% of the total uptake was eliminated unchanged in the urine and ~8% in exhaled air. A high affinity for adipose tissue was indicated (1).

References

1. Falk, A. A. et al *Scand. J. Work, Environ. Health* 1990, **16**(5), 372-378

P197 (±)-α-pinene



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 2437-95-8

Synonyms (±)-2,6,6-trimethylbicyclo[3.1.1]hept-2-ene; (±)-2-pinene

EINECS No. 219-445-9

Occurrence In plant oils.

Physical properties

B. Pt. 155-156°C **Flash point** 32°C **Specific gravity** 0.858 at 20°C with respect to water at 4°C
Solubility Organic solvents: vegetable oils

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

UN No. 2368 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Environmental fate

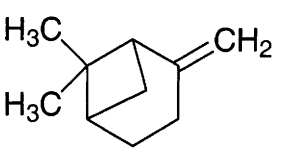
Degradation studies

Degraded by the honey fungus *Armillaria mellea*; transformation proceeds enantioselectively and (±)-α-pinene oxidises (via α-terpineol) to (4*S*)-*trans*-solorerol faster than to the (4*R*)- isomer (1).

References

1. Draczynska-Lusiak, B. et al *J. Basic Microbiol.* 1989, **29**(5), 269-275

P198 β-pinene



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 127-91-3

Synonyms 6,6-dimethyl-2-methylenebicyclo[3.1.1]heptane; nopinene; pseudopinene; 2(10)-pinene

EINECS No. 204-872-5 **RTECS No.** DT 5077000

Uses Chemical intermediate. Insect attractant. Fragrance.

Occurrence Oil of turpentine. In plant oils. Aroma component in some cooked meats and dairy products. Residues have been identified in water samples (1,2).

Physical properties

M. Pt. –61°C **B. Pt.** 165-167°C **Specific gravity** 0.859 at 20°C with respect to water at 4°C
Solubility Organic solvents: benzene, diethyl ether, dimethylformamide, dimethyl sulfoxide, ethanol, vegetable oils

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

Ecotoxicity

Fish toxicity
Pinene, unspecified isomer, was reported to be non-toxic to brown trout, bluegill sunfish, yellow perch and goldfish at 5 ppm for 24 hr (3).

Invertebrate toxicity
LC_{Lo} *Erwinia amylovora* 1500 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4700 mg kg^{-1} (5).

Carcinogenicity and chronic effects
A CASE study reported a negative result for prediction of carcinogenicity (6).

Metabolism and toxicokinetics
In the brushtail possum β-pinene was metabolised to myrtenic acid (7).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (5).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (8).
In vitro Chinese hamster ovary cells sister chromatid exchanges negative (metabolic activation unspecified) (9).

Other effects

Any other adverse effects
Inhibited oxidative phosphorylation in isolated rat liver mitochondria in a dose-dependent manner (10).

Other comments

Taste taint in water, especially when chlorinated (11).

References

1. Dykhanov, N. N. et al *Form. Kontrol Kach. Poverkhn. Vod.* 1976, **3**, 21 (*Chem. Abstr.* **91**, 205626j).
2. Richardson, M. L. *Compendium of Toxicological Ecological Data on Chemicals Found by GC/MS in Water Samples* 1985, Thames Water Authority, Reading, UK.
3. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, PB 87-200-275, Washington, DC, USA.
4. Scortichini, M. et al *J. Appl. Bacteriol.* 1991, **71**(2), 109-112.
5. Opdyke, D. L. J. *Food Cosmet. Toxicol.* 1978, **16**, 859.
6. Rosenkranz, H. S. et al *Carcinogenesis* 1990, **11**(2), 349-353.
7. Southwell, I. A. et al *Xenobiotica* 1980, **10**, 17.
8. Florin, I. et al *Toxicology* 1980, **15**, 219.
9. Sasaki, Y. F. et al *Mutat. Res.* 1989, **226**(2), 103-110.
10. Uribe, S. et al *Xenobiotica* 1991, **21**(5), 679-688.
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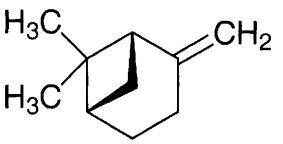
P199 (1*S*)-(–)-β-pinene



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 18172-67-3

Synonyms (1*S*)-6,6-dimethyl-2-methylenebicyclo[3.1.1] heptane; *l*-β-pinene; (–)-norpinene

EINECS No. 242-060-2 **RTECS No.** DT 5077000

Occurrence In plant oils.

Physical properties

M. Pt. –61°C **B. Pt.** 165-167°C **Flash point** 32°C **Specific gravity** 0.859 **Volatility** v.p. ~2 mmHg at 20°C ; v.den. 4.7

Solubility Organic solvents: vegetable oils

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit 4700 mg kg^{-1} (1).

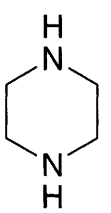
Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (1).

References

1. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2841, Sigma-Aldrich, Milwaukee, WI, USA

P200 piperazine



$C_4H_{10}N_2$ **Mol. Wt.** 86.14 **CAS Registry No.** 110-85-0

Synonyms 1,4-diethylenediamine; *N,N*-diethylenediamine; dispermine; hexahydropyrazine; hexahydro-1,4-diazine; Lumbrical; piperazidine; pyrazine hexahydride; Worm-away; Wurmirazin

EINECS No. 203-808-3 **RTECS No.** TK 7800000

Uses Anthelmintic. Organic synthesis. Corrosion inhibitor. Insecticide.

Physical properties

M. Pt. 108-110°C **B. Pt.** 145-146°C **Flash point** 81°C (open cup) **Specific gravity** 1.1 at 20°C
Volatility v.p. >1.0 mmHg at 20°C ; v.den. 3.0
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol, glycerol, glycols

Occupational exposure

FR-VME 5 mg m^{-3} (as the dihydrochloride)
SE-LEVL 0.1 ppm (0.3 mg m^{-3}) **SE-STEL** 0.3 ppm (1 mg m^{-3})
UK-LTEL 5 mg m^{-3} (as the dihydrochloride)

UN No. 2579 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Causes burns – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment – May cause sensitisation by inhalation and skin contact (R34, R52/53, R42/43)
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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S22, S26, S36/37/39, S45, S61)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 600, 1900 mg kg^{-1}, respectively (1,2).
LC_{50} (2 hr) inhalation mouse 5400 mg m^{-3} (2).
LD_{50} dermal rabbit 4000 mg kg^{-1} (3).
LD_{50} subcutaneous rat 3700 mg kg^{-1} (4,5).
LD_{50} intravenous rat 1300 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Inhalation guinea pig 100 ppm 3 hr day^{-1} 7 × in 11 days caused no gross adverse effects (6).

Metabolism and toxicokinetics
Following inhalation exposure of human volunteers to 0.3 mg m^{-3} ~5% of absorbed piperazine was converted into *N*-mononitrosopiperazine which was eliminated in the urine. The degree of nitrosation was increased with high nitrate diets provided by spinach and beetroot (7).
Readily absorbed from the gastro-intestinal tract and excreted in the urine partly as metabolites (8).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation (3).
250 μg instilled into rabbit eye for 24 hr caused severe irritation (9).

Sensitisation
A study of exposed workers showed a strong association between piperazine exposure and asthma-like symptoms and chronic bronchitis (10).

Genotoxicity

No significant difference in chromosomal aberrations or frequency of micronuclei in lymphocytes was found in exposed workers in a chemical factory (11).
An increase in the size and frequency of micronuclei has been found in exposed workers at a chemical factory (12).

Other effects

Other adverse effects (human)

May produce severe neurotoxicity with high doses (8).

Has been used therapeutically during pregnancy with no adverse effects (13).

Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (15).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).

Other comments

Salmonella typhimurium TA1535 with and without metabolic activation, positive after nitrosation (17).

Used therapeutically as the adipate, citrate, hydrate or phosphate (8).

Physical properties, use, health hazards, mammalian toxicity and safety precautions reviewed (18,19).

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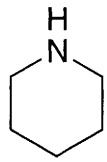
P201 piperidine



$C_5H_{11}N$ **Mol. Wt.** 85.15 **CAS Registry No.** 110-89-4

Synonyms azacyclohexane; cyclopentimine; cypentil; hexahydropyridine; hexazane; pentamethyleneimine; perhydropyridine

EINECS No. 203-813-0 **RTECS No.** TM 3500000

Uses Organic synthesis. Curing agent for epoxy resins. Catalyst. Solvent.
Occurrence Aroma component of cooked fish. Isolated from black pepper. Detected in cigarette smoke. Found in the brain, skin, milk and urine of mammals. Residues have been detected in natural and drinking waters (1).

Physical properties

M. Pt. –13°C **B. Pt.** 106°C **Flash point** 4°C (closed cup) **Specific gravity** 0.8622 at 20°C *with respect to* water at 4°C **Partition coefficient** log P_{ow} 0.84 **Volatility** v.p. 30 mmHg at 25°C ; v.den. 3.0
Solubility Water: miscible. Organic solvents: acetone, benzene, chloroform, ethanol

Occupational exposure

UK-LTEL 1 ppm (3.5 mg m^{-3})

UN No. 2401 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive
Supply classification highly flammable, toxic
Risk phrases Highly flammable – Toxic by inhalation and in contact with skin – Causes burns (R11, R23/24, R34)
Safety phrases Keep locked up and out of the 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 – 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, S16, S26, S27, S45)

Environmental fate

Degradation studies
Utilised as sole carbon, nitrogen and energy source by *Pseudomonas* sp. (2).
Biodegradation >30% ThOD in 2 wk with mixed soil and sewage inoculum (3).

Abiotic removal
Reacts with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 3.4 days (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rabbit, rat 30, 145, 490 kg^{-1} respectively (5-8).
LC_{50} (2 hr) inhalation mouse 6000 mg m^{-3} (5).
LD_{50} dermal rabbit 320 mg kg^{-1} (6).
LD_{50} intraperitoneal mouse 50 mg kg^{-1} (9).

Sub-acute and sub-chronic data
Inhalation rat, rabbit 10 mg m^{-3} daily for 4 months caused changes in the liver, kidneys, cardiovascular system, brain electrical activity and sperm production (10).

Teratogenicity and reproductive effects
Inhalation rat, lowest toxic concentration 3 mg m^{-3} for 24 hr on 4th day of gestation, teratogenic effects (5).
Inhalation rat, 2.9 ppm 4 hr day^{-1} for 4 months altered spermatogenesis in rats (10).

Metabolism and toxicokinetics
Reported to be readily absorbed through mammalian skin, gastro-intestinal tract and via lungs (11,12).
Major metabolites identified following intraperitoneal administration to rats were 3- and 4-hydroxypiperidine (13).

Irritancy
100 µg instilled into rabbit eye for 24 hr caused irritation (6).
Inhalation human volunteer, threshold concentration for irritation 90 mg m^{-3} (14).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1538 with and without metabolic activation positive (15).
In vitro mouse lymphoma L5178Y cells, tk^+/tk^- forward mutation assay with and without metabolic activation positive (16).
In vitro primary rat hepatocytes, DNA damage negative (17).

Other effects

Other adverse effects (human)
Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (18).

Other comments

Can undergo nitrosation *in vivo* to yield the carcinogenic 1-nitrosopiperidine (19).
Environmental fate reviewed (1).
Physical properties, use, hazards, toxicity and safety precautions reviewed (12,13,20,21).

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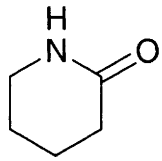
P202 2-piperidinone



C_5H_9NO **Mol. Wt.** 99.13 **CAS Registry No.** 675-20-7

Synonyms 2-piperidone; δ-valerolactam

EINECS No. 211-622-9 **RTECS No.** TO 0110000

Uses Organic synthesis.

Physical properties

M. Pt. 38-40°C **B. Pt.** 256°C **Flash point** >110°C

Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 600 mg kg^{-1} (1).

References

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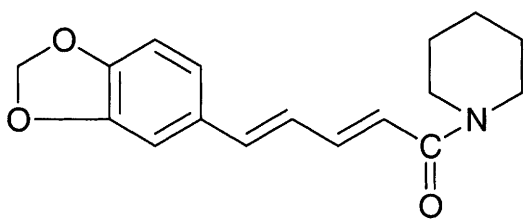
P203 piperine



$C_{17}H_{19}NO_3$ **Mol. Wt.** 285.34 **CAS Registry No.** 94-62-2

Synonyms (*E*,*E*)-1-[5-(1,3-benzodioxol-5-yl)-1-oxo-2,4-pentadienyl]piperidine; 1-piperoylpiperidine

EINECS No. 202-348-0 **RTECS No.** TN 2321500

Uses Flavouring agent. Insecticide.

Occurrence In black and white pepper.

Physical properties

M. Pt. 131-135°C

Solubility Water: 40 mg l^{-1} at 18°C. Organic solvents: acetic acid, benzene, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 510, 1600 mg kg^{-1}, respectively (1,2).
LD_{50} intramuscular mouse 400 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, hamster, mouse 34, 105, 1637 mg kg^{-1}, respectively (2).
LD_{50} subcutaneous mouse 200 mg kg^{-1} (2).
LD_{50} intravenous mouse 15 mg kg^{-1} (2).

Teratogenicity and reproductive effects

Oral mouse, lowest toxic dose 150 mg kg^{-1} day^{-1} on days 15-20 of gestation, teratogenic effects (3).

Other effects

Any other adverse effects

Intraperitoneal rat, single dose of 100 mg kg^{-1} produced a significant decrease in hepatic cytochrome P_{450} and in the activities of benzphetamine *N*-demethylase, aminopyrine *N*-demethylase and aniline hydroxylase 1 hr after treatment. After 24 hr, these parameters along with cytochrome b_5 and NADPH-cytochrome *c* reductase remained depressed (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).

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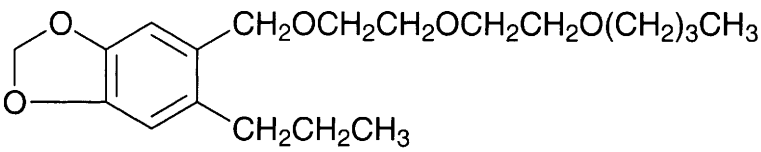
P204 piperonyl butoxide



$C_{19}H_{30}O_5$ **Mol. Wt.** 338.44 **CAS Registry No.** 51-03-6

Synonyms 5[(2-[2-butoxyethoxy]ethoxy)methyl]-6-propyl-1,3-benzodioxole; α-[2-(2-*n*-butoxyethoxy)ethoxy]-4,5-methylenedioxy-2-propyltoluene; butyl carbinol 6-propylpiperonyl ether; ENT 14250; (3,4-methylenedioxy-6-propylbenzyl)(butyl) diethylene glycol ether; NCI-C02813; 6-propylpiperonyl butyl diethylene glycol ether; pybuthrin; PBO-9; Butacide; Prentox

EINECS No. 200-076-7 **RTECS No.** XS 8050000

Uses Insecticide.

Physical properties

B. Pt. 155°C at 0.3 mmHg **Flash point** 170°C **Specific gravity** 1.059 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} 4.75
Solubility Water: practically insoluble. Organic solvents: acetone, dichlorofluoromethane, diethyl ether, ethanol, hexane, methanol, mineral oils, petroleum ether

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) carp 5.3 mg l^{-1} (1,2).
LC_{50} (96 hr) bluegill sunfish, rainbow trout 3.4, 4.2 μg l^{-1}, respectively (3).

Invertebrate toxicity
LC_{50} (96 hr) *Ascellus* 12 μg l^{-1} (3).
LD_{50} >25μg bee^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, starling >100 mg kg^{-1} (4).
LD_{50} oral rat, mouse, rabbit 2,600-13,000 mg kg^{-1} (5-9).
LD_{50} dermal rabbit 200-1900 mg kg^{-1} (1,10).
LD_{Lo} intraperitoneal mouse 1000 mg kg^{-1} (11).

Sub-acute and sub-chronic data
♂ mice and rats (7 and 42 days) 0, 10, 30, 100 or 300 and 0, 100, 550, 1050 or 1850 mg kg^{-1} day^{-1}, respectively, in diet. In both species relative liver weight increased and midzonal (mouse) or periportal/midzonal (rat) hypertrophy was observed. In rats, individual cell necrosis was observed at 42 days after high doses (12).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (13).
Gavage mouse (60 wk) 0, 100 or 460 mg kg^{-1} day^{-1} for 3 wk, subsequently 300 or 1100 mg kg^{-1} diet, respectively, for 57 wk. There was no significant difference in the incidence of tumours between treated mice and controls (14).
Oral mouse (112 wk) 2500 mg kg^{-1} diet for 30 wk then 500 mg kg^{-1} diet for 82 wk, or 5000 mg kg^{-1} diet for 30 wk then 1000 mg kg^{-1} diet for 82 wk. There was no significant difference in the incidence of tumours between treated and control mice (15).

Oral ♂ and ♀ CD-1 mice (52 wk) 0-1.2% piperonyl butoxide in diet. Hepatocellular carcinomas were found in 11.3 and 52.0% of ♂ mice receiving 0.6 and 1.2% piperonyl butoxide, respectively, and in 41.2% of ♀ mice given 1.2% piperonyl butoxide (16).

Oral rat (107 wk) 5000 or 10,000 mg kg^{-1} diet. Of the treated ♀ rats 7/50 low-dose and 15/50 high-dose animals developed lymphomas compared with 1/20 controls. There was no significant difference in the incidence of tumours between treated ♂ rats and controls. The validity of the dose-related incidence in tumours in ♀ rats was considered questionable in view of the high incidence of lymphomas and leukaemias in historical ♀ controls of that strain (15,17).

Subcutaneous mouse (74 wk) single injection of 100 or 1000 mg kg^{-1} on 28th day of life. No significant difference in tumour incidence was observed between treated and control animals (18).

Subcutaneous mouse (1 yr) single injection of 0.75 mg within 24 hr of birth. No significant difference in tumour incidence was observed between treated and control animals (19).

Teratogenicity and reproductive effects

Oral rat 63, 125, 250 or 500 mg kg^{-1} day^{-1} on days 6-15 of gestation caused no teratogenic effects (20).

Oral rat 0, 100, 1000, 10,000 or 25,000 mg kg^{-1} diet for three generations. None of the ♀ rats given the high dose were fertile, and there were marked reductions in the incidences of pregnancies and weight of weanlings of dams fed 10,000 mg kg^{-1} diet. No adverse effect on reproduction was observed in three generations of progency fed diets containing up to 1000 mg kg^{-1} (21).

Metabolism and toxicokinetics

Following intravenous administration to rats, the compound was widely distributed in tissues and prolonged biliary and urinary metabolites were noted. A large percentage of unchanged piperonyl butoxide was detected in lung and adipose tissue. After oral administration, piperonyl butoxide was poorly absorbed from the gut and rapidly eliminated in the urine and faeces (22).

Metabolism in mammals involves cleavage of the methylenedioxy ring and oxidative degradation of the side groups. Eliminated as the glucoside or amino acid derivative (1,23).

Genotoxicity

Salmonella typhimurium TA92, TA98, TA100, TA1535, TA1537, TA2637 with and without metabolic activation negative (24).

Bacillus subtilis H17 *rec*+ M45 *rec*– *rec* assay negative (25).

Drosophila melanogaster wing spot genotoxicity test negative (26).

In vitro Chinese hamster ovary cells with and without metabolic activation, sister chromatid exchanges and chromosomal aberrations negative (27).

In vivo rat bone marrow chromosomal aberrations negative (25).

In vivo mouse dominant lethal mutation assay negative (11).

Other effects

Other adverse effects (human)

A single oral dose of 50 mg (~0.71 mg kg^{-1}) to adult volunteers did not influence the metabolism of antipyrine, and no sign of toxicity was observed (28).

Any other adverse effects

Oral rat 600, 1200 or 8100 mg kg^{-1} caused a dose-related increase in liver GST activity. The low dose caused a slight decrease in cytochrome P_{450} activity (29).

Acute administration of high levels to mammals inhibited mixed-function oxidase activities. Chronic administration had a stimulating effect on these enzyme activities (28,30).

Signs of acute toxicity in laboratory animals include anorexia, vomiting, diarrhoea, haemorrhagic enteritis and bloody discharge from the nose and eyes (31).

Legislation

WHO Toxicity Class Table 5 (32).

EPA Toxicity Class IV (formulation) (2).

ADI (JMPR) 0.2 mg kg^{-1} body weight (2).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (33).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (34).

Other comments

Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (35).

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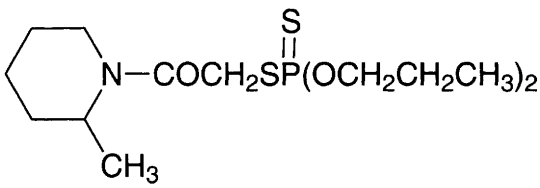
P205 piperophos



$C_{14}H_{28}NO_3PS_2$ **Mol. Wt.** 353.49 **CAS Registry No.** 24151-93-7

Synonyms *S*-[2-(2-methyl-1-piperidinyl)-2-oxoethyl] *O,O*-dipropyl phosphorodithioate; *S*-2-methylpiperidinocarbonylmethyl *O,O*-dipropyl phosphorodithioate; Rilof

RTECS No. TE 3690000

Uses Herbicide

Physical properties

B. Pt. 190°C (decomp.) **Specific gravity** 1.13 at 20°C **Partition coefficient** log P_{ow} 4.3 (1)
Volatility v.p. 2.4×10^{-7} mmHg at 20°C
Solubility Water: 25 mg l^{-1} at 20°C. Organic solvents: miscible with acetone, benzene, dichloromethane, hexane, octanol

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) crucian carp, rainbow trout 5-6 mg l^{-1} (1,2).

Invertebrate toxicity
LD_{50} bee, oral >22, contact 30 μg bee^{-1} (2).

Environmental fate

Degradation studies
$t_{1/2}$ ~70 days in soil (1,2).

Abiotic removal
Hydrolysis $t_{1/2}$ >200 days at pH 7.0, 178 days at pH 9 at 20°C (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 320-330 mg kg^{-1} (1-3).
LC_{50} (1 hr) inhalation rat >1960 mg m^{-3} (1,2).
LD_{50} dermal rat >2150 mg kg^{-1} (1,2).
LD_{50} intraperitoneal rat, mouse 94-250 mg kg^{-1} (3).
LD_{50} subcutaneous rat, mouse 3300->6000 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral rat, dog (90 day) no-adverse-effect level 5 mg kg^{-1} diet for dogs, 10 mg l^{-1} diet for rats (1,2).

Irritancy
Reported to be non-irritant to the skin and slightly irritating to the eyes of rabbits (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).
The log P_{ow} exceeds the European Community recommended level of 3.0 (Directive on Classification, Packaging and Labelling of Dangerous Substances, 6th and 7th Amendments) (6).
WHO Class II (7).
EPA Toxicity Class II (formulation) (2).

Other comments

Toxicity to freshwater organisms considered (8-11).
Metabolic pathways reviewed (12).

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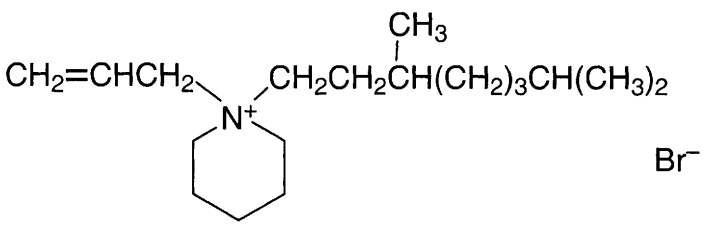
P206 piproctanyl bromide



$C_{18}H_{36}BrN$ **Mol. Wt.** 346.39 **CAS Registry No.** 56717-11-4

Synonyms Alden; 1-allyl-1-(3,7-dimethyloctyl)piperidinium bromide; 1-(3,7-dimethyloctyl)-1-(2-propenyl)piperidinium bromide

RTECS No. TN 4426000

Uses Superseded plant growth regulator.

Physical properties

M. Pt. 75°C **Volatility** v.p. $<3.7 \times 10^{-7}$ mmHg at 20°C
Solubility Water: miscible. Organic solvents: acetone, cyclohexane, ethanol, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 12.7, 62 mg l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 180, 820-990 mg kg^{-1}, respectively (1,2).
LC_{50} inhalation rat 1500 mg m^{-3} (exposure not specified) (1).
LD_{50} dermal rat 110-240 mg kg^{-1} (1,2).

Sub-acute and sub-chronic data
LD_{50} (8 day) oral mallard duck, bobwhite quail >10,000 mg kg^{-1} diet (1).
Oral rat, dog (90 day) no significant ill-effects were observed in rats receiving 150 mg kg^{-1} day^{-1} and in dogs receiving 25 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics
Following oral administration to mammals, piproctanyl bromide is eliminated largely unchanged in the faeces (1).

Irritancy
Reported to be non-irritating to rabbit eyes and guinea pig skin (1).

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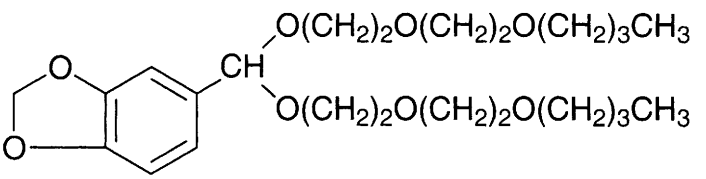
P207 piprotal



$C_{24}H_{40}O_8$ **Mol. Wt.** 456.58 **CAS Registry No.** 5281-13-0
Synonyms 5-[bis[2-(2-butoxyethoxy)ethoxy]methyl]-1,3-benzodioxole; 1,1-bis[2-(2-butoxyethoxy)ethoxy]methyl-3,4-methylenedioxybenzene; piperonal bis[2-(2-butoxyethoxy)ethyl]acetal; heliotropin acetal; tropital
RTECS No. DF 4911000
Uses Insecticide.

Physical properties

B. Pt. 200-230°C at 0.04 mmHg **Specific gravity** 1.075 at 20°C
Solubility Organic solvents: ethanol, glycols, methanol, methylene chloride

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2900-4400 mg kg^{-1} (1,2).

LD_{50} dermal rabbit >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral rat (90 day) 150, 300 or 600 mg kg^{-1}. The high dose was slightly toxic to the liver, kidneys, urinary bladder and thymus tissue (2).

Metabolism and toxicokinetics

When fed to rats, mice, rabbits and hamsters degradation occurred primarily at the side chain with excretion of the metabolites in the urine. The glycine and glucuronide conjugates were found. Metabolites included piperonal, piperonylic acid and *N*-piperonylglycine (3).

Irritancy

Not irritating to skin and mucous membranes (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).

References

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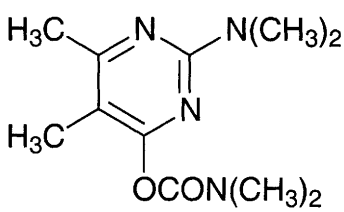
6. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

P208 pirimicarb



$C_{11}H_{18}N_4O_2$ **Mol. Wt.** 238.29 **CAS Registry No.** 23103-98-2

Synonyms 2-(dimethylamino)-5,6-dimethyl-4-pyrimidinyl dimethylcarbamate; Ferros; Pirimor; PP 062; Pyrimor

EINECS No. 245-430-1 **RTECS No.** EZ 9100000

Uses Insecticide.

Physical properties

M. Pt. 90.5°C **Partition coefficient** log P_{ow} 1.7 **Volatility** v.p. 3×10^{-5} mmHg at 30°C
Solubility Water: 3.0 g l^{-1} at 20°C and pH 7.4. Organic solvents: acetone, chloroform, diethyl ether, ethanol, 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 dust – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 29, 55 mg l^{-1}, respectively (1).

Invertebrate toxicity
LD_{50} (24 hr) bee, oral 3.5, contact 51 μg bee^{-1} (tech.) (1).
Effects on soil microflora were simulated in the laboratory at recommended and excessive rates and incubated with soil samples for 11 wk. Recommended rates of single application decreased soil microflora by 0-6% and dehydrogenase by 0-10%. Excessive rates (10-fold) showed negligible toxicity and slight interactions (unspecified). Cellulose degradation and nitrification were depressed, but adaption took place and the toxicity decreased over 11 wk (2).

Environmental fate

Abiotic removal
$t_{1/2}$ for solution exposed to sunlight <1 day at pH 5, 7 or 9 (1).

Adsorption and retention
Strongly adsorbed by clay soils, particularly montmorillonite soils. Adsorption by oxidised soils showed that organic matter can block adsorption by clay (3).
Leaching experiments and testing of groundwater under ploughland showed groundwater pollution does not occur because Pirimicarb is strongly sorbed and virtually immobile in soil (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken, mallard duck, bobwhite quail 8-50 mg kg^{-1} (5).
LD_{50} oral rat, mouse, dog 100-147 mg kg^{-1} (6,7).
LD_{50} dermal rat >500 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Dermal rabbit (14 day) 500 mg kg^{-1} day^{-1} produced no toxic effects (1).
Inhalation rat (21 day) exposure for 6 hr day^{-1} for 5 day wk^{-1} to air which had been passed over pirimicarb (technical grade) at room temperature caused no adverse effects, nor inhibited cholinesterase activity (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 250 mg kg^{-1} diet (5).

Metabolism and toxicokinetics
In mammals the major metabolites are 2-dimethylamino-5,6-dimethyl-4-hydroxypyrimidine, 2-methylamino-5,6-dimethyl-4-hydroxypyrimidine, 2-amino-5,6-dimethyl-4-hydroxypyrimidine and 2-dimethylamino-6-hydroxymethyl-5-methyl-4-hydroxypyrimidine (5).

Irritancy
5 g l^{-1} solution instilled into rabbit eye did not cause irritation (period of exposure and volume unspecified (1).

Sensitisation
Did not cause sensitisation in guinea pigs (5).

Other effects

Any other adverse effects
Cholinesterase inhibitor (5).

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).
ECC maximum residue level: fruit and vegetables 0.5 ppm; cereal 0.05 ppm (5).
WHO Toxicity Class II (10).
EPA Toxicity Class II (formulation) (1).
ADI 0.02 mg kg^{-1} body weight (1).

Other comments

Residues have been isolated from soil and water (11,12).
Hazard of multiple applications in modern agriculture discussed (13).

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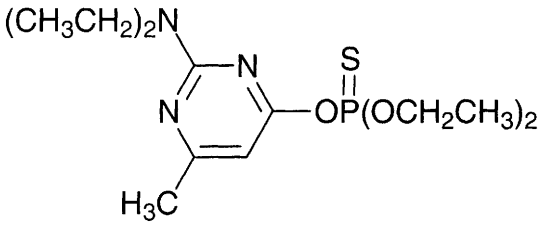
P209 pirimiphos-ethyl



$C_{13}H_{24}N_3O_3PS$ **Mol. Wt.** 333.39 **CAS Registry No.** 23505-41-1

Synonyms *O*-[2-(diethylamino)-6-methyl-4-pyrimidinyl] *O,O*-diethyl phosphorothioate; *O*-2-(diethylamino)-6-methylpyrimidin-4-yl *O,O*-diethyl phosphorothioate; Fernex; Primicid; Primotec; Solgard; Bullit

EINECS No. 245-704-0 **RTECS No.** TF 1610000

Uses Insecticide.

Physical properties

M. Pt. 15-18°C (tech.) **B. Pt.** decomposes above c. 194°C **Specific gravity** 1.14 at 20°C
Partition coefficient log P_{ow} 4.459 (1) **Volatility** v.p. 2.9×10^{-4} mmHg at 25°C
Solubility Water: <1 mg l^{-1} at 30°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

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) – Do not breathe vapour – 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, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) brown trout, carp 0.02, 0.22 mg l^{-1}, respectively (1).

Environmental fate

Degradation studies
$t_{1/2}$ 21-70 days in soil (non-sterile, aerobic, organic material 1.8-6.3%, pH 6.0-7.5) (2).

Abiotic removal
Hydrolysis $t_{1/2}$ 52-1200 days at pH 5.5-8.5 at 25°C (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, mallard duck, bobwhite quail 2.5-140 mg kg^{-1} (3-5).
LD_{50} oral rat 140-200 mg kg^{-1} (1,3).
LD_{50} dermal rat 1000-2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral rat, dog (90 day) no-adverse-effect level 0.08 mg kg^{-1} day^{-1} in rats, 0.20 mg kg^{-1} day^{-1} in dogs (1).

Irritancy
Dermal rabbit 100 mg did not cause irritation when applied for 24 hr day^{-1} on alternate days for 10 days (2).

Sensitisation
Reported not to cause skin sensitisation in guinea pigs (1).

Genotoxicity

Salmonella typhimurium TA1530, TA1535, G46, C117 without metabolic activation positive (6).
Escherichia coli WP2 without metabolic activation positive (6).

Legislation

EEC maximum residue level – fruit and vegetables 2 ppm, cereals 4 ppm (1).
The log P_{ow} value exceeds the European Community recommended level of 3.0 (Directive on Classification, Packaging and Labelling of Dangerous Substances, 6th and 7th Amendments) (7).
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).
WHO Toxicity Class Ib (10).
EPA Toxicity Class II (formulation) (2).

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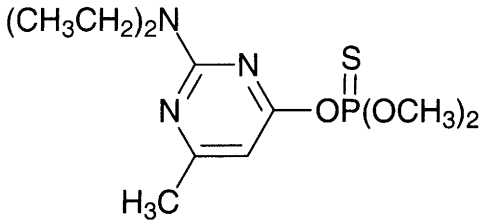
P210 pirimiphos-methyl



$C_{11}H_{20}N_3O_3PS$ **Mol. Wt.** 305.34 **CAS Registry No.** 29232-93-7

Synonyms *O*-[2-(*N*,*N*-diethylamino)-6-methyl-4-pyrimidinyl] *O*,*O*-dimethylphosphorothioate; phosphorothioic acid, *O*-[2-(diethylamino)-6-methyl-4-pyrimidinyl] *O*,*O*-dimethyl ester; Actellic; ENT 27699Ge; PP 511

EINECS No. 249-528-5 **RTECS No.** TF 1410000

Uses Fast acting insecticide. Acaricide.

Physical properties

M. Pt. 15-18°C (technical grade) **B. Pt.** Decomposes on distillation **Flash point** >46°C **Specific gravity** 1.157 at 30°C **Partition coefficient** log P_{ow} 4.2 (20°C, un-ionised) **Volatility** v.p. 1×10^{-4} mmHg at 30°C **Solubility** Water: 2.5 mg l^{-1} at pH 7.2. Organic solvents: miscible with alcohols, ketones, halogenated hydrocarbons

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) mirror carp 1.6 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 1.4 mg l^{-1} (1).
LC_{50} (4 hr) *Paramecium caudatum* <575 ppb (2).

Mammalian & avian toxicity

Acute data
LD_{50} mallard duck, bobwhite quail 2.5, 10-20 mg kg^{-1}, respectively (1).
LD_{50} oral rabbit, mouse, guinea pig 1000-1180 mg kg^{-1} (3).
Acutely toxic doses in chicks and chickens produced lachrymation and salivation and other frequently observed consequences of inhibition of cholinesterase activity. Lethal doses were associated with 65-85% inhibition of cholinesterase activity in blood (4).

Sub-acute and sub-chronic data
When administered for 28 days proteinuria and an increase in blood urea were seen, but no pathological changes could be detected. Inhibition of cholinesterase activity in the central nervous system may have been responsible for the physiological changes (5).
The same regime reduced activities of acetylcholinesterase (true) and cholinesterase (pseudo) in central and peripheral nervous system as well as plasma non-specific carboxylesterase. Effects were reversible (6).

Carcinogenicity and chronic effects

Rats receiving 10 mg kg^{-1} for 2 yr in diet, showed no adverse effects (1).

Metabolism and toxicokinetics

The metabolism in ruminants has been shown to be mainly by hydrolysis, loss of the phosphorothioate side-chain, and *N*-dealkylation. Products formed are then conjugated (7).

Other effects

Any other adverse effects

When administered to rats, kidney function becomes abnormal within 1-4 hr. Urine flow increased four fold, albumin excretion increased, β-2-micro globulin and *N*-acetyl-glucosaminidase were excreted. Metabolic alkalosis was seen at 24 hr (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticide: maximum admissible concentration 0.1 μg l^{-1} (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).
Log P_{ow} exceeds the European Community recommended limit of 3.0 (11).
WHO Toxicity Class III (12).
EPA Toxicity Class III (formulation).
ADI 0.03 mg kg^{-1} body weight (12).

Other comments

Environmental pollutant. Food contaminant.

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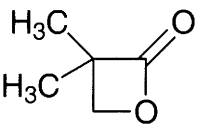
P211 pivalolactone



$C_5H_8O_2$ **Mol. Wt.** 100.12 **CAS Registry No.** 1955-45-9

Synonyms 3,3-dimethyl-2-oxethanone; dimethyl propiolactone; 3,3-dimethyl-β-propiolactone; pivalic acid lactone

RTECS No. RQ 7525000

Uses Manufacture of polymers.

Physical properties

M. Pt. –13°C **B. Pt.** 58°C at 15 mmHg **Partition coefficient** log P_{ow} 1.007 (1)
Solubility Organic solvents: acetone, dimethyl sulfoxide, ethanol

Environmental fate

Abiotic removal
Decomposes in water (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 320, 1500 mg kg^{-1}, respectively (3).

Carcinogenicity and chronic effects
Gavage rat, mouse 0, 150 or 300 mg kg^{-1} day^{-1} for 108 wk to rats or 0, 75 or 150 mg kg^{-1} day^{-1} for 102 wk to mice. A significant increase in the incidence of squamous cell papillomas and carcinomas of the forestomach were observed in rats. Negative carcinogenic results were reported in mice (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (5).

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P212 platinum

Pt

Pt **Mol. Wt.** 195.08 **CAS Registry No.** 7440-06-4

Synonyms C.I. 77795; liquid bright platinum; platinum black; platinum sponge

EINECS No. 231-116-1 **RTECS No.** TP 2160000

Uses Catalyst. In preparation of anti-cancer agents. Used in dental ceramics, electrodes and jewellery. Control of automotive emissions.

Occurrence Abundance in Earth's crust ~0.01 ppm.

Physical properties

M. Pt. 1772°C **B. Pt.** 3827°C **Specific gravity** 21.45 at 20°C

Solubility Water: aqua regia

Occupational exposure

FR-VME 1 mg m^{-3}

UK-LTEL 5 mg m^{-3}

US-TWA 1 mg m^{-3}

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Incubation of fresh human sperm with platinum strip reduced motility by 40% after 2 hr and by 70% after 5 hr (1). Implantation on day 3 into rat uterus reduced the number of implantation sites of fertilised ova by 83%. When implanted on day 6 of gestation, no effect on embryonic or foetal survival was observed (2,3).

Metabolism and toxicokinetics

Following inhalation exposure rat to ^{191}Pt for up to 8 days, 94% radioactivity was detected in the lungs and 4% in the trachea. After oral administration <1% was retained in the body after 3 days (4-6).

Other effects

Other adverse effects (human)

Allergic dermatitis has been reported in susceptible individuals. Symptoms of respiratory distress, ranging from irritation to an "asthmatic syndrome" with coughing, wheezing, and shortness of breath, have been reported after exposure to platinum dust. The skin and respiratory changes are termed platinosis (7).

Any other adverse effects

Oral rat, single dose of 25 mg kg^{-1} as dust caused only slight necrotic changes in the gastro-intestinal epithelium, granular dystrophy of hepatocytes and swelling of the convoluted renal tubules (8,9).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

Environmental impact and toxicity of platinum and its compounds reviewed (1,11).

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P213 platinum dichloride

$PtCl_2$

Cl_2Pt **Mol. Wt.** 265.99 **CAS Registry No.** 10025-65-7

Synonyms muriate of platinum; platinum(II) chloride; platinous chloride

EINECS No. 233-034-1 **RTECS No.** TP 2275000

Uses Catalyst.

Physical properties

M. Pt. 581°C (decomp.) **Specific gravity** 6.050
Solubility Water: insoluble

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 18 mg kg^{-1} (1).
LD_{50} oral rat 3400 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 670 mg kg^{-1} (3).

Irritancy
Dermal rabbit (24 hr) 100 mg caused mild irritation (4).

Genotoxicity

In vitro mouse lymphoma L5178Y cells tk^+/tk^- forward mutation negative (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides: guide level 25 mg l^{-1} (6).
Limited under UK Water Supply (Water Quality) Regulations. Chloride: maximum concentration 400 mg l^{-1} (12 monthly average) (7).

Other comments

Environmental impact and toxicity reviewed (8).
Soluble in hydrochloric acid and ammonium hydroxide.

References

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2. Roshchin, A. V. et al *J. Hyg. Epidemiol. Microbiol. Immunol.* 1984, **28**, 17-24.
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8. *IPCS Environmental Health Criteria No. 125* 1991, WHO, Geneva, Switzerland

P214 platinum tetrachloride

$PtCl_4$

Cl_4Pt **Mol. Wt.** 336.89 **CAS Registry No.** 13454-96-1

Synonyms platinum(IV) chloride

EINECS No. 236-645-1 **RTECS No.** TP 2275500

Uses Catalyst.

Physical properties

M. Pt. 370°C (decomp.) **Specific gravity** 4.303 at 25°C with respect to water at 4°C
Solubility Water: slightly soluble. Organic solvents: diethyl ether, ethanol

Occupational exposure

UK-LTEL 0.002 mg m^{-3} (as Pt)
US-TWA 0.002 mg m^{-3} (as Pt)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 240-280 mg kg^{-1} (1,2).
LD_{50} intraperitoneal rat 38 mg kg^{-1} (2).
LD_{50} intravenous rat 26-41 mg kg^{-1} (3).

Teratogenicity and reproductive effects
Intratesticular rat, lowest toxic dose, single administration 27 mg kg^{-1}, reproductive effects (4).

Irritancy
Dermal rabbit (24 hr) 100 mg caused severe irritation (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 without metabolic activation positive (6).
Escherichia coli WP2 DNA damage (base exchange) positive (6).
Drosophila melanogaster sex-linked recessive lethal assay positive (7).
In vitro Chinese hamster ovary cells, reverse mutation positive (8).
In vitro mouse lymphoma L5178Y cells tk^+/tk^- forward mutation positive (9).
In vitro yeast cells, caused a reduction, but not delay, in growth and in RNA, DNA and ribsome syntheses. The results were indicative of DNA damage (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides: guide level 25 mg l^{-1} (11).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chloride: maximum concentration 400 mg l^{-1} (12 monthly average) (12).

Other comments

Environmental impact and toxicity reviewed (13).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (14).

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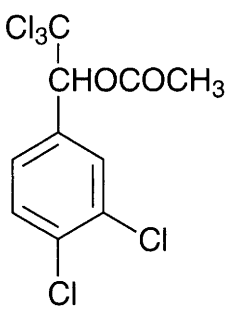
P215 plifenate



$C_{10}H_7Cl_5O_2$ **Mol. Wt.** 336.43 **CAS Registry No.** 21757-82-4

Synonyms acetoferate; Baygon MEB; 3,4-dichloro-α-(trichloromethyl)benzenemethanol acetate; 3,4-dichloro-α-(trichloromethyl)benzylalcohol acetate; MB-6046; penferate; 2,2,2-trichloro-1-(3,4-dichlorophenyl)ethyl acetate

EINECS No. 244-573-7 **RTECS No.** KK 5000000

Uses Superseded insecticide.

Physical properties

M. Pt. 84.5°C **Volatility** v.p. 1.1×10^{-7} mmHg at 20°C
Solubility Water: 50 mg kg^{-1}. Organic solvents: cyclohexanone

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) golden orfe 0.5-1.0 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken >2500 mg kg^{-1} (1).
LD_{50} oral rat 10,000 mg kg^{-1} (1,2).
LC_{50} (4 hr) inhalation rat >560 mg m^{-3} (1).
LD_{50} dermal rat >1000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral rat (90 day) no-adverse-effect level 1000 mg kg^{-1} diet (1).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation negative (3).
Salmonella typhimurium TA98 with metabolic activation fluctuation test positive (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 l^{-1} (5).

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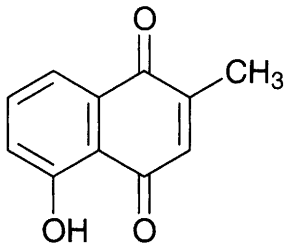
P216 plumbagin



$C_{11}H_8O_3$ **Mol. Wt.** 188.18 **CAS Registry No.** 481-42-5

Synonyms 5-hydroxy-2-methyl-1,4-naphthalenedione; 5-hydroxy-2-methyl-1,4-naphthoquinone; Plumbagine

EINECS No. 207-569-6 **RTECS No.** QL 8500000

Occurrence Found in the roots of *Plumbago europaea*.

Physical properties

M. Pt. 78-79°C

Solubility Water: slightly soluble in hot water. Organic solvents: acetone, acetic acid, benzene, chloroform, ethanol

Occupational exposure

UN No. 3143

Environmental fate

Degradation studies

Partially degraded to the 3-hydroxy derivative by *Pseudomonas putida* J1 and J2 in the presence of a growth-supporting carbon source (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 16, 65 mg kg^{-1}, respectively (2,3).

LD_{50} intraperitoneal mouse 5 mg kg^{-1} (4).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation weakly positive; TA100 with metabolic activation negative; TA2637 with metabolic activation positive (5).

Other comments

Phytotoxin.

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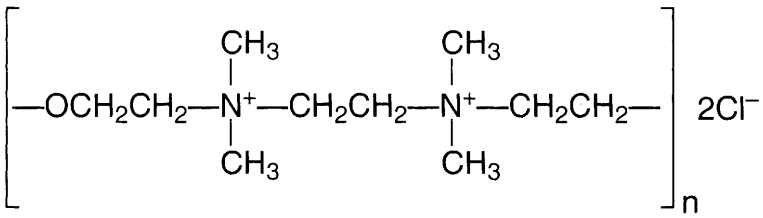
P217 polixetonium chloride



CAS Registry No. 31512-74-0

Synonyms poly[oxyethylene(dimethyliminio)ethylene(dimethyliminio)ethylene]dichloride; bualta; Bubond 60; Busan 77; TB 66

RTECS No. TR 1650000

Uses Biocide. Pesticide.

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1850 mg kg^{-1} (1).

LD_{50} dermal rabbit >2000 mg kg^{-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).

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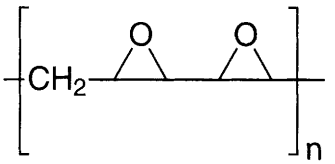
P218 poloxamer



$(C_5H_{10}O_2)_x$ **CAS Registry No.** 9003-11-6

Synonyms bis[hydroxyethylpoly(ethyleneoxy)ethyl]polypropyleneglycol; dipolyoxyethylated polypropyleneglycol ether; Adeka Carpol MH500; Berol 370; exocorpol; methyl oxirane, polymer with oxirane; Nissan Unilube DE60; Niscolen; oxalgon; polyethylene-polypropylene glycol; Poloxalcol; poloxalene; proxanol; Pluronic L44; Pluronic L-81; Tergitol XH

RTECS No. MD 0911050

Uses Plasticiser. Emulsifying agent. Manufacture of polymers. Food additive.

Physical properties

Specific gravity 1.01-1.04

Environmental fate

Abiotic removal

Removal from wastewater at concentrations ≤1% effected by adsorption onto bentonite, pretreated and regenerated by heating at 650-750°C (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1800, 2300-15,000 mg kg^{-1}, respectively (2-4).
LD_{50} intraperitoneal mouse, rat 420, 1100 mg kg^{-1}, respectively (2).
LD_{50} subcutaneous rat, mouse 5500-6900 mg kg^{-1} (5).
LD_{50} intravenous mouse 1000-3000 mg kg^{-1} (5,6).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation. 500 mg instilled into rabbit eye for 24 hr caused mild irritation (3).

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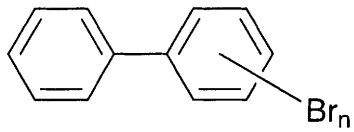
P219 polybrominated biphenyls



$C_{12}H_4Br_6$ **Mol. Wt.** 627.59 **CAS Registry No.** 59536-65-1 (Firemaster BP-6)
CAS Registry No. 67774-32-7 (Firemaster FF-1)

Synonyms Firemaster FF-1; Firemaster BP-6; hexabromobiphenyl; PBB

RTECS No. LK 5060000

RTECS No. LK 5065000

Uses Flame retardant.

Physical properties

M. Pt. ~72°C **B. Pt.** 300°C (decomp.) **Partition coefficient** log P_{ow} 7.72 (1)
Volatility v.p. 7.5×10^{-5} mmHg at 90°C
Solubility Water: 11 μg l^{-1}. Organic solvents: acetone, benzene, toluene

Occupational exposure

UN No. 3151 (liquid)

UN No. 3152 (solid) **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 21.5 g kg^{-1} (Firemaster BP-6) (2).
LD_{50} dermal rabbit 2200-10,000 mg kg^{-1} (Firemaster BP-6) (2,3).

Sub-acute and sub-chronic data

Oral rat (90 day) 30, 100, 300 or 1000 mg (Firemaster FF-1) kg^{-1} day^{-1} 5 day wk^{-1} for a total of 22 doses. Morphological changes included enlargement of the liver and atrophy of the thymus and spleen. Microscopic degenerative changes were seen in the liver, kidney, prostate and thyroid in ♂ rats and in the liver of ♀, ♀ rats. LD_{50} values were 150 mg kg^{-1} for ♂ and 65 mg kg^{-1} for ♀ rats (4,5).
Gavage rat, mouse 3 or 30 mg Firemaster FF-1 kg^{-1} day^{-1} for 22 days suppressed to mitogen response of splenic lymphocytes (6).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (7).
Gavage rat and mouse (30 month) 0.1, 0.3, 1.0, 3.0 or 10 mg (Firemaster FF-1) kg^{-1} day^{-1} 5 day wk^{-1} for 25 wk. A dose-dependent reduction in survival was noted in ♂ rats, and reduced survival was rated in high-dose ♂ mice. The incidence of hepatocellular carcinomas was also significantly increased in high-dose ♂ mice. Hepatocellular carcinomas were observed in treated ♂ and ♀ rats compared with none in control rats. Cholangiocarcinomas were seen only in the high-dose ♂ (2/31) and ♀ (7/20) rats. Statistically significant increases in the incidences of neoplastic nodules in the liver were found in the 2 highest dose ♀ rat groups and in ♂ rats receiving 1.0 mg kg^{-1}. In addition, statistically significant increases in the incidence of atypical foci were observed in the livers of high ♀ rats and in ♂ rats in the 4 highest dose groups. Chronic progressive nephropathy was observed in treated ♂ rats. Gastric ulcers and hyperplastic gastrophy were also observed in the higher dose groups (8,9).
Perinatal rat (2 yr) pregnant ♀ were administered oral doses of 0 or 200 mg kg^{-1} Firemaster FF-1 on days 7 and 14

gestation. The survival rate up until weaning, and growth rate were significantly reduced for the offspring of treated rats. The incidences of trabecular hepatocellular carcinomas were 3/51 and 4/41 in ♀ and ♂ offspring, respectively, exposed transplacentally and through milk compared with 0/48 and 0/42 ♂ and ♀ controls, respectively. These differences were not statistically significant (10,11).
Gavage rat (23 month) single dose of 0, 200 or 1000 mg kg^{-1}, or 12 × 100 mg kg^{-1} doses at 3 wk intervals caused a significant increase in the incidence of neoplastic nodules of the liver and atypical foci on altered areas in the liver (form unspecified) (12).

Teratogenicity and reproductive effects
Gavage rat 0, 0.25, 0.50, 1.0, 5.0 or 10 mg Firemaster BP-6 kg^{-1} day^{-1} on days 7-15 of gestation. Doses of 1.0 mg kg^{-1} and above caused enlarged maternal livers. No teratogenicity was observed. Growth rates of the high-dose group were decreased (13).
Oral mouse 0-1000 mg Firemaster BP-6 kg^{-1} diet on days 7-20 of gestation. No maternal toxicity was observed. Mean foetal weight decreased with increasing dose. A higher incidence of exencephaly and cleft palate were observed in treated offspring compared with a historical control group from another laboratory, but the effect was not significant when compared with concurrent controls (14).
Oral chicken (5 wk) 0.2-120 mg Firemaster BP-6 kg^{-1} diet. Feed with >125 mg kg^{-1} was rejected. Egg production, hatchability and offspring viability were reduced for levels of 45 mg kg^{-1} diet and above. Oedema of the abdominal and cervical regions was the predominant morphological finding in embryos and newly hatched chicks (15,16).

Metabolism and toxicokinetics
>90% hexabromobiphenyl was absorbed from the gastro-intestinal tract in rats. Tissue distribution was similar following oral and intravenous administration. Within 4 days adipose tissue contained >60% of the total body burden (17-20).
Elimination $t_{1/2}$ 145 days following oral administration of 10 mg kg^{-1} to rats (20).
Transplacental distribution was demonstrated in guinea pigs and rats (21,22).
Negligible metabolism of several tetra-, penta- and hexabromobiphenyls was demonstrated in rat liver microsomes *in vitro* (23).
Following incubation of ^{14}C-polybrominated biphenyls with rat liver microsomes, no binding to exogenous DNA was detected and the extent of irreversible binding to protein was very small (24).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (hexabromobiphenyl) (25).
In vitro primary rat, mouse and hamster hepatocytes, DNA repair synthesis negative (Firemaster BP-6) (26,27).
In vitro inhibition of gap-junction communication between primary rat hepatocytes and a 6-thioguanine-resistant rat liver epithelial cell line positive (form unspecified) (27,28).
In vitro mouse lymphoma L5178Y cell tk^+/tk^- assay negative (metabolic activation unspecified) (Firemaster FF-1) (29).
In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations negative (metabolic activation unspecified) (Firemaster FF-1) (29,30).
In vivo rat bone marrow and spermatogonal cells, chromosomal aberrations negative (Firemaster BP-6) (31).

Other effects

Other adverse effects (human)
Higher rates of dermatological, neurological and musculoskeletal disorders were reported in a group of 933 Michigan farmers than in 299 unexposed farmers, and a high prevalence of abnormal liver function tests was observed in 614 Michigan adults compared with 141 unexposed adults following unintentional addition of Firemaster FF-1 to animal feed (32,33).
Damage to the immune system was indicated by a reduction in the response to T- and B-lymphocyte mitogens, a reduced number of T- and B-lymphocytes in peripheral blood, a decrease in a T-lymphocyte proliferation test among exposed Michigan farmers. Increases in immunoglobulin A and G levels were also observed (34,35).

No major differences were observed in sperm counts, motility or morphology between exposed production workers and farmers when compared with a reference group of graduate students (36).

Any other adverse effects

Increased tissue accumulation and urinary excretion of porphyrins have been reported in treated rats and mice (5,9,15).

Toxic effects in dairy cattle fed polybrominated biphenyls included decreased milk production, excessive lachrymation and salivation, increased frequency of urination, abnormal hair growth, hair loss thickening and wrinkling of the skin and underdeveloped udders (37,38).

Chronic administration of Firemaster FF-1 to rats for 6 months decreased haemoglobin content, corpuscular volume and erythrocyte counts. However, comparable administration of 2,2',4,4',5,5'-hexabromobiphenyl had no haematological effects (4,8).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (39).

The log P_{ow} value exceeds the European Community recommended level of 3.0 (Directive on Classification Packaging and Labelling of Dangerous Substances, 6th and 7th Amendments) (40).

Other comments

Residues have been isolated from sediments, soil and fish (10).

Technical grade contains 60-90% hexabromobiphenyl of which the 2,2',4,4',5,5'-isomer is the principal component. Heptabromo-, pentabromo-, with traces of tribromo- and tetrabromobiphenyl. Firemaster FF-1 is Firemaster B6-6 to which 2% calcium silicate has been added as an anticaking agent (10).

Uses, occurrence, analysis, carcinogenicity, mutagenicity, mammalian toxicity and metabolism reviewed (10).

Removed from the market after the "Michigan Incident" in 1973 in which Firemaster BP-6 was accidently added to animal feed (41).

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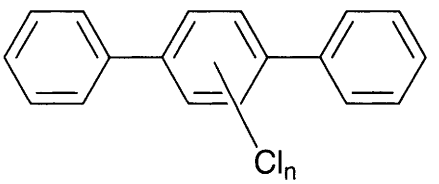
P220 polychlorinated terphenyls



CAS Registry No. 61788-33-8

Synonyms PCT; Kanechlor 500

EINECS No. 262-968-2 **RTECS No.** WZ 6500000

Uses Formerly used as insecticide.

Occupational exposure

UN No. 3151 (liquid)

UN No. 3152 (solid) **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Oral mouse (40 wk) 250 or 4500 mg kg^{-1} diet or 250 mg kg^{-1} diet for 24 wk induced liver tumours, nodular hyperplasia and hepatocellular carcinomas (1).

Teratogenicity and reproductive effects

Oral rat, lowest toxic dose 500 mg kg^{-1} day^{-1} on days 1-21 of gestation (foetal death and teratogenic effects) (2).
Oral mouse, lowest toxic dose 110 mg kg^{-1} day^{-1} on days 1-18 of gestation (foetal death and teratogenic effects) (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 l^{-1} (4).

Other comments

Environmental impact and toxicity of polychlorinated terphenyls reviewed (5).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

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P221 polychloroterpenes

CAS Registry No. 8001-50-1

Synonyms heptachloro-2,2-dimethyl-3-methylenenorborane; dichloricide aerosol; strobane; dichloricide mothproofer; terpene polychlorinate

RTECS No. WZ 6400000

Uses Superseded insecticide and acaricide.

Physical properties

Specific gravity 1.6267 at 25°C **Volatility** v.p. 3×10^{-7} mmHg
Solubility Organic solvents: miscible with aromatic and aliphatic hydrocarbons

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) green sunfish 0.05 mg l^{-1} (1).
Three-spined stickleback, steelhead trout, sockeye salmon died at 3-4, 2-3 and 2-3 hr, respectively, when placed in water containing 3 mg l^{-1} (technical grade). Water characteristics: 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).
Killed trout, bluegill sunfish, yellow perch and goldfish in 5, 22, 22 and 22 hr, respectively, at 5 ppm. Water characteristics: pH, 7.0; dissolved oxygen, 7.5 ppm; total hardness (soap method), 300 ppm; methyl orange alkalinity, 310 ppm; free carbon dioxide, 5 ppm; temperature 12.8°C (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, dog 200 mg kg^{-1} (4).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).
C57BL/6×C3H/Anf F1 and C57BL/6×AKR F1 mice were given 4.64 mg kg^{-1} body weight by stomach tube at 7

days of age and this same absolute amount was then given daily until 28 days of age. Until 80 wk the mice were given 11 ppm in the diet. Hepatomas were found in 2/15 of C57BL/6×C3H/Anf ♂ (8/79 controls) and in 11/18 C57BL/6 ×AKR ♂ (5/90 controls). No hepatomas were found in ♀. 7/33 (5 ♂ and 2 ♀) C57BL/6×C3H/Anf mice had malignant lymphomas (9/166 controls). No malignant lymphomas were found in the other strain with treatment (6).

Metabolism and toxicokinetics
Found in the milk fat of cows after spraying. Maximum residues of 0.68-0.74 ppm occurred 1 or 2 days after spraying (7).

Irritancy
May be mildly irritating to human skin (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).

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P222 polydimethylsiloxane

$$[\text{-Si}(CH_3)_2\text{O-}]_n$$

$(C_2H_6OSi)_x$ **CAS Registry No.** 9016-00-6

Synonyms aeropax; dimethione 350; Dow Corning 346; geon; goodrite; gum; hycar; latex; methyl silicone; poly[oxy(dimethylsilylene)]; dimethyl polysiloxane; Syltherm XLT; Ceranine HFC Liquid

RTECS No. TQ 2690000

Uses In mammary prosthetic devices. Water repellant. Lubricant. In antiallergenic creams and lotions.

Physical properties

B. Pt. >149°C **Flash point** 203°C **Specific gravity** 0.976
Solubility Organic solvents: carbon tetrachloride, chloroform, diethyl ether, ethanol, ethyl acetate, methyl ethyl ketone, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, rainbow trout >10 g l^{-1}, static bioassay (1).

Environmental fate

Abiotic removal

Twelve Ca-saturated clay minerals tested at 22°C and 32% relative humidity were all catalysts for polymethylsiloxane degradation. Kaolinite, beidellite, and nontronite were the most active and goethite and allophane were the least active (2).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse >5500 mg kg^{-1} (3).
LD_{50} intraperitoneal rat >2000 mg kg^{-1} (3).
LD_{50} intraperitoneal dog >410 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Oral rat, 1% diet for 90 days caused no observable toxic symptoms or pathological changes (4).

Teratogenicity and reproductive effects

Subcutaneous rat 500, 1000 or 2000 mg kg^{-1} day^{-1} on days 6-15 of gestation, or a single dose of 1000, 5000, 10,000, or 20,000 mg kg^{-1} 1 wk to prior to mating. The only toxic effect observed was a significant post-implantation loss in animals given the single doses. No clinical signs of toxicity were evident in the dams and no teratogenic effects were observed (5).

Subcutaneous rats 200, 1000 mg kg^{-1} (medical grade polydimethylsiloxane) caused an apparent dose-related *in utero* mortality, however a 2nd study failed to confirm this. Subcutaneous rabbits 200 mg siloxane kg^{-1}, talipes varus occurred in 8.8% of animals treated but the condition did not occur in animals administered 1000 mg kg^{-1}. Dermal rabbits 200 mg kg^{-1} (10 centistoke fluid) non-teratogenic. Oral rats 1000 mg kg^{-1} (7 centistoke pump fluid) non-teratogenic (6).

Genotoxicity

In vitro human lymphoctytes, chromosomal aberrations positive (7).
In vivo intraperitoneal mice 5 and 10 g kg^{-1} (7 centistoke pump fluid) non-mutagenic (6).

Other effects

Any other adverse effects

If vapour is inhaled in very high concentrations, fatal narcosis may result. Exposed animals which have survived narcosis have recovered completely (8).

Other comments

Genotoxicity of possible intermediates in the synthesis and degradation of polydimethylsiloxanes reviewed (9). Reviews on human health effects, experimental toxicology, physico-chemical properties listed (10).

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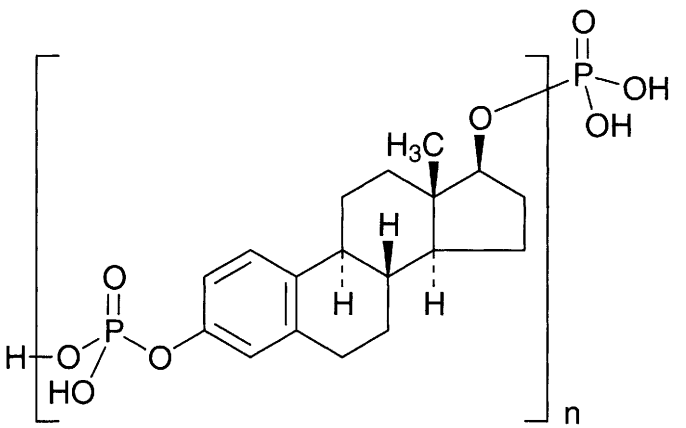
P223 polyestradiol phosphate



Mol. Wt. 26000 **CAS Registry No.** 28014-46-2

Synonyms (17β)-estra-1,3,5(10)-triene-3,17-diol polymer with phosphoric acid; estradiol phosphate polymer; polyoestradiol phosphate; PEP; Estradurin

RTECS No. KG 5792000

Uses Antineoplastic (hormonal) used in the treatment of prostate cancer. Polyestradiol phosphate (molecular weight ~26,000) is gradually depolymerised in the body to release estradiol-17(β). See the DOSE entry on estradiol for the full data on this compound.

Occurrence Estradiol-17β is a widely occurring natural oestrogen but is not naturally found in the form of polyestradiol phosphate.

Physical properties

M. Pt. 195-202°C

Solubility Water: very slightly soluble. Organic solvents: very soluble in aqueous pyridine, soluble in aqueous alkali, very slightly soluble in ethanol, ethanol + water (1:1), acetone, chloroform, dioxane

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rat, mouse 5800, 6100 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects

Polyestradiol phosphate is gradually depolymerised in the mammalian body to release estradiol-17(β), for which there is sufficient evidence for carcinogenicity to animals. In the absence of adequate data in humans IARC advise that it is reasonable, for practical purposes, to regard estradiol-17(β) as if it presented a carcinogenic risk to humans (2).

Polyestradiol phosphate administered to CBA mice as 3 subcutaneous injections of 0.25 mg 7 days before and 30

and 60 days after an intraperitoneal injection of ^{90}Sr, or as 3 subcutaneous implants (0.25-1.0 mg) over 60 days in combination with ^{90}Sr, led to an increased incidence of bone tumours over that found with ^{90}Sr alone and also to a shorter latent period. No bone tumours were found in mice treated only with estrogen. Osteoclastic and mixed osteosarcomas were frequent only in the combination treatment groups. The authors suggest that estrogen increased the carcinogenicity of ^{90}Sr by stimulating bone cells to proliferate (3-5).
Intermittent intramuscular injections (173 mg kg^{-1} over 9 yr) caused liver cancer in a woman patient (6).

Teratogenicity and reproductive effects
A single intramuscular injection 50 mg kg^{-1} on day 19 of gestation caused teratogenic effects in rats (7).

Other comments

Carcinogenic risk to humans of estradiol-17(β) reviewed (8,9).

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P224 polyethylene

$$[CH_2{=}CH_2]_n$$

$(\text{-}C_2H_4\text{-})_n$ **CAS Registry No.** 9002-88-4

Synonyms diothene; ethene homopolymer; HDPE; LDPE; polyethene; Agilene; Alkathene; Bakelite DYNH; Polywax 1000; Tenite 800; microthene; Polythene; Pylen; Reevon

RTECS No. TQ 3325000

Uses In manufacture of adhesives. Surface coating. Binder. Manufacture of films, bottles, fibres, fillers, foam, laminates, pipes, packaging, toys and utensils.

Physical properties

M. Pt. 108-126°C (low density); 126-136°C (high density) **Specific gravity** 0.910-0.925 (low density) at 20°C with respect to water at 4°C; 0.941-0.965 (high density)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >3000 mg kg^{-1} (polymer unspecified) (1).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (2).
Subcutaneous implant mouse (13 month) polyethylene disc (15 mm diameter, 0.38 mm thick). The first sarcoma appeared at the site of implantation after 7.5 months. After 13 months the fatal number of sarcomas was 35/71 in mice with implanted smooth discs and 7/60 mice given roughened discs (3).

Subcutaneous implant rat and mouse (2 yr) polyethylene film (polymer unspecified without plasticiser) (15 mm diameter, 0.02 mm thick) induced malignant tumours at the site of implantation in 1-11% of animals. In 42 rats implanted with polyethylene powder no such tumours occurred. When rats were implanted with polyethylene powder in conjunction with glass cover-slips of 18 mm diameter local sarcomas developed in ~25% of animals (4,5).
Subcutaneous implant rat (39 month) high density polyethylene discs (18 mm diameter, 0.14 mm thick) on glass discs. Fibrosarcomas were found in 5/55 rats at the site of implantation of polyethylene discs between 347 and 644 days after implantation. No tumours were associated with the glass discs (6).
Intraperitoneal implant rat (2 yr) polyethylene particles (polymer unspecified) of <3 mm greatest dimension weighing 1500 mg. 43/74 rats developed intraperitoneal fibrosarcomas and 6/74 developed other unspecified tumours. The incidence of tumours in controls was 11/74 (7).
Intra-uterine implantation rat (2 yr) 10 mm portion of polyethylene intra-uterine contraceptive device (polymer unspecified), 5/102 rats developed epidermoid carcinomas and 1/102 developed a sarcoma of the uterus. All animals that had epidermoid carcinomas also had pyometra, which is associated with squamous metaplasia. Among 406 controls, 3 squamous-cell and 1 adenocarcinoma of the uterus were observed. Among 106 rats given stainless steel inserts, 6 epidermoid carcinomas and 1 sarcoma of the uterus developed (8).

Metabolism and toxicokinetics

In rats given subcutaneous implants of ^{14}C-labelled polyethylene (polymer unspecified), radioactivity was excreted in the urine only after 26 wk. No radioactivity was excreted in the urine after removal of the film (5).
Polyethylene pellets (polymer unspecified) lost 1% mass after 12 days in the stomach of seabirds, indicating a $t_{1/2}$ of >1 yr (9).

Other effects

Other adverse effects (human)

In 209 consecutive endometrial biopses from women who also attended a contraceptive clinic, two cases of endometrial squamous metaplasia and one atypical glandular hyperplasia were found among users of polyethylene intra-uterine contraceptive devices for up to 105 months (10).
Follow-up biopses of nine women with squamous metaplasia who used a polyethylene device (polymer unspecified) failed to reveal persistence or progression of the metaplasia (11).

Other comments

Physical properties, use, carcinogenicity, mammalian toxicity and metabolism of ethylene and polyethylene reviewed (12,13).
LC_{50} (30 min) inhalation mouse 12000 mg m^{-3} (pyrolysis products) (14).
Environmental degradation of polyethylene reviewed (15).
Available as low, medium and high density polmer. Molecular weight 100,000 to 500,000.

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P225 polyethylene glycol

$$HO(CH_2CH_2O)_nH$$

$(-C_2H_4O-)_nH_2O$ **CAS Registry No.** 25322-68-3

Synonyms polyglycol 200; polyglycol 300; polyoxyethylene; poly(oxyethylene)glycol; poly(ethylene glycol); polyethylene oxide; α-hydro-ω-hydroxypoly(oxy-1,2-ethanediyl); Alcox; Carbowax; E200 (polyglycol); ethylene glycol homopolymer; Macrogol; oxirane polymer; PEG; PEO; Pliviol E; polyox

RTECS No. TQ 3600000

Uses Surfactant. Anti-static agent. Binder. Catalyst. Electrolyte. Flocculant. Plasticiser. Solvent. Suppository base. Lubricant.

Physical properties

M. Pt. −10 to 63°C **Flash point** 182-284°C (open cup) **Specific gravity** 1.11-1.14 at 25°C with respect to water at 25°C

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

Occupational exposure

DE-MAK 1000 mg m^{-3} (av. mol. wt. 200-600)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) goldfish >5000 mg l^{-1} (PEG 200, 400, 800) (1).

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* >100 g l^{-1} Microtox test (polymer unspecified) (2).

Environmental fate

Degradation studies

BOD_5: PEG 200, 0.02 mg O_2 l^{-1} (1% of ThOD); PEG 400, 0.01 mg O_2 l^{-1} (1% of ThOD). PEG 800 nil. COD: PEG 200 1.62 mg O_2 l^{-1} (98% of ThOD); PEG 400, 1.71 mg O_2 l^{-1} (98% of ThOD); PEG 800, 1.74 mg O_2 l^{-1} (98% of ThOD) (1).

Biodegradability was reported to be significantly improved by pre-ozonation (3).

Abiotic removal

Degraded by UV irradiation at 254 nm in conjunction with ozone treatment (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, guinea pig 17-76 g kg^{-1} (PEG 200, 300, 400, 1000, 1500, 4000) (5-7).

LD_{50} intraperitoneal rat, mouse 2-18 g kg^{-1} (PEG 200, 300, 1000, 1500, 4000, 6000) (7-9).

LD_{Lo} intravenous dog 3 g kg^{-1} (PEG 1000) (9).

Metabolism and toxicokinetics

Absorption by the nasal and gastro-intestinal mucosa is dependent on molecular weight (10).
Polyethylene glycols entering the systemic circulation are predominantly excreted in the urine unchanged (11).

Irritancy

500 mg of PEG 1000 instilled into rabbit eye for 24 hr caused mild irritation (12).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (PEG 200) (13).
In vitro human fibroblasts, inhibition of DNA synthesis negative (polymer unspecified) (14).

Other effects

Other adverse effects (human)

Use in therapeutic formulations has been associated with hypersensitivity reactions such as urticaria.
Hyperosmolarity, metabolic acidosis and renal failure have been reported following topical application to burn patients (11).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).
Average molecular weight 200-9000. Fractions with molecular weight of ≤600 are liquid, ≥100 are solid.

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P226 polymethyl methacrylate

$$[CH_2=C(CH_3)CO_2CH_3]_n$$

CAS Registry No. 9011-14-7

Synonyms methyl methacrylate homopolymer; methyl 2-methyl-2-propenoate, homopolymer; Delaglas-A; Delaprism; Delpet; Acryloid A-30; Altuglas; Luminous

RTECS No. TR 0400000

Uses Main constituent of acrylic sheets, acrylic mouldings and extrusion powders.

Physical properties

M. Pt. >300°C **Specific gravity** 1.179 at 25°C
Solubility Organic solvents: moderately soluble in butanol, dimethylformamide, ethanol, ethyl acetate, toluene

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (1).
In rats, intramuscular, subcutaneous and intraperitoneal implantation of discs or films produced local sarcomas. Local sarcomas were also produced in mice following subcutaneous implantation of films. Intramuscular implantation in guinea-pigs and implantation into the cheek pouch of hamsters produced no implantation site tumours (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3).

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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

P227 polysorbate 20

CAS Registry No. 9005-64-5

Synonyms E432; polyethylene glycol sorbitan monolaurate; capmul; polyoxyethylene (20) sorbitan monolaurate; sorbimacrogol laurate; Tween 20

RTECS No. TR 7400000

Uses Surfactant. Stabiliser. Dispersing agent.

Physical properties

Flash point >110°C **Specific gravity** 1.095
Solubility Water: miscible. Organic solvents: 1,4-dioxane, ethanol, ethyl acetate, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 37 ml kg^{-1} (1).
LD_{50} oral mouse >33,000 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse 2600, 3900 mg kg^{-1}, respectively (2,3).
LD_{50} intravenous rat 770 mg kg^{-1} (2).

Teratogenicity and reproductive effects

Intraperitoneal mouse, lowest toxic dose 1000 mg kg^{-1} on day 9 of gestation (teratogenic effects to musculoskeletal system) (4).

Irritancy

Reported to be a mild eye irritant to rabbits (5).
Dermal rabbit (3 days) 15 mg caused mild irritation (6).
15 mg applied to human skin caused mild irritation (7).

Legislation

TDI (human) 25 mg kg^{-1} day^{-1} (8).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).
A complex mixture of partial lauric esters of sorbitol and its mono- and dianhydrides condensed with ethylene oxide.

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P228 polysorbate 40

$C_{62}H_{122}O_{26}$ **Mol. Wt.** 1283.64 **CAS Registry No.** 9005-66-7

Synonyms polyethylene glycol sorbitan monopalmitate; polyoxyethylene derivatives sorbitan monopalmitate; Crill 7; Durfax 60; Emulgen 6910; ethoxylated sorbitan monopalmitate; Glycosperse P20; Tween 40

RTECS No. WG 2933000

Uses Surfactant. Used in cosmetic formulations.

Physical properties

B. Pt. >110°C **Flash point** >110°C **Specific gravity** 1.083

Ecotoxicity

Invertebrate toxicity

Mycobacterium paratuberculosis ATCC strain 19698, suppressed growth at 0.01-0.1%, but enhanced growth at concentrations of 0-0.001% and 0.1-1.0% (1).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat 1600 mg kg^{-1} (polymer unspecified) (2).
LD_{50} intravenous mouse 50 g kg^{-1} (3).

Teratogenicity and reproductive effects

Gavage mouse 5200 mg of Tween 60 kg^{-1} day^{-1} on days 6-13 of gestation. No maternal toxicity was observed. Reduced foetal weight gain was observed (4).

Irritancy

Not irritating to rabbit eye as assessed by Draize test (polymer unspecified) (5).

Genotoxicity

Salmonella typhimurium Ames test negative (details not specified) (6).
Escherichia coli rec assay, DNA damage negative (polymer unspecified) (6).
In vitro Chinese hamster ovary cells, chromosome aberrations negative (polymer unspecified) (7).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

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P229 polysorbate 60

CAS Registry No. 9005-67-8

Synonyms polyethylene glycol sorbitan monostearate; Ahco DFS100; Grill 8; Liposorb S-20; poly(oxy-1,2-ethanediyl) sorbitan monooctadecanoate; sorbitan polyethoxy monostearate; Tween 60; poly(oxyethylene) sorbitol monostearate

RTECS No. WG 2934000

Uses Surfactant.

Physical properties

B. Pt. >110deg;C **Flash point** >100°C
Solubility Water: miscible. Organic solvents: aniline, ethanol, ethyl acetate, toluene, methanol

Occupational exposure

US-TWA 10 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >60 ml kg^{-1} (1).

LD_{50} intravenous rat 1200 mg kg^{-1} (2).

Teratogenicity and reproductive effects

Oral rat 0, 0.1, 1.0 or 10% diet on days 7-14 of gestation. No teratogenic or foetotoxic effects were observed (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

References

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P230 polysorbate 80

$C_{61}H_{122}O_{24}$ **Mol. Wt.** 1239.63 **CAS Registry No.** 9005-65-6

Synonyms E433; polyethylene glycol sorbitan monooleate; ethoxylated sorbitan monooleate; Glycosperse 0-20; Monitan; polyoxyethylene (20) sorbitan monooleate; Tween 80; Sarlate; Olothorb

RTECS No. WG 2932500

Uses Defoamer. Stabiliser. Plasticiser. Surfactant. Suppository base.

Physical properties

Flash point >149°C **Specific gravity** 1.06-1.10

Solubility Water: miscible. Organic solvents: ethanol, ethyl acetate, methanol, fixed oils, toluene

Ecotoxicity

Invertebrate toxicity

Mycobacterium paratuberculosis ATCC strain 19698, suppressed growth at 0.01-0.1% but enhanced growth at concentrations of 0-0.001% and 0.1-1.0% (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 35 ml kg^{-1} (2).

LD_{50} oral mouse 25 g kg^{-1} (3).

LD_{50} intraperitoneal rat, mouse 3500, 7600 mg kg^{-1}, respectively (4-6).

LD_{50} intravenous rat, mouse 1800, 4500 mg kg^{-1}, respectively (7,8).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via feed. Equivocal evidence of carcinogenicity was demonstrated in ♂ rats. No evidence of carcinogenic activity was demonstrated in ♀ rats or in ♂ and ♀ mice (9).

Teratogenicity and reproductive effects
Oral rat, lowest toxic dose 640 g kg^{-1} over several generations (reduced viability index) (10).

Irritancy
150 mg instilled into rabbit eye caused mild irritation (exposure not specified) (11).
Did not cause irritation to human skin (12).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (13).

Legislation

TDI human 25 mg kg^{-1} day^{-1} (14).

Other comments

A complex mixture of partial oleic acid esters of sorbitol and sorbitol anhydride copolymerised with ethylene oxide.

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P231 polystyrene

$(C_8H_8)_n$ **CAS Registry No.** 9003-53-6

Synonyms ethenylbenzene, homopolymer; bakelite LP80; Bustren; Carinex; Dorvon; Esbrite; Gedex; instrex; styrene polymer; styrofoam; styron; torporex

RTECS No. DA 0520000

Uses Packaging, consumer products, disposable serviceware, construction, electronic parts, furnishings and appliances.

Physical properties

M. Pt. 240°C **Specific gravity** 1.04-1.065 (amorphous); 1.111 (crystalline)
Solubility Organic solvents: ethylbenzene, methyl isobutyl ketone, tetrahydrofuran, benzene, toluene, pyridine, dichloromethane

Mammalian & avian toxicity

Acute data

LC_{50} (10 min) inhalation mouse 120 mg m^{-3} (1).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (2).
Subcutaneous implants to Wistar rats led to 37/47, 25/51 and 15/40 animals showing implantation site sarcomas for smooth discs, perforated discs and rods/spheres/fibres, respectively (3).
In another study, no appreciable difference in the incidence of local sarcomas was found between perforated and unperforated discs (4).

Other effects

Any other adverse effects

Subcutaneous implantation of discs in rats led to increased mucopolysaccharide production in the adjacent tissue during the first 4 months (5).
Sunflower oil containing styrene (0.56 mg l^{-1}) was fed to rats and caused the ratio of blood SH to SS groups initially to decrease at 2 wk and then increase after 6 months. Blood and erythrocyte lipid peroxide values increased, as did the activity of erythrocyte superoxide dismutase (after 6 months) and glucose-6-phophodehydrogenase (after 9 months). Erythrocyte glutathione reductase, blood alanine aminotransferase and cholinesterase activities were also affected. (6).

Other comments

Floating pollutant of seas (7).
In US municipal waste accounts for 20% (weight) of all plastics (7).

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P232 polytetrafluoroethylene

$$(CF_2{=}CF_2)_n$$

$(C_2F_4)_n$ **CAS Registry No.** 9002-84-0

Synonyms Aflon; Fluon; fluoroflex; poly(ethylene tetrafluoride); polytef; PTFE; tetrafluoroethylene homopolymer; Teflon; Velflon

RTECS No. KX 4025000

Uses In anti-friction composites. Binding agent. Lubricant additive. Non-stick surface coating. Manufacture of microporous membranes, laminates and films. Prosthetic aid.

Physical properties

M. Pt. 327°C **B. Pt.** 440°C (decomp.) **Specific gravity** 2.25

Environmental fate

Abiotic removal

Gases identified during pyrolysis at 300-400°C included tetrafluoroethylene, hexafluoroethylene, hexafluoroproplyene, octafluorocyclobutane, octafluoroisubutylene. At temperatures >500°C carbonyl fluoride is the predominant product and at >650°C carbon dioxide is also formed (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1250, 12,500 mg kg^{-1}, respectively (2).

Sub-acute and sub-chronic data

Oral rat (90 day) 25% diet caused no observable toxic effects (3,4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).

Subcutaneous mouse, observed for life following implant of PTFE discs of 15 × 1.2 mm. Sarcomas developed around the disc in 38% mice. Average ages at death of tumour-bearing animals were 72 wk for ♀ and 69 wk for ♂. No subcutaneous fibrosarcomas developed in control mice (6).

Subcutaneous implant ♀ mouse (120 wk) PTFE discs of 15 × 1.2 mm. Fibrosarcomas developed in 17/38 BALB/C mice, in 36/38 C3Hf/Dp mice and 12/39 C57BL/He mice, with mean latent periods of 78, 61 and 82 wk, respectively (7).

Subcutaneous implant rat (112 wk) PTFE plate of 4 × 5 × 0.16 mm. Subcutaneous sarcomas developed in 2/65 rats. 45 rats were still alive at the time of appearance of the first tumour at 659 days. No tumours were observed in 20 controls given glass implants (8).

Intraperitoneal implant rat (27 month) PTFE rods of 10 × 2 × 2 mm, or equivalent amount of PTFE powder. No tumours were found in 16 rod-implanted rats, whereas sarcomas became palpable in 2/17 the in powder-treated rats at 354 and 476 days. Extraperitoneal tumours included 1 fibroadenoma in the inguinal region of rod-implanted rats, and 1 liposarcoma in the upper part of the leg, 1 fibrosarcoma in the shoulder and 1 inguinal fibroadenoma in powder-treated rats. Among 25 untreated controls, 1 adenoma of the testes and 1 possible carcinoma of the inguinal region were observed (9).

Genotoxicity

Not mutagenic in *Salmonella* microsome test (with and without metabolic activation) and in the micronucleus test (details not given) (2).

Other effects

Other adverse effects (human)

A fibrosarcoma was reported in a 31-yr-old man 10.5 yr after implantation of a 5 cm woven PTFE-dacron arterial prosthesis. There was no evidence of metastasis (10).

Exposure to thermal degradation products and to unfinished products has caused polymer-fume fever (11).

Other comments

Physical properties, uses, carcinogenicity and mammalian toxicity reviewed (1,12).

Toxicity of pyrolysis products reviewed (1).

Glass transition temperature 130°C (powder).

Molecular weight 400,000-10,000,000.

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P233 polyvinyl acetate

$$(CH_2{=}CHO_2CCH_3)_n$$

$(C_4H_6O_2)_n$ **CAS Registry No.** 9003-20-7

Synonyms Gelva; Protox; PVAE; Rhodapos; vinyl acetate homopolymer; vinyl acetate resin; Bakelite AYAA; polymers acetic acid vinyl ester

RTECS No. AX 0920000

Uses Manufacture of adhesives. Binding agent. Base for chewing gum. In surface coatings. Lubricants. Plasticiser. Sizing agent.

Physical properties

M. Pt. 35-50°C **Specific gravity** 1.19 at 25°C

Solubility Organic solvents: acetone, benzene, chloroform, *n*-butanol, carbon tetrachloride, ethanol, isopropanol, methylene chloride, trichloroethylene

Environmental fate

Abiotic removal

Removal from wastewater by precipitation with an electrolyte (eg, sodium carbonate, sodium sulfate or sodium chloride). Separation was facilitated by addition of formaldehyde (1).

Principal pyrolysis product at 220-250°C acetic acid (2).

Undergoes hydrolysis in water to give polyvinyl alcohol (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse >2500 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Oral rat, mouse, single dose of 25 g kg^{-1}. Lymphoid infiltration of the liver, epithelial dystrophy of the kidney and a slight increase in the number of polynucleated cells in the spleen were observed (4).

Oral rat, mouse (1 yr) 250 mg kg^{-1} day^{-1} caused fluctuation in weight, changes in blood composition, changes in liver:body weight ratio and changes in catalase and cholinesterase activities (4).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).
Implantation rat and mouse (site not specified) polyvinyl acetate powder did not induce local sarcomas within 16-20 months (6).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).
In vitro Chinese hamster fibroblasts without metabolic activation, chromosomal aberrations negative (7).

Other comments

Physical properties, uses, analysis, carcinogenicity and mammalian toxicity reviewed (1).
Glass transition temperature 30°C (high molecular weight polymer).
Autoignition temperature 427°C.
Molecular weight 11,000-1,500,000.

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P234 polyvinyl alcohol

$$(CH_2{=}CHOH)_n$$

$(C_2H_4O)_n$ **CAS Registry No.** 9002-89-5

Synonyms Airvol 103; Alcotox 75L; alvyl; C05 (vinyl polymer); covol; Elvanol; Ivalor; ethenal, homopolymer; Gohsenol; polyviol; Prosthex; Solvor; PMS artificial tears; PVA; Vinarol; vinyl alcohol polymer

RTECS No. TR 8100000

Uses Non-ionic surfactant. Plastic mouldings. Surface coating. Paper and textile size. In adhesives. In printing inks for plastics and glass. Films. In cosmetics. Ophthalmic lubricant. Absorbent for water. Binding agent, coagulant in water treatment. Manufacture of electrodes.

Physical properties

M. Pt. 228°C (decomp.) **Flash point** 228°C (open cup) **Specific gravity** 1.31-1.91
Solubility Water: miscible with hot water

Environmental fate

Degradation studies
Degraded by *Pseudomonas* sp. in activated sludge process (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, guinea pig 14-22 g kg^{-1} (2,3).

Sub-acute and sub-chronic data

Intravenous or intraperitoneal dog, repeated injection of 5% aqueous solution (total dose not specified) caused anaemic and atheromatous lesions in the aorta and in the carotid and femoral arteries (4,5).

Subcutaneous rat, 1 ml of 5% solution day^{-1} for 49 days. Of 6 grades of molecular weight 35,000-240,000, 2 grades caused hypertension, widespread vascular lesions, hypertrophy of the heart and kidneys, renal damage and increased thyroid weight (6).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (7).

Subcutaneous implant rat (800 day) 20 × 20 × 5 mm or 33 × 33 × 2 mm sponges. 9/24 animals implanted with 5 mm thick sponges developed local sarcomas compared with 1/24 among the 2 mm group. In addition sarcomas developed in 5/24 animals with 12.6 × 12.6 × 5 mm implants, and only 1/24 with 20 × 20 × 2 mm and 1/24 with 8 × 8 × 5 mm implants (8).

Subcutaneous rat (2 yr) 500 mg $animal^{-1}$ polyvinyl alcohol powder (molecular wt 120,000). No local tumours were seen, but 3 benign and 6 malignant tumours at various sites were observed among 25 treated animals compared with 3 benign and 17 malignant tumours among 200 controls (9).

Metabolism and toxicokinetics

Following oral, intravenous or subcutaneous administration to rats and rabbits, polyvinyl alcohol was retained for up to 6 months in various organs, including the brain, liver and kidney. Accumulation has also been reported in cells of the reticular-endothelial system, spleen, suprarenal glands and in histiocytes of the lung, testicles and retroperitoneal tissue (10,11).

Irritancy

Repeated instillation of 1.4% solution into rabbit eyes did not cause injury and did not interfere with healing of experimental epithelial wounds (12).

Other effects

Other adverse effects (human)

Implantation of polyvinyl alcohol sponge as a breast prosthesis has been reported to be associated with fibrosis (13).

A case of haemangiopericytoma of the bladder was reported in a 40-yr-old man who had worked with polyvinyl alcohol. It was speculated that there might be a relationship similar to that between vinyl chloride and angiosarcoma of the liver (14).

Other comments

Available in many grades of differing molecular weight (25,000-300,000, average 120,000) and in degree of hydrolysis (75-100%) (10).

Physical properties, use, analysis, carcinogenicity and mammalian toxicity reviewed (10).

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P235 polyvinyl chloride

$$(CH_2{=}CHCl)_n$$

$(C_2H_3Cl)_n$ **CAS Registry No.** 9002-86-2

Synonyms atactic poly(vinyl chloride); bakelite QSAH; chloroethene homopolymer; vinyl chloride homopolymer; PVC; Syncrolube; Evicom; Lacovyl; Vestolit

RTECS No. KV 0350000

Uses Manufacture of film, bottles, packaging, laminates, foam, pipes, toys and untensils. Binder. Electrical insulator. Surface coating.

Physical properties

Specific gravity 1.406
Solubility Organic solvents: high mol. wt. PVC: cyclohexanone, dimethylformamide, methylcyclohexanone, mesityl oxide, nitrobenzene, tetrahydrofuran; low mol. wt. PVC: acetonylacetone, dichloromethane, 1,4-dioxane, methyl amyl ketone, methyl ethyl ketone, methyl isobutyl ketone

Occupational exposure

DE-MAK 1.5 mg m^{-3} (respirable fraction or aerosol)
SE-LEVL 1 mg m^{-3} (total dust); 0.5 mg m^{-3} (respirable dust)
UK-LTEL 10 mg m^{-3} (total inhalable dust); 4 mg m^{-3} (respirable dust)

Environmental fate

Degradation studies
Degraded by *Penicillium chrysogenum, Aspergillus niger, Aspergillus flavus, Aspergillus fumigatus, Rhizopus oryzae* and *Pseudomonas aeruginosa* when incubated in a mineral medium with or without glucose. The major degradation product was isooctanol (1).

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Inhalation rat, guinea pig exposure to PVC dust (concentration not specified) for 24 hr day^{-1} for 2-7 months caused extensive lung damage (2).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (3).
Subcutaneous implant rat, PVC discs or squares of 15 mm × 0.04 mm thick, known to contain some additives. Malignant tumours at the site of implant were observed in 17/45 animals (fibrosarcomas and 1 liposarcoma) with a latent period of 189-727 days. No local tumours developed in 27 rats implanted with a similar but perforated PVC film. With pure PVC film of 0.03 mm thickness, 4 malignant tumours developed in a similar group after 533 days. No local tumours were observed in 50 rats given subcutaneous implant of cotton wool (4).

Subcutaneous implant rat (800 day) PVC film 4 × 5 × 0.16 mm. Among 30 rats which survived >300 days one sarcoma and 1 fibroma were found after 580 days. No local tumours developed in controls (5).
Rats were implanted with PVC film by laparotomy to surround the kidney. Fibrosarcomas developed at the site of implantation in 6/16 animals (6).

Sensitisation

Cases of "peat wrapper asthma" have been reported in which workers exposed to fumes of PVC film sealed with hot wire developed respiratory symptoms (7).
Cases of dermatitis have been reported which are believed to have been caused by sensitivity to plasticisers in PVC plastics (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (9).

Other effects

Other adverse effects (human)

Workers exposed to PVC dust have shown reduced pulmonary function (10-14).
A case of systemic sclerosis (involving thickening of the skin on the arms, hands, face and trunk) and pneumoconiosis in a 58-yr-old worker was associated with work at an Austrian plastic recycling mill. Over the preceding 10 yr he had fed and cleaned the "poorly ventilated" mill up to five times per day (a total daily exposure of approximately 2 hr). These operations resulted in exposure to polyvinyl chloride (PVC) dust particles in the micrometre range, the inhalation of which was associated with the development of pneumoconiosis. The investigators postulated that non-digestible PVC particles within lung macrophages stimulated the production of growth factors leading to the excess production of collagen associated with the systemic sclerosis (15).
A large proportion of abnormal liver function tests and abnormal platelet counts were found in a group of 37 PVC process workers. 20% had abnormal alkaline phosphatase, 60% abnormal lactate dehydrogenase, 30% abnormal serum glutamic-oxalacetic transaminase, 10% abnormal serum glutamic-pyruvic transaminase levels, and 35% abnormal platelet counts (16).
Mortality studies of plastics workers have shown statistically significant excesses of cancer mortality, particularly that of the digestive system in both sexes, and cancer of the breast and urinary organs among women. These studies are limited, however, by the fact that not all deaths were among workers engaged in activities directly involving PVC (17-18).
A case was reported of a 22-yr-old man who developed a squamous-cell carcinoma of the buccal mucosa as a result of a habit, acquired at the age of 8 yr, of chewing plastic materials containing PVC (19).
In a study of 148 male cancer victims and 315 healthy controls, researchers at the Medical Centre in Oerebro, Sweden, found that workers in PVC processing and handling industries had a seven times greater risk of developing testicular cancer. The suspect chemicals are phthalate softening agents (20).

Other comments

Physical properties, use, analysis, carcinogenicity and toxicity reviewed (21,22).
Carcinogenicity data reviewed (23).
Average molecular weight 60,000-150,000. Formulated with non-phthalate plasticiser.

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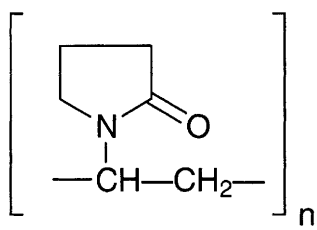
P236 polyvinylpyrrolidone



$(C_6H_9ON)_n$ **CAS Registry No.** 9003-39-8

Synonyms 1-ethenyl-2-pyrrolidinone polymers; 1-vinyl-2-pyrrolidinone polymers; poly[1-(2-oxo-1-pyrrolidinyl)ethylene]; polyvidone; povidone; P.V.P.

RTECS No. TR 8370000

Uses Widely used in the cosmetics, pharmaceutical, plastics, ink, adhesives, textile, beverage, detergent and other industries for its film-forming and adhesive properties, its colloidal and dispersing abilities and its capacity to form complexes with iodine, dyes, drugs, toxins and other chemicals.

Physical properties

Specific gravity 1.23-1.29
Solubility Water: soluble in water giving a colloidal solution. Organic solvents: ethanol, chloroform

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 12 g kg^{-1} (1).
LD_{Lo} oral mouse 3 g kg^{-1} (average molecular weight 20,000) (2).
LD_{Lo} oral mouse 5 g kg^{-1} (average molecular weight 50,000) (2).

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

Polyvinylpyrrolidone has been tested in mice, rats and rabbits by various routes of administration, with polymers of various molecular weights. Subcutaneous injections of an aqueous solution to rats caused local sarcomas. Subcutaneous or intraperitoneal implantation of material in powder form caused a low incidence of local tumours. In rats, repeated intravenous injections or intraperitoneal implantation resulted in tumours at distant sites, but the association between treatment and these distant tumours is not conclusive (4).
Albino rats were fed bracken fern as ⅓ of diet for 12 months, resulting in 30/30 rats with intestinal tumours and 22/30 with urinary bladder tumours. Another group of rats fed the same diet with polyvinylpyrrolidone (50 mg g^{-1} diet) had similar incidence of intestinal tumours (26/28 rats), but much lower incidence of bladder tumours(5/28 rats) (5).

Teratogenicity and reproductive effects
Injection of 500 μg (molecular weight 11,500) in 0.01 ml saline into the yolk sac of rabbits (day 9 of gestation) did not result in any teratogenic effects (6,7).

Metabolism and toxicokinetics
Polyvinylpyrrolidone, intravenously injected into rats, rabbits or dogs, was not significantly metabolised by any species. Only low molecular weight polymer can be excreted, and PVP with a molecular weight >110,000 is retained by the reticuloendothelial system (8,9).
In humans PVP with a molecular weight <25,000 is excreted by the kidneys (9).
Four terminal cancer patients were given ^{14}C-PVP with an average molecular weight of 40,000 by intravenous infusion. About ⅓ of the dose had been excreted in the urine after 6 hr, and ⅔ after 18 hr. Small amounts were excreted in the faeces. At autopsy, PVP was found in the kidneys, lungs, liver, spleen and lymph nodes (10).

Irritancy
Addition of 0.5-1.0% polyvinylpyrrolidone to shampoo formations markedly reduces their irritancy to rabbit eyes (11).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 and TA1537 with and without metabolic activation negative (12).
Polyvinylpyrrolidone produces 48% inhibition of benzo[*a*]pyrene-induced mutagenicity in *Salmonella typhimurium* TA98 at a concentration 50 times that of benzo[*a*]pyrene; it is defined as a relatively weak inhibitor of this mutagenicity (13).

Other effects

Other adverse effects (human)
Injection of products containing polyvinylpyrrolidone as an excipient has resulted in its deposition in various tissues, causing pain and lesions, and occasionally involving the liver (14).
Liver biopsies from 22 patients who had been administered intravenous infusions of 3.5 or 4.5% PVP showed basophilic globular deposits within Kupffer cells or free deposits in the liver sinusoids, occasionally with a mild inflammation (15).
Lymph node biopsies from 6 patients with thesaurismosis (storage disease) after inhalation of PVP-containing hairspray showed pathological changes varying from slight hyperplasia to marked granuloma formation resembling sarcoidosis. Some patients had lung lesions such as fibrosis or pneumonia, with hyperplasia of alveolar lining cells and an accumulation of macrophages. Three of the patients died. (16).

Other comments

Available commercially with average molecular weight ranging from 10,000 to 700,000 (17).
Temporary acceptable daily intake 25 mg kg^{-1} (18).
Physico-chemical properties, human health effects, exposure levels (environment and workplace), experimental toxicology, workplace experience and epidemiology reviewed (3,19,20).

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P237 potassium

K

K **Mol. Wt.** 39.10 **CAS Registry No.** 7440-09-7

Synonyms kalium

EINECS No. 231-119-8 **RTECS No.** TS 6460000

Uses In synthesis of inorganic potassium salts. Organic synthesis. Heat transfer agent.
Occurrence Found mainly as the chloride (sylvite), also in the aluminosilicates (orthoclase, microcline) and as carnallite (KCl, $MgCl_2.6H_2O$).

Physical properties

M. Pt. 64°C **B. Pt.** 774°C **Specific gravity** 0.862 at 20°C **Volatility** v.p. 8 mmHg at 432°C

Occupational exposure

UN No. 2257 **HAZCHEM Code** 4W **Conveyance classification** substance which in contact with water emits flammable gas
Supply classification highly flammable, corrosive
Risk phrases Reacts violently with water, liberating extremely flammable gases – Causes burns (R14/15, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep contents under oil – Keep container dry – In case of fire, use graphite, sand, sodium chloride – do not use water – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – (S5 not required when safe packaging is used) (S1/2, S5, S8, S43, S45)

Ecotoxicity

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 140 mg l^{-1} (K^+) (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 700 mg kg^{-1} (2).

Other effects

Other adverse effects (human)

Solid metal causes burns. Fumes from burning potassium are extremely destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin (3,4).

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. Potassium guide level 10 mg l^{-1}; maximum admissible concentration 12 mg l^{-1} (6).

Other comments

Physical properties, toxicity and safety precautions reviewed (4).
Reacts vigorously with oxygen and with water (7).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

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P238 potassium arsenate

$$KH_2AsO_4$$

AsH_2KO_4 **Mol. Wt.** 180.03 **CAS Registry No.** 7784-41-0

Synonyms Macquer's salt; monopotassium arsenate; monopotassium dihydrogen arsenate; potassium hydrogen arsenate; potassium acid arsenate

EINECS No. 232-065-8 **RTECS No.** CG 1100000

Uses Laboratory reagent. Preserving hides. Insecticide.

Physical properties

M. Pt. 288°C **Specific gravity** 2.867
Solubility Water: 190 g l^{-1} at 6°C. Organic solvents: glycerol

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)

UN No. 1677 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation and if swallowed (R45, R23/25)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Invertebrate toxicity
Minimum inhibitory concentration (24 hr) *Photobacterium fischeri* 305 mg l^{-1} (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (arsenic and arsenic compounds) (2).

Teratogenicity and reproductive effects
Oral sheep, 0.5 mg kg^{-1} day^{-1} either throughout gestation or for the first 45 days produced no teratogenic effects (3).

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}. Arsenic maximum admissible concentration 50 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
WHO guideline value for drinking water, arsenic 10 μg l^{-1} (6).

Other comments

Physical properties, uses, carcinogenicity, mammalian toxicity and mutagenicity of arsenic and arsenic compounds reviewed (7,8).

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P239 potassium arsenite

$KAsO_2.HAsO_2$

As_2HKO_4 **Mol. Wt.** 253.95 **CAS Registry No.** 10124-50-2

Synonyms arsenous acid, potassium salt; arsonic acid, potassium salt; Fowler's solution; potassium metaarsenite

RTECS No. CG 3800000

Uses A haematinic used in the treatment of chronic myelogenous leukaemia. In treatment of skin and pulmonary diseases. In manufacture of mirrors, reducing silver salt to metallic silver.

Physical properties

M. Pt. 300°C (decomp.)
Solubility Water: miscible. Organic solvents: ethanol

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)

UN No. 1678 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic by inhalation and if swallowed (R23/25)
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)

Ecotoxicity

Fish toxicity
Not toxic to brown trout, bluegill sunfish, yellow perch or goldfish at 5 ppm for 24 hr. Water conditions: pH, 7.0; dissolved oxygen, 7.5 ppm; total hardness (soap method), 300 ppm; methyl orange alkalinity, 310 ppm; phenolphthalein alkalinity, 0; free carbon dioxide, 5 ppm; temperature, 12.8°C (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 14 mg kg^{-1} (2).
LD_{50} dermal rat 150 mg kg^{-1} (3).
LD_{Lo} subcutaneous mouse, rabbit, guinea pig, dog, cat 0.7-12 mg kg^{-1} (4).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (arsenic and arsenic compounds) (5).
Oral mouse (2 yr) 170 or 340 mg kg^{-1} diet for 48 wk 1 wk after a single dermal application of 5 μg 7,12-dimethyl benz[*a*]anthracene. 2 wk later they were also given dermal applications of 25 μl of a 0.5% solution of croton oil in benzene wk^{-1} throughout the experiment. The incidence of papillomas did not differ from that in controls given DMBA and croton oil (6).

Metabolism and toxicokinetics
Following daily subcutaneous administration to rabbits, guinea pigs and apes, low blood levels of arsenic and relatively higher tissue levels of arsenic. In contrast, rats showed higher arsenic levels in the blood than in the major organs. Some arsenic appeared to pass from the blood into the spinal fluid in apes (7).
Passes through the placental barrier (8).

Irritancy

Irritating to the eyes, skin and upper respiratory tract of humans (8).

Genotoxicity

In vitro human lymphocytes, mitotic arrest and chromosomal aberrations positive (9).
In vivo human lymphocytes, an increased incidence of sister chromatid exchanges, but not chromosomal aberrations was reported for workers exposed to Fowler's solution (10).
Vicia faba induction of sister chromatid exchanges positive (11).

Other effects

Other adverse effects (human)

The therapeutic use of Fowler's solution has lead to chronic changes in the skin (arsenicism) and invasive carcinomas of the skin. The period from the beginning of treatment to occurrence of tumours range from 5-60 yr (average 18 yr), and most cancers occurred only after the drug had been taken for a long time: 90% of cases after 1 yr and 60% after 5 yr. The average dose was 28 g (range 0.2-121 g) (12).

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}. Arsenic maximum admissible concentration 50 μg l^{-1} (13).
WHO guideline value for drinking water, arsenic 10 μg l^{-1} (14).

Other comments

Readily oxidised to arsenate in aqueous solution (15).
Physical properties, use, carcinogenicity, mammalian toxicity and mutagenicity reviewed (15,8,12).

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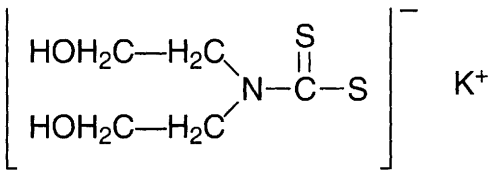
P240 potassium bis(2-hydroxyethyl)dithiocarbamate



$C_5H_{10}NO_2S_2K$ **Mol. Wt.** 219.37 **CAS Registry No.** 23746-34-1

Synonyms bis(2-hydroxyethyl)carbamodithioic acid, monopotassium salt; bis(2-hydroxyethyl)dithiocarbamic acid, monopotassium salt; bis(2-hydroxyethyl)dithiocarbamic acid, potassium salt

RTECS No. EY 9450000

Uses Fungicide. As an analytical reagent in the quantitative determination of cobalt, copper, gold, mercury, nickel and palladium (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (2).

TD_{Lo} (78 wk, continuous) oral rat 82 g kg^{-1}, was not carcinogenic under the test conditions (3).

Groups of ♂ and ♀ (C57BL/6xC3H/Anf)F_1 mice and (C57BL/6xAKR)F_1 mice were given 464 mg kg^{-1} in gelatine daily from 7 days until 4 wk old; this was the maximum tolerated dose for infant and young mice. After 4 wk of age, mice were orally fed 1112 mg kg^{-1} of diet, until about 78 weeks old. 14/18, 17/18, 15/18 and 16/18 mice in the four groups, respectively, were still alive at the end of treatment. Hepatomas were found in 13/16 ♂ and 12/18 ♀ mice of the first strain, compared with 8/79 and 0/87 controls, respectively, and in 13/17 ♂ and 13/16 ♀ mice of the second strain, compared with 5/90 and 1/82 controls. Lung adenomas and malignant lymphomas did not occur more frequently in treated mice than in controls (4,5).

Mice (28 days old) given single subcutaneous injections of 464 mg kg^{-1} in dimethyl sulfoxide were observed until 78 weeks old; 15/18, 15/18, 17/18 and 18/18 mice out of the four groups tested were still alive. The incidence of tumours was not increased, compared with control mice (5).

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} (6).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

Other comments

Suspected genotoxic carcinogen (8).

Reviews on human health effects and experimental toxicology listed (1).

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P241 potassium bromate

$KBrO_3$

$BrKO_3$ **Mol. Wt.** 167.00 **CAS Registry No.** 7758-01-2

Synonyms bromic acid, potassium salt; E924

EINECS No. 231-829-8 **RTECS No.** EF 8725000

Uses Brominating agent. Catalyst. Analytical reagent. Oxidising agent. In malting of barley for beer.

Physical properties

M. Pt. 350°C **B. Pt.** 370°C (decomp.) **Specific gravity** 3.270 at 17.5°C
Solubility Water: 75 g l^{-1} at 25°C. Organic solvents: ethanol

Occupational exposure

UN No. 1484 **HAZCHEM Code** 1YE **Conveyance classification** oxidising substance
Supply classification toxic, oxidising
Risk phrases May cause cancer – Explosive when mixed with combustible material – Toxic if swallowed (R45, R9, R25)
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 rat 160-320 mg kg^{-1} (1,2).
LD_{50} intraperitoneal mouse 180 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral rat (1, 2, 3, 4 or 14 wks) 500 ppm in drinking water. A rapid increase in the levels of 8-hydroxydeoxy guanosine was noted in ♂ kidney DNA. This elevation persisted until the end of the experiment. An increase in cell proliferation in the proximal convoluted tubule was also observed. In ♀ subjects the increase in 8-hydroxydeoxy guanosine only became apparent after 3 wk (4).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (5).
Oral rat, 0, 250 or 500 mg l^{-1} in drinking water for 110 wk (total dose 0, 10 and 20 g kg^{-1}. A >2% reduction in body weight gain was observed in the high-dose animals, especially in ♂ rats. Survival rates were decreased in high-dose ♂ rats. Treatment-related increases in the incidence of renal adenocarcinomas and renal adenomas were observed in both sexes. A significant increase in the incidence of mesotheliomas was also observed in ♂ rats. No such tumour occurred in ♀ rats. Benign and malignant tumours of the thyroid were also observed in ♂ rats but the incidence did not differ among groups (6).
Oral rat and mouse, 50 or 75 mg kg^{-1} diet for 104 wk to rats and for 80 wk to mice caused no adverse effects (7,8).

Dermal mouse, 0.008 mg animal^{-1} wk^{-1} for 51 wk after a single application of 0.05 ng 7, 12-dimethybenz[*a*]anthracene or alone. No skin tumour was observed in either group (9).

Metabolism and toxicokinetics

When mice were given diets containing 50 or 75 mg kg^{-1} for 80 wk, concentrations of 1 and 2 mg kg^{-1} bromine, respectively, were detected in the adipose tissue. However, bromine did not accumulate in the adipose tissue of rats given similar diets for 104 wk (7,8).

Ionic compounds such as potassium bromate are poorly absorbed through the mammalian skin (10).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract to humans (11).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with metabolic activation positive (12,13).
In vitro Chinese hamster lung cells, chromosomal aberrations with metabolic activation positive (13).
In vivo mouse micronucleus test positive (14,15).
In vivo rat bone marrow cells, chromosome aberrations positive (16).

Other effects

Other adverse effects (human)

Ingestion may cause vomiting, diarrhoea, methaemoglobinaemia and renal injury (17).
In both children and adults, oliguria and death from renal failure have been reported (18,19).
Hearing loss and deafness have also been reported (20,21).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1}; maximum admissible concentration 12 mg l^{-1} (22).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).
WHO guideline value for drinking water, bromate 25 µg l^{-1} (24).

Other comments

Disinfectant by-product in brominated drinking water (24,25).
Physical properties, use, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (9,26-30).
Water chemistry reviewed (25).

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P242 potassium chlorate

$KClO_3$

$ClKO_3$ **Mol. Wt.** 122.55 **CAS Registry No.** 3811-04-9

Synonyms Berthallet salt; chlorate of potash; potassium oxymuriate; potcrate

EINECS No. 223-289-7 **RTECS No.** FO 0350000

Uses Oxidising agent. Manufacture of explosives. Manufacture of dyestuffs. Antiseptic.

Physical properties

M. Pt. 368.4°C **B. Pt.** 400°C (decomp.) **Specific gravity** 2.320 at 20°C
Solubility Water: 6%. Organic solvents: glycerol

Occupational exposure

UN No. 1485

UN No. 2427 (aqueous solution) **HAZCHEM Code** 1YE **HAZCHEM Code** 2S (aqueous solution)
Conveyance classification oxidising substance
Supply classification oxidising, harmful
Risk phrases Explosive when mixed with combustible material – Harmful by inhalation and if swallowed (R9, R20/22)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Keep away from sources of ignition – No smoking – Take off immediately all contaminated clothing (S2, S13, S16, S27)

Environmental fate

Nitrification inhibition
75% inhibition of ammonia oxidation by activated sludge at 57 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat, dog 1200, 1900 mg kg^{-1}, respectively (2,3).

LD_{Lo} intraperitoneal rat, guinea pig 1500, 1800 mg kg^{-1}, respectively (4).

Irritancy

Irritating to the gastro-intestinal tract (5).

Irritating to the skin, eye, mucous membranes and upper respiratory tract of humans (6).

Genotoxicity

Escherichia coli PQ37 (uvr B^-), PQ35 (uvr B^+) SOS chromotest negative (7).

Other effects

Other adverse effects (human)

May cause haemolysis of red blood cells, methaemoglobinaemia and kidney damage (5).

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. Potassium: guide level 10 mg l^{-1}; maximum admissible concentration 12 mg l^{-1} (9).

Other comments

Disinfectant by-product in chlorinated drinking water (10).

Physical properties, toxicity and safety precautions reviewed (11,12).

Applications and effects in chlorinated drinking waters comprehensively reviewed (13).

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P243 potassium chloride

KCl

ClK **Mol. Wt.** 74.55 **CAS Registry No.** 7447-40-7

Synonyms chloropotassuril; camcopat; chlorvescent; Kalium-Duriles; muriate of potash; muriate of potassium; potavescent; Super K; Kaochlor; Kay Ciel

EINECS No. 231-211-8 **RTECS No.** TS 8050000

Uses Chlorination catalyst in electroplating. In pharmaceutical preparations. In colour photographic developers. Electrolyte. Fertiliser. Therapeutic electrolyte replenisher. Food additive. Salt substitute.
Occurrence In the mineral sylvite.

Physical properties

M. Pt. 770°C **B. Pt.** 1500°C **Specific gravity** 1.99 at 20°C
Solubility Water: 240 g l^{-1} at 100°C. Organic solvents: diethyl ether, ethanol, glycerol, methanol

Ecotoxicity

Fish toxicity
Concentrations of 5000 mg l^{-1} produced signs of toxicity in perch within 90 min of exposure (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, guinea pig 380-2600 mg kg^{-1} (2-4).
LD_{50} intravenous rat, mouse 39, 120 mg kg^{-1}, respectively (4,5).
LD_{50} intraperitoneal rat, mouse 660, 1200 mg kg^{-1}, respectively (6-8).

Metabolism and toxicokinetics
Potassium salts are readily absorbed from the gastro-intestinal tract. Potassium is actively transported into body cells where its concentration is up to 40 × that in extracellular fluids (9,10).

Irritancy
500 mg instilled into rabbit eye for 24 hr caused mild irritation (2).
Irritating to the skin, mucous membranes and upper respiratory tract (11).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (12).
Escherichia coli WP2 (λ) without metabolic activation negative (13).
In vitro Chinese hamster V79 cells, chromosomal aberrations positive (14).
In vitro primary rat hepatocytes, DNA damage and repair assays negative (15).

Other effects

Other adverse effects (human)
Large oral doses may cause gastro-intestinal irritation, purging, weakness and circulatory disorders (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chloride: guide level 25 mg l^{-1} (17).
UK maximum permitted concentration in drinking water, chloride 400 mg l^{-1} (12 monthly average) (18).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (19).

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P244 potassium chromate

$$K_2CrO_4$$

CrK_2O_4 **Mol. Wt.** 194.19 **CAS Registry No.** 7789-00-6

Synonyms bipotassium chromate; dipotassium monochromate; potassium chromate(VI); tarapacaite

EINECS No. 232-140-5 **RTECS No.** GB 2940000

Uses Oxidising agent. Analytical reagent. Corrosion inhibitor. Manufacture of pigments and dyestuffs.

Physical properties

M. Pt. 975°C **Specific gravity** 2.732 at 18°C

Solubility Water: 629 g l^{-1} at 20°C

Occupational exposure

FR-VME 0.05 mg m^{-3} (as Cr)

SE-LEVL 0.02 mg m^{-3} (as Cr)

UK-LTEL MEL 0.05 mg m^{-3} (as Cr)

US-TWA 0.05 mg m^{-3} (as Cr)

Supply classification toxic

Supply classification dangerous for the environment

Risk phrases Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact – May cause cancer by inhalation – May cause heritable genetic damage – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R36/37/38, R43, R49, R46, 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 (S53, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) sheephead minnow, fathead minnow, bluegill sunfish, threespine stickleback 25-180 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia pulex* 0.18 mg l^{-1} (1).
LC_{50} (48 hr) *Mysidopsis bahia* (mysid shrimp) 6.0 mg l^{-1} (1).

Environmental fate

Nitrification inhibition

75% inhibition of ammonia oxidation by activated sludge at 680 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 180 mg kg^{-1} (3).
LD_{50} intramuscular rabbit 11 mg kg^{-1} (4).
LD_{Lo} subcutaneous rabbit, guinea pig 12, 60 mg kg^{-1}, respectively (5).
LD_{Lo} intravenous dog 2.9 mg kg^{-1} (5).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (chromium(VI) compounds) (6).

Teratogenicity and reproductive effects

Intraperitoneal mouse, lowest toxic dose 30 mg kg^{-1} day^{-1} on days 8-10 of gestation caused greyish or brownish spots in the fur of the offspring (7).
In vitro mouse embryo cells 0.02-2.0 mg l^{-1} damaged blastocyst formation, and hatching of the blastocyst from the zona pellucida to the formation of the inner cell mass was inhibited (8).

Metabolism and toxicokinetics

Gastro-intestinal absorption in rats has been reported to be 3-6% (9,10).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (11).

Genotoxicity

Salmonella typhimurium TA1535 umu test positive (12).
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (13).
Escherichia coli WP2 (λ) without metabolic activation, Microscreen assay, positive (14).
In vitro Chinese hamster ovary fibroblasts, DNA damage positive (15).
In vitro human peripheral blood lymphocytes, sister chromatid exchanges and chromosomal aberrations positive (16).
In vivo Chinese hamster bone marrow, sister chromatid exchanges positive. The frequency of micronucleated polychromatic erythrocytes was also increased (17).

Other effects

Other adverse effects (human)

A number of epidemiological studies carried out among workers involved in chromate and chromate pigments have consistently shown an excess risk for lung cancers (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).
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}. Chromium: maximum admissible concentrations 50 μg l^{-1} (19).
WHO guideline value for drinking water, chromium 50 μg l^{-1} (20).

Other comments

Environmental impact and toxicity of chromium compounds reviewed (6,10,21-24).

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P245 potassium cyanide

KCN

CKN **Mol. Wt.** 65.12 **CAS Registry No.** 151-50-8

Synonyms hydrocyanic acid, potassium salt

EINECS No. 205-792-3 **RTECS No.** TS 8750000

Uses Catalyst. Organic synthesis. In electroplating baths.

Physical properties

M. Pt. 634.5°C **B. Pt.** 1625°C **Specific gravity** 1.520 at 16°C
Solubility Water: 50%. Organic solvents: ethanol, glycerol, methanol

Occupational exposure

DE-MAK 5 mg m^{-3} (as CN) (inhalable dust fraction)
FR-VME 5 mg m^{-3} (as HCN) **SE-CEIL** 5 mg m^{-3} (as CN)
UK-LTEL 5 mg m^{-3} (as CN) **US-STEL** ceiling limit 5 mg m^{-3} (as CN)

UN No. 1680 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Contact with acids liberates very toxic gas (R26/27/28, R32)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed – After contact with skin, wash immediately with plenty of water – Do not empty into drains – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7, S28, S29, S45)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) guppy, bluegill sunfish, brook trout, zebra fish 0.09-0.48 mg l^{-1} (1-3).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* sp. 0.8 mg l^{-1} (3).

Environmental fate

Nitrification inhibition
Limiting concentration for inhibition of nitrification 0.05 mg l^{-1} (4).

Degradation studies
BOD_7 activated sludge 6% of ThOD, 99% in trickling filter (1).

Abiotic removal
>99% removal from wastewater at 10 mg l^{-1} was achieved by precipitation with copper salts or by treatment with copper-bearing ion exchange resin in the presence of a reducing agent (sulfite, hydrosulfite, iron(II) salt, or hydrazine) (5,6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 5, 10 mg kg^{-1}, respectively (7-10).
LD_{50} intraperitoneal rat, mouse 4, 6 mg kg^{-1}, respectively (11,12).
LD_{50} subcutaneous rat, mouse, rabbit, dog 4-9 mg kg^{-1} (13-16).
LD_{50} intravenous mouse 2.6 mg kg^{-1} (16).

Sub-acute and sub-chronic data
Oral 0.3 mg kg^{-1} diet for 2 wk led to body weight loss and to falls in haemoglobin, protein and thyroxine levels in the blood, with concurrent increased in the blood levels of thiocyanates. Some animals developed intestinal tumours and all showed impaired reproductive performance (17).
Subcutaneous rat, 0.5 mg kg^{-1} wk^{-1} for 22 wk caused demyelinisation and degenerative changes in the cerebral cortex, hippocampus and cerebellum (18).

Metabolism and toxicokinetics
Rapidly absorbed through skin and gastro-intestinal tract (19).
Elimination $t_{1/2}$ 23 min following intravenous administration of 0.82 mg kg^{-1} to dogs (20).
In humans excretion is principally via the urine (83-89%). ~4% is removed in expired air (21).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (22).
Escherichia coli WP2, WP67, CM871, DNA repair test with and without metabolic activation positive (22).
Plant gene or point mutation negative (species unspecified) (1).
Plant chromosomal aberrations positive (species unspecified) (1).

Other effects

Other adverse effects (human)

Exposure may cause nausea, dizziness and headache, lung irritation and cyanosis. May be fatal as a result of inhalation, swallowing or absorption through the skin (23).

Any other adverse effects

Inhibits cyctochrome c oxidase in the rat brain inducing a blockade of cell respiratory processes which is reflected in a dose-dependent manner, by a decrease in phosphocreatine content and pH, and an increase in inorganic phosphate, whereas ATP levels remain constant for intraperitoneal doses up to 6 mg kg^{-1} (24).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Cyanides: maximum admissible concentration 50 $\mu g\ l^{-1}$ (25).
WHO guideline value for drinking water, cyanide 70 $\mu g\ l^{-1}$ (26).

Other comments

Physical properties, environmental impact and toxicity and safety precautions reviewed (1,19,27).

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P246 potassium dichromate

$K_2Cr_2O_7$

$Cr_2K_2O_7$ **Mol. Wt.** 294.18 **CAS Registry No.** 7778-50-9

Synonyms potassium bichromate; potassium dichromate(VI); iopezite

EINECS No. 231-906-6 **RTECS No.** HX 7680000

Uses Analytical reagent. Catalyst. Corrosion inhibitor. Electrolyte. Oxidising agent. Bleaching agent. Tanning leather. Manufacture of pigments and dyestuffs.

Physical properties

M. Pt. 398°C **B. Pt.** 500°C (decomp.) **Specific gravity** 2.676 at 25°C with respect to water at 4°C
Solubility Water: 43 g l^{-1} at 0°C and 502 g l^{-1} at 100°C

Occupational exposure

FR-VME 0.05 mg m^{-3} (as Cr)
SE-LEVL 0.02 mg m^{-3} (as Cr)
UK-LTEL MEL 0.05 mg m^{-3} (as Cr)
US-TWA 0.05 mg m^{-3} (as Cr)
Supply classification very toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer by inhalation – May cause heritable genetic damage – Harmful in contact with skin – Toxic if swallowed – Very toxic by inhalation – Irritating to respiratory system and skin – Risk of serious damage to eyes – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R49, R46, R21, R25, R26, R37/38, R41, R43, 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 (S53, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) sheephead minnow, fathead minnow, bluegill sunfish, threespine stickleback 25-150 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) 29.9 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) 211 mg l^{-1} (2).
EC_{50} (48 hr) *Daphnia pulex* 0.18 mg l^{-1} (1).
LC_{50} (48 hr) *Mysidopsis bahia* (mysid shrimp) 6.3 mg l^{-1} (1).

Environmental fate

Nitrification inhibition
10% inhibition of nitrification at 6 mg l^{-1} in biological film reaction (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 190 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 37 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Subcutaneous rat (9 days) single dose of 3-20 mg kg^{-1} induced renal damage as indicated by the urinary excretion of *N*-acetyl-β-D-glucosaminidase activity (6).

Inhalation rabbit and cat, 11-23 mg m^{-3} for 2-3 hr day^{-1} for 5 days caused bronchitis and pneumonia in cats. No adverse effects were observed in rabbits (7).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (chromium (VI) compounds) (8).

Teratogenicity and reproductive effects

Groups of 30 ♀ mice were fed with 250 ppm, 500 ppm and 750 ppm Cr(VI), as potassium dichromate in drinking water for 20 days and groups of 10 mice were fed with 0.05 ppm, 0.5 ppm and 5 ppm Cr(VI) for 90 days. Ovaries of the highest dose group (750 ppm) exhibited large numbers of atretic follicles and congestion in stromal tissue compared with all other treated groups and there was a dose-dependent reduction in the number of follicles at different stages of their maturation. The number of ova recovered from ice treated with 500 ppm and 750 ppm Cr(VI) were decreased significantly from those treated with 250 ppm or control groups and the length of the oestrus cycle increased in mice treated with 750 ppm Cr(VI) (9).

Oral mouse 250, 500 or 1000 ppm in drinking water throughout gestation caused an increase in foetal deaths. Complete absence of implantation sites was noted in the mothers treated with the highest dose. A dose-dependent increase in the incidences of external and skeletal malformations was observed (10).

Intratesticular or intraperitoneal ♂ mice, 880 mg wk^{-1}. A decrease in sperm count was observed after 3 wk treatment, and morphological abnormalities in ~50% of total sperm after 4 wk treatment. Following mating with untreated ♀ mice, decreases in the number of implantation sites, in litter size and foetal body weight were observed. No conspicuous foetal malformations were observed. None of the ♀ became pregnant after 3 wk treatment of ♂ mice (11).

The effect on sexual behaviour, aggresive behaviour, and fertility of 1000 ppm potassium dichromate in the drinking water for 12 wk of ♂ rats was investigated. The number of mounts was reduced and time to ejaculation was increased. The number of animals ejaculating was reduced and the post ejaculatory period was increased. Lateralisations, boxing bouts, and fights with stud males were reduced. There was no effect on fertility. Testes, seminal vesicle and preputial gland weights were significantly reduced (12).

Metabolism and toxicokinetics

After inhalation exposure of rats, the highest concentrations of chromium were detected in the liver and kidneys (13,14).

Rats were administered 3 mg kg^{-1} alternate days for 8 wk. Urinary elimination of chromium increased progressively during the experiment and was correlated with the concentration of chromium in the renal cortex (15).

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract of humans (16).

Sensitisation

Positive in 2% men and 1.5% women in patch tests (17).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 with and without metabolic activation positive (18).

Drosophila melanogaster sex-linked recessive lethal assay positive (19).

In vitro human peripheral blood lymphocytes, sister chromatid exchanges and chromosome aberrations positive (20).

In vitro Chinese hamster ovary cells, DNA damage postive (21).

In vitro human lymphocytes, unscheduled DNA synthesis positive (22).

In vivo mouse, dominant lethal assay positive (23).

In vivo Chinese hamster bone marrow, sister chromatid exchanges positive. The frequency of micronucleated polychromatic erythrocytes was also increased (24).

Vicia faba roots tips, induction of micronuclei positive (25).

Other effects

Other adverse effects (human)

A number of epidemiological studies carried out among workers involved in chromate and chromate pigments have consistently shown an excess risk for lung cancers (8).

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}. Chromium: maximum admissible concentration 50 μg l^{-1} (26).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (27).
WHO guideline value for drinking water, chromium 50 μg l^{-1} (provisional) (28).
US EPA primary and secondary drinking water maximum contaminant level chromium, 100μg l^{-1} (29).

Other comments

Environmental impact and toxicity of chromium compounds reviewed (8,30-33).

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P247 potassium dimethyldithiocarbamate

$(CH_3)_2NCS_2K$

$C_3H_6KNS_2$ **Mol. Wt.** 159.32 **CAS Registry No.** 128-03-0

Synonyms *N,N*-dimethyldithiocarbamic acid, potassium salt; dimethylcarbamodithioic acid, potassium salt; Busan 85

EINECS No. 204-875-1 **RTECS No.** FA 0850000

Uses Disinfectant. Preservative. Pesticide. Coagulant.

Mammalian & avian toxicity

Acute data

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

Metabolism and toxicokinetics

In mammals the major metabolite is the glucuronide which is excreted in the urine and faeces. Other metabolites include carbon disulfide and methyldiethyldithiocarbamate (2).

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).

Other comments

Use, environmental fate, metabolism and mammalian toxicity of dithiocarbamate pesticides reviewed (2).

References

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P248 potassium fluoride

KF

FK **Mol. Wt.** 58.10 **CAS Registry No.** 7789-23-3

EINECS No. 232-151-5 **RTECS No.** TT 0700000

Uses Fluorinating agent. Catalyst. Electrolyte. Component of fluxes. In ceramics.

Physical properties

M. Pt. 858°C **B. Pt.** 1505°C **Specific gravity** 2.480 at 20°C **Volatility** v.p. 1 mmHg at 885°C

Solubility Water: 92% at 18°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (inhalable dust fraction)
FR-VME 2.5 mg m^{-3} (as F)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)
US-TWA 2.5 mg m^{-3} (as F)

UN No. 1812 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
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) – 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, S26, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, guinea pig 250 mg kg^{-1} (1,2).
LD_{50} intraperitoneal rat, mouse 40, 64 mg kg^{-1}, respectively (1,3).

Teratogenicity and reproductive effects
Intraperitoneal mouse, lowest toxic dose 1050 mg kg^{-1} day^{-1} on days 1-21 of gestation (foetoxicity and teratogenicity) (3).

Genotoxicity

In vitro mouse lymphoma L5178Y cells, tk^+/tk^- forward mutation assay positive (4).

Other effects

Other adverse effects (human)
Chronic exposure may result in fluorosis, brittle bones, joint stiffness and calcification of the ligaments (2).
Extremely destructive to the eyes, skin and tissue of the upper respiratory tract (5).

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}. Fluoride: maximum admissible concentration 1500 μg l^{-1} for water temperatures of 8-12°C, 700 μg l^{-1} for water temperatures of 25-30°C (6).
WHO guideline value for drinking water, fluoride 1500 μg l^{-1} (7).

Other comments

Physical properties, use, toxicity and safety precautions reviewed (2,8).

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P249 potassium fluoroacetate

$$FCH_2CO_2K$$

$C_2H_2FKO_2$ **Mol. Wt.** 116.13 **CAS Registry No.** 23745-86-0

Synonyms potassium cymonate

RTECS No. AH 8800000

Occupational exposure

UN No. 2628 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rabbit 0.5 mg kg^{-1} (1).
LD_{Lo} oral chicken 50 mg kg^{-1} (2).
LD_{Lo} subcutaneous mouse, rabbit 0.5, 4 mg kg^{-1}, respectively (1,2).
LD_{Lo} subcutaneous chicken 10 mg kg^{-1} (2).
LD_{Lo} intravenous rabbit 0.5 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium guide level 10 mg kg^{-1}; maximum admissible concentration 12 mg l^{-1}. Fluoride maximum admissible concentration 1500 µg l^{-1} for water temperatures of 8-12°C, 700 µg l^{-1} for water temperatures of 25-30°C (3).
WHO guideline value for drinking water, fluoride 1500 mg l^{-1} (4).

References

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P250 potassium fluorosilicate

$$K_2SiF_6$$

F_6K_2Si **Mol. Wt.** 220.27 **CAS Registry No.** 16871-90-2

Synonyms dipotassium hexafluorosilicate; potassium hexafluorosilicate; potassium silicofluoride

EINECS No. 240-896-2 **RTECS No.** VV 8400000

Uses Component of fluxes. In electroplating. Manufacture of ceramics and pesticides.

Physical properties

M. Pt. decomposes **Specific gravity** 2.27
Solubility Water: 69 g l^{-1} at 19°C

Occupational exposure

SE-LEVL 2 mg m^{-3} (as F)

UN No. 2655 **HAZCHEM Code** 1Z **Conveyance classification** toxic substance
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) – 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, S26, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, guinea pig 160, 70, 500 mg kg^{-1}, respectively. Main toxic effects were decreased numbers of blood cells and decreased activities of cholinesterase and lactate dehydrogenase in blood serum (1,2).
LC_{50} (4 hr) inhalation rat, mouse 7.4, 9.6 mg m^{-3}, respectively (2).
LD_{Lo} subcutaneous guinea pig 500 mg kg^{-1} (3).

Irritancy
Irritating to the skin, eyes, mucous membrane and upper respiratory tract of humans (4).

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}. Fluoride: maximum admissible concentration 1500 μg l^{-1} for water temperatures of 8-12°C, 700 μg l^{-1} for water temperatures of 25-30°C (5).
WHO guideline value for drinking water 1500 μg l^{-1} (6).

Other comments

Physical properties, use, toxicity and safety precautions reviewed (4).
Decomposes on heating (4).

References

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P251 potassium fluorozirconate(IV)

$$K_2ZrF_6$$

F_6K_2Zr **Mol. Wt.** 283.41 **CAS Registry No.** 16923-95-8

Synonyms zirconate(2–), hexafluoro-, dipotassium (OC-6-11)-; potassium fluozirconate; potassium hexafluorozirconate; zirconium potassium fluoride

EINECS No. 240-985-6 **RTECS No.** ZH 7028400

Uses In welding flux. Manufacture of metallic zirconium. Fire-proofing agent for textiles.

Physical properties

Solubility Water: 7.8 g l^{-1} at 2°C

Occupational exposure

DE-MAK 5 mg m^{-3} (as Zr) (inhalable dust fraction)
UK-LTEL 5 mg m^{-3} (as Zr) **UK-STEL** 10 mg m^{-3} (as Zr)
US-TWA 5 mg m^{-3} (as Zr) **US-STEL** 10 mg m^{-3} (as Zr)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 98 mg kg^{-1} (1).

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}. Fluorides: maximum admissible concentration 1500 μg l^{-1} for water temperatures of 8-12°C, 700 μg l^{-1} for water temperatures of 25-30°C (2).

References

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P252 potassium hydrogen fluoride

KHF_2

F_2HK **Mol. Wt.** 78.10 **CAS Registry No.** 7789-29-9

Synonyms potassium bifluoride; potassium acid fluoride; potassium hydrogen difluoride; hydrogen potassium fluoride

EINECS No. 232-156-2 **RTECS No.** TS 6650000

Uses Catalyst for olefin alkylation reactions. Electrolyte in the manufacture of fluorine. Used in the preparation of pure potassium fluoride. Frosting glass applications. Flux for silver solders.

Physical properties

M. Pt. 238.7°C **B. Pt.** 195°C (transforms) **Specific gravity** 2.370 at 25°C
Solubility Water: 392 g l^{-1}

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (inhalable dust fraction)
FR-VME 2.5 mg m^{-3} (as F)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)
US-TWA 2.5 mg m^{-3} (as F)

UN No. 1811 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance, toxic

Supply classification toxic, corrosive
Risk phrases Toxic if swallowed – Causes burns (R25, R34)
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 gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S26, S37, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig ~150 mg kg^{-1} (1).

Other effects

Other adverse effects (human)
May be fatal if inhaled, swallowed or absorbed through the skin. Inhalation may be fatal as a result of spasm, inflamation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (2). Extremely destructive to tissue of the mucous membranes and upper respiratory tract, skin and eyes (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1} maximum admissible concentration 12 mg l^{-1}. Fluoride: maximum admissible concentration 1500 μg l^{-1} for water temperatures 8-12°C; 700 μg l^{-1} for water temperature 25-30°C (3).
WHO guideline value for fluoride in drinking water 1500 μg l^{-1} (4).

Other comments

Physical properties, use, mammalian toxicity and safety precautions reviewed (5,6).

References

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P253 potassium hydrogen sulfate

$KHSO_4$

HKO_4S **Mol. Wt.** 136.17 **CAS Registry No.** 7646-93-7
Synonyms potassium bisulfate; potassium acid sulfate; salenixum
EINECS No. 231-594-1 **RTECS No.** TS 7200000
Uses Used in the analysis of ores and silica componds. Cathartic. Catalyst.

Physical properties

M. Pt. 214°C **Specific gravity** 2.24
Solubility Water: in 1.8 parts water

Occupational exposure

UN No. 2509 **HAZCHEM Code** 2X **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) – 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 2300 mg kg^{-1} (1).

Other effects

Other adverse effects (human)
Extremely destructive to tissue of the mucous membrane and upper respiratory tract, eyes and skin (2). Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium guide level 10 mg kg^{-1} maximum admissible concentration 12 mg l^{-1}. Sulfates guide level 25 mg l^{-1}, maximum admissible concentration 250 mg l^{-1} (3).

References

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P254 potassium hydroxide

KOH

HKO **Mol. Wt.** 56.11 **CAS Registry No.** 1310-58-3
Synonyms potassium hydrate; caustic potash; potassa; E525; Lye
EINECS No. 215-181-3 **RTECS No.** TT 2100000

Uses Used in veterinary medicine. Used in organic syntheses and chemical analysis. Used in paint and varnish removers, electroplating, photoengraving and lithography. Mordant in wood. Printing ink and textile industries. Processing of black olives and cocoa.

Physical properties

M. Pt. 380°C (anhydrous) **B. Pt.** 1320°C **Specific gravity** 2.044 **Volatility** v.p. 1 mmHg at 714°C
Solubility Water: 1 in 0.9 parts water. Organic solvents: ethanol, glycerol

Occupational exposure

FR-VLE 2 mg m^{-3}
JP-OEL ceiling limit 2 mg m^{-3}
UK-STEL 2 mg m^{-3}
US-STEL ceiling limit 2 mg m^{-3}

UN No. 1813 (solid)

UN No. 1814 (solution) **HAZCHEM Code** 2R **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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable 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, S37/39, S45)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) mosquito fish 80 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 270, 365, 1230 mg kg^{-1} (2-4).

Carcinogenicity and chronic effects
Dermal mouse, frequent application for 46 wk resulted in tumours identical with those induced by coal tar (total exposure not specified) (5).

Irritancy
Dermal rabbit (24 hr) 50 mg cause severe irritation. 1 mg instilled into rabbit eye for 24 hr (rinsed) caused moderate irritation (3).

Genotoxicity

In vitro Chinese hamster ovary K1 cells, with metabolic activation positive (6).

Other effects

Other adverse effects (human)
After ingestion causes violent pain in throat and epigastrium, haematemesis and collapse. If not immediately fatal, stricture of the oesophagus may occur (7).
Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (8).
10% of workers exposed to KOH during the production of ascorbic acid developed allergic dermatitis (9).

Legislation

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

Other comments

Physical properties, uses, mammalian toxicity and safety precautions reviewed (11-13).
Rapidly absorbs moisture and carbon dioxide from air and deliquesces.

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P255 potassium iodate

KIO_3

IKO_3 **Mol. Wt.** 214.00 **CAS Registry No.** 7758-05-6

Synonyms iodic acid (HIO_3), potassium salt; potassium iodine oxide

EINECS No. 231-831-9 **RTECS No.** NN 1350000

Uses Oxidising agent. Analytical reagent. Catalyst. Topical antiseptic. Dietary iodine supplement.

Physical properties

M. Pt. 560°C (decomp.) **Specific gravity** 3.930 at 32°C with respect to water at 4°C
Solubility Water: slowly soluble in 12 parts water, in 3 parts boiling water

Mammalian & avian toxicity

Acute data

LD_{Lo} oral mouse, guinea pig, dog 200-530 mg kg^{-1} (1-3).
LD_{50} intraperitoneal mouse 140 mg kg^{-1} (3).

Teratogenicity and reproductive effects

Oral mouse, 0.25-1.0% in diet for 1-2 wk induced sterility. ♀ were more susceptible than ♂ mice (4).

Irritancy

Eyes, skin, mucous membranes and upper respiratory tract irritant in humans (5).

Other effects

Any other adverse effects

Caused necrotic lesions of the liver, kidneys and gastric and intestinal mucosa (species unspecified) (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

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P256 potassium iodide

KI

IK **Mol. Wt.** 166.00 **CAS Registry No.** 7681-11-0

Synonyms Antistrumin; Ceoiodin; Kaiod; Knollide

EINECS No. 231-659-4 **RTECS No.** TT 2975000

Uses Analytical reagent. In photographic emulsions. Dietary iodine supplement. Expectorant. Antiseptic. In the preparation of hair dyes.

Physical properties

M. Pt. 681°C **B. Pt.** 1330°C **Specific gravity** 3.130 **Volatility** v.p. 1 mmHg at 745°C
Solubility Water: 2080 g l^{-1} at 20°C. Organic solvents: acetone, diethyl ether, ethanol, glycol, glycerol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (5 day) rainbow trout 3200 mg l^{-1} (1).
In a 90-day study, 12.5 mg l^{-1} caused no toxic effects to rainbow trout (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral mouse, rabbit 910, 1860 mg kg^{-1}, respectively (2,3).
LD_{Lo} intraperitoneal mouse 1120 mg kg^{-1} (2).
LD_{Lo} intravenous rat 120 mg kg^{-1} (4).

Teratogenicity and reproductive effects

Oral rat, lowest toxic dose 11 g kg^{-1} day^{-1} on days 1-9 of gestation (pre-implantation mortality and foetotoxicity) (5).
Oral rat, lowest toxic dose 300 mg kg^{-1} in 9th day of gestation (post-implant mortality, foetotoxicity and foetal death) (6).
Oral mink, basal diet of 0, 10, 100 or 1000 ppm caused a decrease in gestational periods (7).

Metabolism and toxicokinetics

Iodine is eliminated chiefly by the kidneys, but may also be found in saliva, tears, milk and perspiration. Some retained iodine is stored in the thyroid and incorporated into thyroxine (8).

Irritancy
Eyes, skin, mucous membrane and upper respiratory tract irritant (species unspecified) (9).

Sensitisation
Has been reported to cause allergic respiratory and skin reactions (species unspecified) (9).

Genotoxicity

Salmonella typhimurium TA1535/psk1002 umu negative (10).
Escherichia coli SOS chromotest negative (11).
In vitro rat, embryonic liver cells, chromosomal aberrations positive (12).

Other effects

Any other adverse effects
Lambs administered high doses of potassium iodide died from bronchopneumonia (13).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1} maximum admissible concentration 12 mg l^{-1} (14).

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P257 potassium nitrate

KNO_3

KNO_3 **Mol. Wt.** 101.10 **CAS Registry No.** 7757-79-1

Synonyms E252; niter; nitric acid, potassium salt; saltpeter; vicknite

EINECS No. 231-818-8 **RTECS No.** TT 3700000

Uses Food preservative. Oxidising agent. In fertilisers. In fireworks, matches and gunpowder. Manufacture of glass. In fluxes. Veterinary diuretic. In silver plating baths.

Physical properties

M. Pt. 334°C; decomp. at 400°C with evolution of O_2 **B. Pt.** decomposes at 400°C
Specific gravity 2.109 at 16°C
Solubility Water: 36%. Organic solvents: glycerol

Occupational exposure

UN No. 1486 **HAZCHEM Code** 1Z **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, rabbit 1600, 3750 mg kg^{-1}, respectively (1,2).
LD_{Lo} intravenous cat 100 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral cattle, 340-450 mg kg^{-1} as nitrate for several months. Chronic poisoning was characterised by decreased levels of blood phosphate and magnesium and increased levels of blood calcium, urinary magnesium and urea, and milk urea. Blood catalase activity was decreased by ~20%. Markedly increased blood total protein and γ-globulin levels and activities of glutamate-alanine and glutamate-aspartine aminotransaminases were also observed (4).
Oral pig, 3% diet (exposure not specified) induced hypothyroidism and low blood levels of thyroxine, triiodothyroxine and reverse-triiodothyroxine. Feed consumption fell by 30-50% and weight gain by 38-55%. Serum somatomedin activity was also reduced (5).
Oral rat, 10-100 mg kg^{-1} for 4 months resulted in bronchopneumonia oedema of the pulmonary parenchyma, local haemorrhages and other circulatory disturbances (6).

Teratogenicity and reproductive effects
Oral rabbit, lowest toxic dose 6500 mg kg^{-1} day^{-1} on days 23-27 of gestation induced abortion (1).
Oral guinea pig, lowest toxic dose, 15,000 mg kg^{-1} 24 wk prior to gestation (stillbirths) (7).
Oral guinea pig, lowest dose 1670 g kg^{-1} 29 wk prior to mating (reduced ♂ fertility index) (7).

Metabolism and toxicokinetics
Rapidly absorbed from the upper gastro-intestinal tract and excreted unchanged. If not totally absorbed, nitrate may be reduced to nitrite by bacteria in the bowel (species unspecified) (8).

Irritancy
Skin, eye, mucous membrane and upper respiratory tract irritant in humans (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (10).
Bacillus subtillis rec assay negative (11).
In vivo rat, dominant lethal assay positive (12).

Other effects

Other adverse effects (human)
Acute toxicity of nitrate results from reduction to nitrite (13).
Ingestion of large amounts may cause gastroenteritis. Prolonged exposure to small amounts may cause anaemia, methaemoglobinaemia and nephritis (14).
Three men aged 23-49 yr developed toxic methaemoglobinaemia after absorption of sodium nitrate and potassium nitrate through burned skin after an industrial explosion. One patient died of cardiac arrest, methaemoglobin concentration was 65% (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1} maximum admissible concentration 12 mg l^{-1}. Nitrates: guide level 25 mg l^{-1}, maximum admissible concentration 50 mg l^{-1} (16).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (17).
WHO guideline value for drinking water, nitrate 50 mg l^{-1} (18).

Other comments

Physical properties, uses, mammalian toxicity and safety precautions reviewed (19,20).

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P258 potassium nitrite

$$KNO_2$$

KNO_2 **Mol. Wt.** 85.10 **CAS Registry No.** 7758-09-0

Synonyms E249; nitrous acid, potassium salt

EINECS No. 231-832-4 **RTECS No.** TT 3750000

Uses Meat curing agent. Food preservative. Corrosion inhibitor. Polymerisation inhibitor. Analytical reagent. Antidote for cyanide poisoning. Therapeutic vasodilator.

Physical properties

M. Pt. 441°C (decomp. starts at 350°C) **B. Pt.** decomposes **Specific gravity** 1.915 at 25°C
Solubility Water: 2800 g l^{-1} at 0°C. Organic solvents: hot ethanol

Occupational exposure

UN No. 1488 **HAZCHEM Code** 1Z **Conveyance classification** oxidising susbstance
Supply classification oxidising, toxic
Risk phrases Contact with combustible material may cause fire – Toxic if swallowed (R8, R25)
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)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rabbit 110, 300 mg kg^{-1}, respectively (1-3).
LC_{50} (2 hr) inhalation mouse 85 g m^{-3} (4).

Sub-acute and sub-chronic data
No-observed-effect level (13 wk) rat 50 mg l^{-1} in drinking water, equivalent to ~5 mg kg^{-1} day^{-1} (5).
Oral rat 0, 100, 300, 1000 or 3000 mg l^{-1} in drinking water for 13 wk. The potassium concentration was equalised with potassium chloride equivalent to the high dose of 3000 mg l^{-1} potassium nitrite. Body weight, food intake and food efficiency were decreased in the high dose group among ♂ rats, whereas liquid intake was decreased in ♂ in the 1000 and 3000 mg l^{-1} and in ♀ in the 3000 mg l^{-1} group. Slight decreases in red blood cell variables occurred at the 1000 and 3000 mg l^{-1} doses. No impaired renal function was observed although relative kidney weight and plasma urea level was increased at 3000 mg l^{-1}. Plasma alkaline phosphatase activity was slightly decreased at 3000 mg l^{-1}. A small amount of nitrite was present inthe saliva of the high-dose group but there was no evidence of increased mutagenic activity in the urine of these rats. Hypertrophy of the adrenal zone glomerulosa was observed in all dose groups in a dose-dependent manner (6).
Oral chicken, 400 ppm in diet for 3 wk. Symptoms of toxicity included reduced weight gain, anorexia, muscle tremors and lack of coordination, dyspnoea, and frothing around the mouth (7).

Teratogenicity and reproductive effects
Oral guinea pig, lowest toxic dose 137 mg kg^{-1} 18 wk prior to mating (foetoxicity). ♂ Fertility was not affected (8).

Irritancy
Skin, eye, mucous membrane and upper respiratory tract irritant (species unspecified) (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (9).
Escherichia coli induction of reverse mutation positive (10).
In vivo rat, dominant lethal assay negative (11).

Other effects

Other adverse effects (human)
Caused methaemoglobinaemia, nausea, vomiting, rapid pulse, headache and visual disturbances (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1} maximum admissible concentration 12 mg l^{-1}. Nitrites: maximum admissible concentration 0.1 mg l^{-1} (12).
WHO Guideline value for nitrite in drinking water 3 mg l^{-1} (provisional) (13).
US EPA primary and secondary drinking water maximum contaminant level 1 mg l^{-1} (14).
Tolerable daily intake (TDI) human 0.2 mg kg^{-1} (temporary) (15).

Other comments

Physical properties, uses, mammalian toxicity and safety precautions reviewed (16).

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P259 potassium perchlorate

$KClO_4$

$ClKO_4$ **Mol. Wt.** 138.55 **CAS Registry No.** 7778-74-7

Synonyms periodin; perchloric acid, potassium salt; potassium hyperchloride

EINECS No. 231-912-9 **RTECS No.** SC 9700000

Uses Oxidising agent. Electrolyte. Manufacture of explosives and fireworks. Analytical reagent. Antithyroid agent.

Physical properties

M. Pt. 400°C **B. Pt.** decomposes at 400°C **Specific gravity** 2.520
Solubility Water: 1.5%

Occupational exposure

UN No. 1489 **HAZCHEM Code** 2W **Conveyance classification** oxidising substance
Supply classification oxidising, harmful
Risk phrases Explosive when mixed with combustible material – Harmful if swallowed (R9, R22)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Do not breathe dust – Take off immediately all contaminated clothing (S2, S13, S22, S27)

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Oral mouse 1.0-7.5% diet for 160 days caused thyroid enlargement and enhanced thyroid function, apathy, hair loss, paralysis of the hind limbs, skeletal deformations, abnormal protrusion of the eyeball, weight loss and increase mortality (1).

Carcinogenicity and chronic effects
Injection rat 300 mg animal wk^{-1} for 2 yr did not result in any increase in the rate of tumorigenesis (2).

Teratogenicity and reproductive effects

Oral rat, lowest toxic dose 27 g kg^{-1} day^{-1} on days 1-9 of gestation (teratogenic effects, endocrine system) (3).
Oral rabbit, lowest toxic dose 2100 mg kg^{-1} day^{-1} on days 1-21 of gestation (teratogenic effects, endocrine system) (4).

Metabolism and toxicokinetics

Readily absorbed by gastro-intestinal tract in humans. Perchlorate ions concentrate in the thyroid, choroid plexsus, salivary glands and gastric mucosa. Peak plasma levels are reported to occur 3 hr after oral administration. Perchlorate and iodine ions excreted unchanged in the urine (5,6).

Irritancy

Causes severe irritation in humans. High concentrations are extremely destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin (7).

Other effects

Other adverse effects (human)

Therapeutic doses have been associated with gastric irritation, nausea, vomiting, fever, skin rashes lymphodenopathy, nephrotic syndrome and rarely leucopenia, agranulocytosis, pancytopaenia, and fatal aplastic anaemia (5).
May interfere with iodine uptake in the thyroid (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium guide level 10 mg kg^{-1} maximum admissible concentration 12 mg l^{-1} (8).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).
Included in the UK List of Classified and Authorised Explosives 1994. UK Class and Division 2.0. Competent Authority Reference GB 20032 (10).

Other comments

Physical properties, uses, mammalian toxicity and safety precautions reviewed (11,12).

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P260 potassium permanganate

$KMnO_4$

$KMnO_4$ **Mol. Wt.** 158.03 **CAS Registry No.** 7722-64-7

Synonyms cairox; chameleon mineral; C.I. 77755; condy's crystals; permanganate of potash; manganese potassium oxide

EINECS No. 231-760-3 **RTECS No.** SD 6475000

Uses Analytical reagent. Oxidising agent. Disinfectant. Bleaching agent. Catalyst. Etchant. Deodorant.

Physical properties

M. Pt. 240°C (decomp.) **Specific gravity** 2.703 at 25°C

Solubility Water: 70 g l^{-1} in cold water. Organic solvents: acetic acid, acetic anhydride, acetone, benzonitrile, pyridine, sulfalone, trifluoroacetic acid

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Mn) (total dust)
JP-OEL 0.3 mg m^{-3} (as Mn)
SE-LEVL total dust 1 mg m^{-3} (as Mn), respirable dust 0.5 mg m^{-3} (as Mn)
UK-LTEL 5 mg m^{-3} (as Mn)
US-TWA 0.2 mg m^{-3} (as Mn)

UN No. 1490 **HAZCHEM Code** 1Y **Conveyance classification** oxidising substance
Supply classification oxidising, harmful
Risk phrases Contact with combustible material may cause fire – Harmful if swallowed (R8, R22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) milkfish, bluegill sunfish, channel catfish 1.5-18 mg l^{-1} (1-3).
LC_{50} (24 hr) striped bass 1.5-5.0 mg l^{-1}, static bioassay (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1100 mg kg^{-1} (5).
LD_{50} subcutaneous mouse 500 mg kg^{-1} (6).
LD_{Lo} intravenous rabbit 70 mg kg^{-1} (7).
Oral rats, 1500 mg kg^{-1} resulted in hypochromic anaemia and neutrophilic leukocytosis, changes in the blood, dystrophic changes and bleeding in the parenchymatous organs (8).

Teratogenicity and reproductive effects

Intratesticular rat, lowest toxic dose, single administration 400 mg kg^{-1} (reproductive effects) (9).
Oral rat, 150 mg kg^{-1} day^{-1} during second half of gestation caused foetal death and some maternal deaths (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 with and without metabolic activation positive (11).
In vitro human peripheral blood lymphocytes, DNA damage positive (11).
In vitro mouse induction of sperm head abnormalities positive (12).
In vivo mouse bone marrow cells chromosomal aberrations and micronucleation of erythrocytes positive (12).
Allium cepa, Pisum sativum, Vallisneria spinclis chromosomal aberrations positive (13).

Other effects

Other adverse effects (human)

Gynaecological disturbances have been reported in women occupationally exposed, sensitivity being more pronounced in young women (8).

Its use as a local abortifacient caused severe trauma, and vaginal injury and haemorrhaging (14).

Dilute solutions are mildly irritating and high concentrations are caustic (15).

Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (16).

A case history describes fatal acute hepatorenal toxicity following suicidal ingestion of potassium permanganate. The clinical course resembled severe paracetamol overdose. The authors conclude that toxicity is due to oxidative injury from free radicals generated by the absorbed permanganate ion and recommend prompt treatment with *N*-acetyl cysteine to all patients poisoned with potassium permanganate. Most deaths from poisoning with the compound result from respiratory oedema and airway obstruction or circulatory collapse. The pathogenesis of systemic toxicity is discussed (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1}; maximum admissible concentration 12 mg l^{-1} (18).

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

Other comments

Physical properties, uses, environmental impact, mammalian toxicity and safety precautions reviewed (20-22).

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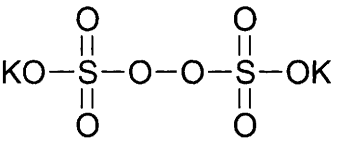
P261 potassium persulfate



$K_2O_8S_2$ **Mol. Wt.** 270.32 **CAS Registry No.** 7727-21-1

Synonyms potassium peroxydisulfate; Anthion; dipotassium persulfate; peroxydisulfuric acid, dipotassium salt

EINECS No. 231-781-8 **RTECS No.** SE 0400000

Uses Bleaching agent. Polymerisation catalyst. Oxidising agent. Analytical reagent.

Physical properties

M. Pt. 100°C (decomp.) **Specific gravity** 2.477
Solubility Water: 2%

Occupational exposure

UK-LTEL 1 mg m^{-3} (as $[S_2O_8]$)
US-TWA 0.1 mg m^{-3}

UN No. 1492 **HAZCHEM Code** 2W **Conveyance classification** oxidising substance
Supply classification oxidising, harmful
Risk phases Contact with combustible material may cause fire – Harmful if swallowed – Irritating to eyes, respiratory system and skin – May cause sensitisation by inhalation and skin contact (R8, R22, R36/37/38, R42/43)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – Avoid contact with the skin – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves (S2, S22, S24, S26, S37)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 800 mg kg^{-1} (1).

Irritancy
Skin, eye, mucous membrane and upper respiratory tract irritant in humans (2).

Sensitisation
Reported to cause allergic reactions in humans (2,3).

Other effects

Other adverse effects (human)
One incidence of burning of the cornea has been recorded; healing occurred within 48 hr (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium guide level 10 mg kg^{-1}, maximum admissible concentration 12 mg l^{-1}. Sulfates: guide level 25 mg kg^{-1}, maximum admissible concentration 50 mg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

References

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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.
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P262 potassium silver cyanide

$$KAg(CN)_2$$

C_2AgKN_2 **Mol. Wt.** 199.00 **CAS Registry No.** 506-61-6

Synonyms Potassium bis(cyano-C)-argenate(1–); potassium dicyanoargenate; silver potassium cyanide

EINECS No. 208-047-0 **RTECS No.** TT 5775000

Uses In electroplating. Bacteriocide. Extraction of silver from silver ores.

Physical properties

Specific gravity 2.36 at 25°C
Solubility Water: miscible. Organic solvents: ethanol

Occupational exposure

DE-MAK 5 mg m^{-3} (as CN) (inhalable dust fraction)
FR-VME 0.01 mg m^{-3} (as Ag)
JP-OEL 0.01 mg m^{-3} (as Ag)
SE-LEVL 0.01 mg m^{-3} (as Ag) **SE-CEIL** 5 mg m^{-3} (as CN)
UK-LTEL 0.01 mg m^{-3} (as Ag)

UN No. 1588 (solid) **HAZCHEM Code** 4X (solid) **Conveyance classification** toxic substance (solid)

Environmental fate

Abiotic removal
Removed from wastewater as a copper precipitate by treatment with a copper-bearing ion-exchange resin in the presence of a reducing agent, such as sulfite, hydrosulfite, hydrazine or ferrous salts (1).
Removal from water effected by adsorption onto activated carbon (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 21 mg kg^{-1} (3).

Irritancy
Dermal rabbit (24 hr) 50 mg caused severe irritation. 250 μg instilled into rabbit eye for 24 hr caused severe irritation (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1}; maximum admissible concentration 12 mg l^{-1}. Cyanides: maximum admissible concentration 50 μg l^{-1}. Silver: maximum admissible concentration 10 μg l^{-1} (4).
WHO guideline value for cyanides in drinking water 70 μg l^{-1}.

References

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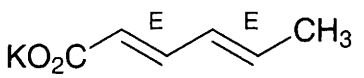
P263 potassium sorbate



$C_6H_7KO_2$ **Mol. Wt.** 150.22 **CAS Registry No.** 24634-61-5

CAS Registry No. 590-00-1 (unspecified stereochemistry)

Synonyms E202; 2,4-hexadienoic acid, potassium salt; sorbic acid, potassium salt; sobitat-K; potassium 2,4-hexadienoate

EINECS No. 246-376-1 **RTECS No.** WG 2160000

Uses Food preservative. Antioxidant.

Physical properties

M. Pt. >270°C (decomp.) **Specific gravity** 1.363 at 25°C
Solubility Water: 582 g l^{-1} at 20°C. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 3800, 4900 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal mouse 1300 mg kg^{-1} (1).

Irritancy
Eye irritant (species unspecified) (3).

Genotoxicity

Salmonella typhimurium TA98, TA100 negative (use of metabolic activation not specified) (4).
In vitro Chinese hamster V79 lung cells chromosomal aberrations and sister chromatid exchanges marginally positive (metabolic activation unspecified) (4).
In vitro Chinese hamster fibroblasts, with and without metabolic activation chromosomal aberrations positive (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1}; maximum admissible concentration 12 mg l^{-1} (6).

Other comments

Tolerable daily intake (TDI) human 2.5 mg kg^{-1} (7).

References

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P264 potassium sulfate

$$K_2SO_4$$

K_2O_4S **Mol. Wt.** 174.26 **CAS Registry No.** 7778-80-5

Synonyms areanum; dipotassium sulfate; arcanum duplicatum; sal polychrestum; sulfuric acid, dipotassium salt

EINECS No. 231-915-5 (containing in the dry state more than 52% by weight of K_2O) **RTECS No.** TT 5900000

Uses Oxidation catalyst. Concrete additive. Fertiliser. Analytical reagent. Therapeutic cathartic.
Occurrence In the mineral arcanite.

Physical properties

M. Pt. 1069°C **B. Pt.** 1689°C **Specific gravity** 2.662
Solubility Water: 120 g l^{-1} at 25°C. Organic solvents: glycerol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 6600 mg kg^{-1} (1).
LD_{50} intraperitoneal rat, mouse, guinea pig 1100-1250 mg kg^{-1} (2).
LD_{Lo} subcutaneous guinea pig 3000 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Inhalation rat 5.5 or 15 mg m^{-3} 4 hr day^{-1} 5 day wk^{-1} for 4 months increased motor activity, caused changes in absorptive capacity of the liver, kidneys and spleen and decreased the relative weights of these organs. Irritation of the upper respiratory tract and lungs, and alteration in the immune status of the animals were also observed (2).

Irritancy
Skin, eye, mucous membrane and upper respiratory tract irritant in humans (4).

Other effects

Other adverse effects (human)
Large oral doses cause severe gastro-intestinal irritation (5).

Any other adverse effects

Oral rat, single dose of 620 mg kg^{-1} produced cardiovascular effects, including a fall in blood pressure, ECG changes, bradycardia and arrhythmia. Histopathologic examination demonstrated cardiac hypertrophy and damage to the cardiac muscles (2).

Cattle which grazed in a field treated with potassium sulfate died within 2 days, showing symptoms of paresis, hypothermia, cessation of rumination and constipation. The only lesion seen at post mortem was congestion of the mucous membrane of the abomasum and intestines (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1} maximum admissible concentration 12 mg l^{-1}. Sulfates: guide level 25 mg l^{-1}, maximum admissible concentration 250 mg l^{-1} (7).

References

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P265 potassium superoxide

KO_2

KO_2 **Mol. Wt.** 71.10 **CAS Registry No.** 12030-88-5

Synonyms potassium dioxide

EINECS No. 234-746-5 **RTECS No.** TT 6053000

Uses Oxidising agent. Catalyst

Physical properties

M. Pt. 509°C

Occupational exposure

UN No. 2466 **Conveyance classification** oxidising substance

Environmental fate

Abiotic removal

Decomposes in water with the formation of potassium hydroxide and evolution of oxygen (1).

Genotoxicity

In vitro Chinese hamster ovary cells, single strand DNA breaks positive (2).

In vitro human P3 teratocarcinoma cells, single strand DNA breaks positive (2).

In vitro Chinese hamster ovary cells, clone CAO-K_1-BH_4 xanthine-guanine phosphoribosyltransferase assay positive (3).

Other effects

Other adverse effects (human)

Extremely destructive to tissue of the mucous membranes and upper respiratory tract, skin and eyes (4). Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and oedema (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Potassium: guide level 10 mg kg^{-1} maximum admissible concentration 12 mg l^{-1} (5).

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

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P266 potassium tetraiodomercurate(II)

$$K_2HgI_4$$

HgI_4K_2 **Mol. Wt.** 786.40 **CAS Registry No.** 7783-33-7

Synonyms mercury potassium iodide; Channing's solution; Nessler reagent; mercuric potassium iodide; potassium iodohydragyrate; potassium mercuric iodide; dipotassium tetraiodomercurate

EINECS No. 231-990-4 **RTECS No.** OU 9670000

Uses Topical anti-infective. Disinfectant. Ammonia analysis.

Physical properties

Solubility Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 0.01 ppm (0.1 mg m^{-3})
FR-VME 0.1 mg m^{-3} (as Hg)
JP-OEL 0.05 mg m^{-3} (as Hg)
SE-LEVL 0.03 mg m^{-3} (as Hg)
UK-LTEL 0.025 mg m^{-3}
US-TWA 0.025 mg m^{-3} (as Hg)

UN No. 1643 **HAZCHEM Code** 2X **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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S13, S28, S45)

Ecotoxicity

Fish toxicity

Intestinal transport rate for nutrients decreased in snakehead fish exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days (1).
Disrupted metabolism in kitefish exposed to 44 μg l^{-1} (Hg^{2+}) for 30 days (1).
Teratogenic to rainbow trout after exposure of eggs to 0.12-0.21 μg l^{-1} (Hg^{2+}) 4 days post hatch, and after parental exposure to 0.70-0.79 μg l^{-1} (Hg^{2+}) for 400 days (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 9.3 μg l^{-1} (Hg^{2+}) (1).
EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (Hg^{2+}) (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} dermal guinea pig 1000 mg kg^{-1} (2).
LD_{Lo} intraperitoneal guinea pig 1000 mg kg^{-1} (2).

Legislation

Community Right-To-Know List.
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 μg l^{-1} (3).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
Quality objectives under EC Directives 82/176/EEC and 84/156/EEC 0.3 mg kg^{-1} (wet weight) in a representative sample of fish flesh; 1 μg l^{-1} (annual mean) total mercury in inland surface waters; 0.5 μg l^{-1} (annual mean) dissolved mercury in estuarine waters; 0.3 μg l^{-1} (annual mean) dissolved mercury in marine waters. A 'standstill' provision applies to concentrations in shellfish or sediments. Limit values under EC Directive 84/156/EEC 0.05 mg l^{-1} effluent and 0.1 g l^{-1} vinyl chloride production capacity for chemical industries using mercury catalysts in vinyl chloride production; 0.05 mg l^{-1} effluent and 5 g kg^{-1} mercury processed for chemical industries using mercury catalysts in other processes; 0.05 mg l^{-1} effluent and 0.7 g kg^{-1} mercury processed for manufacture of mercury catalysts used in vinyl chloride production; 0.05 mg l^{-1} effluent and 0.05 g kg^{-1} mercury processed for manufacture of organic and non-organic mercury compounds (other than mercury catalysts for vinyl chloride production); 0.05 mg l^{-1} effluent and 0.03 g kg^{-1} mercury processed for manufacture of primary batteries containing mercury; 0.05 mg l^{-1} effluent for mercury recovery plants and extraction and refining of non-ferrous metals; 0.05 mg l^{-1} effluent for plants treating toxic wastes containing mercury (5).

Other comments

Physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience reviewed (6).
Toxicity of inorganic mercury and environmental effects reviewed (7,8).

References

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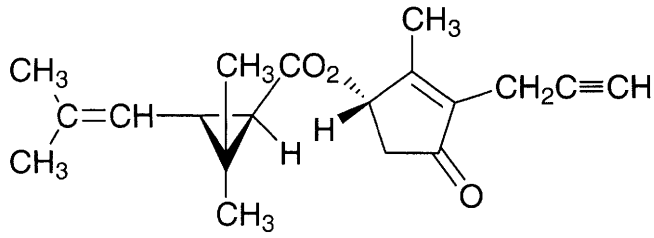
P267 prallethrin



$C_{19}H_{24}O_3$ **Mol. Wt.** 300.40 **CAS Registry No.** 23031-36-9

Synonyms *S*-2-methyl-4-oxo-prop-2-ynylcyclopent-2-enyl (1*R*)-*cis*-*trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate; *S*-2-methyloxo-3-(2-propynyl)-2-cyclopenten-1-yl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate; pralléthrine

EINECS No. 245-387-9

Uses Contact insecticide used to control public health insects (Blattodea, Culicidae, Muscidae)

Physical properties

B. Pt. >313.5°C at 760 mmHg **Specific gravity** 1.03 at 20°C **Partition coefficient** log P_{ow} 4.49 at 25°C
Volatility v.p. <0.013 mPa at 23.1°C
Solubility Water: 8 mg l^{-1} at 25°C. Organic solvents: hexane, methanol, xylene

Ecotoxicity

Fish toxicity
(*S*)-2-methyl-4-oxo-3-(2-propynyl)cyclopent-2-enyl (1*R*)-*trans*-3-(*E*)-(2-carboxyl-1-propynyl)-2,2-dimethyl-cyclopropane carboxylate was identified as the major metabolite in the gallbladder of bluegill sunfish exposed to 1 ppb prallethrin, indicating that taurine conjugate formation of the pyrethroid metabolite occurred before the ester bond cleavage (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂ and ♀ rats 640 and 460 mg kg^{-1}, respectively (2).
LD_{50} dermal rats >5000 mg kg^{-1} (2).
LC_{50} inhalation rats (4 hr) 288-333 mg m^{-3} (2).

Metabolism and toxicokinetics
Two major metabolites in the rat were identified as new types of *S*-linked sulfonic acid and mercapturic acid conjugates. Both types of conjugates were found in the excreta (3).

Irritancy
Non-irritating to the eyes and skin of rabbits (2).

Sensitisation
Not a skin sensitiser in guinea pigs (2).

Legislation

WHO Toxicity Class II (4).
EPA Toxicity Class III (formulation) (2).

Limited under EC Directive on Drinking Water Quality 80/788/EEC. Pesticides: maximum admissible concentration 0.5 μg l^{-1} (5).
Included in Schedules 5 and 6 (Release into Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

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6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

P268 praseodymium

Pr

Pr **Mol. Wt.** 140.91 **CAS Registry No.** 7440-10-0

EINECS No. 231-120-3

Occurrence Constitutes 7.8-9 × 10^{-4}% of Earth's crust. Found in rare earth minerals.

Physical properties

M. Pt. 931°C **B. Pt.** 3290°C **Specific gravity** 6.710

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous mouse 2 mg kg^{-1} (chloride) (1).

References

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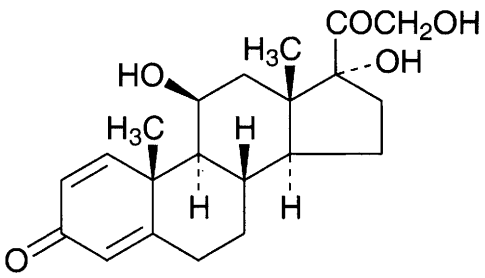
P269 prednisolone



$C_{21}H_{28}O_5$ **Mol. Wt.** 360.45 **CAS Registry No.** 50-24-8

Synonyms Δ^1-cortisol; 1-dehydrocortisone; 11β,17α,21-trihydroxypregna-1,4-diene-3,20-dione; 1,4-pregnadione-3,20-dione-11β,17α,21-triol; Codelcortone; Deltacortil; Hedeltra; Paracortol; Sterane

EINECS No. 200-021-7 **RTECS No.** TU 4152000

Uses Glucocorticoid. Antiinflammatory and analgesic drug. Immunosuppresent. Antineoplastic agent.

Physical properties

M. Pt. 240°C (decomp.)

Solubility Water: very soluble. Organic solvents: acetone, chloroform, 1,4-dioxane, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1700 mg kg^{-1} (1).

LD_{50} subcutaneous rat 150 mg kg^{-1} (2).

LD_{50} intravenous rat, mouse 120, 180 mg kg^{-1}, respectively (3).

Metabolism and toxicokinetics

Metabolites identified in *in vitro* study with human placenta were: prednisone (49%), 20α-dihydroprednisone (0.8%), 20β-dihydroprednisone (39%), 20β-dihydroprednisolone (6.5%) and unmetabolised prednisolone (4.5%). No evidence was found for metabolites formed by 6β-hydroxylation or cleavage at the C_{17}-C_{20} bond (4).

Absorbed through human and guinea pig skin (5,6).

Identified in milk of lactating women within 2 hr of oral administration (7).

Genotoxicity

In vitro mouse lymphoma cells, tk^+/tk^- forward mutation assay negative, DNA damage positive (8).

Other effects

Other adverse effects (human)

Induced acute psychoses within 10 days in 3 Chinese patients receiving 15-75 mg day^{-1} (9).

Prolonged therapy may result in suppression of pituitary-adrenal function (10).

Any other adverse effects

Delayed the growth of bone in mice (11).

Other comments

Metabolism reviewed (12).

References

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2. *Toxicol. Appl. Pharmacol.* 1966, **8**, 250.
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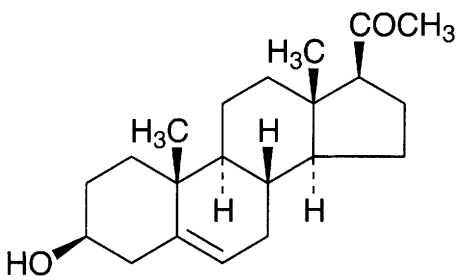
P270 pregnenolone



$C_{21}H_{32}O_2$ **Mol. Wt.** 316.48 **CAS Registry No.** 145-13-1

Synonyms 3-hydroxypregn-5-en-20-one; Δ^5-pregnon-3β-ol-20-one; 17β-(1-ketoethyl)-Δ^5-androsten-3β-ol

EINECS No. 205-647-4 **RTECS No.** TU 5560700

Uses Glucocorticoid.

Occurrence Precursor of testosterone.

Physical properties

M. Pt. 193°C

Solubility Water: very sparingly soluble in water. Organic solvents: acetone, benzene, benzyl alcohol, chloroform, 1,4-dioxane, ethanol, ethyl acetate, isopropanol, propylene glycol

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Injection rat, lowest toxic dose, 35 mg kg^{-1} 7 days before mating (teratogenic effects) (1).

Metabolism and toxicokinetics

Metabolised by mouse adrenal cells *in vitro* to yield 11β,20α-dihydroxy-4-pregnen-3-one (2).

Metabolised in human testicular homogenate (*in vitro*) to testosterone via the δ5 pathway and via the δ4 pathway in monkeys. δ16-synthetase activity, a prerequisite for the synthesis of the sex pheromone precursors 5,16-androstadien-3β-ol and 4,16-androstadiene-3-one, was measurable in human but not monkey homogenates (3).

Other effects

Any other adverse effects

Pregnenolone-16α-carbonitrile (CAS RN 1434-54-4) induces liver growth and an excessive liver DNA increase and associated induction of monoxygenases in rats (4).

References

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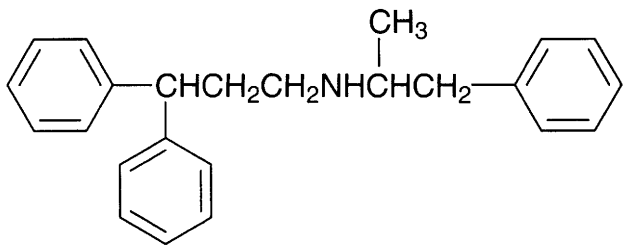
P271 prenylamine



$C_{24}H_{27}N$ **Mol. Wt.** 329.49 **CAS Registry No.** 390-64-7

Synonyms *N*-(3,3-diphenylpropyl)-α-methylphenethylamine; *N*-(1-methyl-2-phenylethyl)-γ-phenylbenzenepropanamine

EINECS No. 206-869-4 **RTECS No.** SH 6480000

Uses Formerly used as the lactate in angina pectoris treatment.

Physical properties

M. Pt. 36.5-37.5°C

Mammalian & avian toxicity

Acute data

TD_{Lo} oral human 13 mg kg^{-1} (1).

LD_{50} intravenous rat, mouse 11, 250 mg kg^{-1}, respectively (2,3).

Teratogenicity and reproductive effects

Reproductive and teratogenic effects reported in mice following oral administration of 180-270 mg kg^{-1} (4).

Other effects

Other adverse effects (human)

Ventricular arrhythmias, ECG abnormalities, tremor and other side-effects reported (5,6).

Unsafe for patients with acute porphyria (7).

Cases of prenylamine-induced Parkinsonism have been reported (8).

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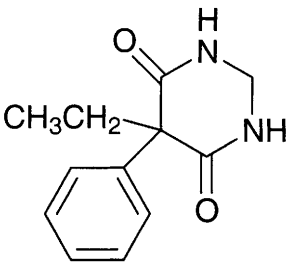
P272 primidone



$C_{12}H_{14}N_2O_2$ **Mol. Wt.** 218.26 **CAS Registry No.** 125-33-7

Synonyms 2-desoxyphenobarbital; 5-ethyldihydro-5-phenyl-4,6(1*H*,5*H*)-pyrimidinedione; 5-ethylhexahydro-4,6-dioxo-5-phenylpyrimidine; 5-phenyl-5-ethylhexahydropyrimidine-4,6-dione; Primaclone; Mysoline

EINECS No. 204-737-0 **RTECS No.** UV 9100000

Uses Barbiturate-related antiepileptic agent.

Physical properties

M. Pt. 281-282°C

Solubility Water: 0.6 g l^{-1} at 37°C. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 280, 1500 mg kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal mouse 332 mg kg^{-1} (3).

Teratogenicity and reproductive effects

Incidence of major malformations in children was the same in those exposed or not exposed to antiepileptics *in utero*; minor malformations were more common in children exposed to antiepileptics *in utero*, particularly if more than one drug was used (4-6).

Foetal exposure (the mother took 375 mg day^{-1}) was associated with Goldenhar syndrome, hemifacial microsomia, tetralogy of Fallot, aqueductal stenosis and anterior encephalocoele (7).

Familial embryopathy associated with maternal primidone therapy reported (8).

Metabolism and toxicokinetics

Readily absorbed from gastro-intestinal tract in humans; plasma $t_{1/2}$ 10-15 hr; principal metabolites are phenylethylmalonamide and phenobarbitone, both of which are pharmacologically active (9).

Partially (20%) bound to plasma protein, crosses the placenta and is excreted in breast milk and in urine as unchanged primidone and metabolites (9).

Genotoxicity

Salmonella typhimurium TA1535 with or without metabolic activation positive (10).

Other effects

Other adverse effects (human)

Adverse effects in patients given primidone for essential tremor may be due to absence of induced hepatic enzymes in patients previously unexposed to antiepileptics (11).

There is some evidence for tolerance to side-effects including ataxia, nystagmus, drowsiness and confusion (12).

Crystalluria has been reported and appears associated with serum primidone levels of >80 $\mu g\ l^{-1}$ (13).

A possible case of primidone toxicity presenting as severe catatonic schizophrenia was associated with a blood level of 13.9 $\mu g\ ml^{-1}$ (14).

Other comments

Effect of formulation and administration vehicles on bioavailability, potency and time course reviewed (15).

Toxicity reviewed (16).

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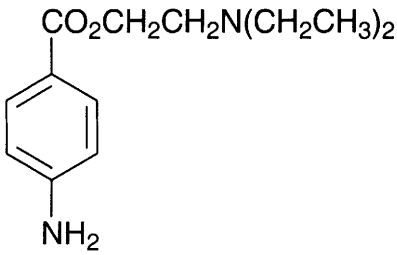
P273 procaine



$C_{13}H_{20}N_2O_2$ **Mol. Wt.** 236.31 **CAS Registry No.** 59-46-1

Synonyms 4-aminobenzoic acid, 2-(diethylamino)ethyl ester; 2-(diethylamino)ethyl *p*-aminobenzoate; allocaine; uovocaine; *p*-aminobenzoyldiethylaminoethanol

EINECS No. 200-426-9 **RTECS No.** DG 2100000

Uses Short acting, slow onset local anaesthetic used for infiltration anaesthesia, peripheral nerve block and spinal block.

Physical properties

M. Pt. 61°C

Solubility Water: soluble (hydrochloride). Organic solvents: benzene, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 500 mg kg^{-1} (1).

LD_{50} subcutaneous mouse, rat 300, 600 mg kg^{-1}, respectively (2,3).

LD_{50} intravenous mouse 45 mg kg^{-1} (4).

LD_{50} intraperitoneal mouse 124 mg kg^{-1} (5).

Metabolism and toxicokinetics

Poorly absorbed from mucous membranes but readily absorbed parenterally. Rapidly hydrolysed by plasma cholinesterase to *p*-aminobenzoic acid and diethylaminoethanol; some may also be metabolised in the liver (6). 6% bound to plasma proteins; 80% *p*-aminobenzoic acid excreted unchanged or conjugated in urine and 30% diethylaminoethanol is excreted in urine and the remainder metabolised in the liver (6).

In studies of procaine absorption in the rat small intestine, more unchanged procaine was absorbed in the ileum than duodenum or jejunum. In addition to procaine, two metabolites, *p*-aminobenzoic acid and acetylated *p*-aminobenzoic acid were formed in the intestinal mucosa and appeared in the absorbate (7).

Pharmacokinetics of intravenous procaine fitted a two-compartment open model in surgical patients; distribution and elimination $t_{1/2}$ 2.09 and 10.48 min, respectively, volume of distribution 1.07 mg l^{-1} and clearance 0.06 mg l^{-1} kg^{-1} min^{-1} (8).

Irritancy

In human trials 4.8% reacted positively to patch testing with a 2% aqueous solution (hydrochloride) (9).

Genotoxicity

Induced sister chromatid exchanges but not chromosomal aberrations in cultured Syrian hamster embryo cells (metabolic activation unspecified) (10).

Other comments

Pharmacokinetics reviewed (11).
Toxicity reviewed (12).
Pharmacokinetics and metabolism testing underway at the University of California, San Diego (13).

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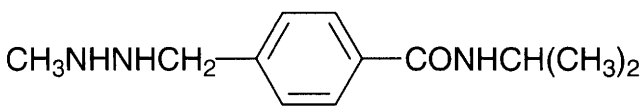
P274 procarbazine



$C_{12}H_{19}N_3O$ **Mol. Wt.** 221.30 **CAS Registry No.** 671-16-9

Synonyms 2-[(*p*-isopropylcarbamoyl)benzyl]-1-methylhydrazine; *N*-isopropyl-α-(2-methylhydrazino)-*p*-toluamide; 4-[(2-methylhydrazino)methyl]-*N*-isopropylbenzamide

EINECS No. 211-582-2 **RTECS No.** XS 4550000

Uses Antineoplastic in treatment of Hodgkin's disease and other lymphomas (as the hydrochloride).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat 350 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 614 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Ionising radiation had a potentiating effect on tumorigenicity of procarbazine, inducing increased incidence of pulmonary adenoma, thymomas and lachrymal gland adenocarcinoma, in mice receiving 300 mg kg^{-1} wk^{-1} for 4 wk (3).

Metabolism and toxicokinetics

Readily absorbed from the gastro-intestinal tract and crosses the blood-brain barrier. Plasma $t_{1/2}$ 10 min. Rapidly metabolised in kidneys and liver, only 5% excreted unchanged, to *N*-isopropylterephthalamic acid. 70% of a dose is excreted in 24 hr. Some excretion is via lungs as carbon dioxide and methane (4).

Genotoxicity

Salmonella typhimurium TA1530 with metabolic activation negative (5).
Induced DNA damage and sister chromatid exchanges in rat hepatocytes and V79 cells *in vitro* (5,6).
Induced DNA damage in rats *in vivo*. Benzylic C-H oxidation is an important step in the activation of procarbazine to genotoxic metabolites in rats (5).
In vivo mouse bone marrow micronucleus test positive (7).

Other effects

Other adverse effects (human)
Side-effects include nausea, vomiting, bone marrow depression, leucopenia, thrombocytopenia, anaemia, haemolysis, neurotoxicity (somnolence, depression, confusion, headache and peripheral neuropathies), fever, myalgia, pulmonary fibrosis, dermatitis and infertility (4).

Other comments

Urine from patients should be handled with protective clothing for up to 24 hr after dosing (4).
Neuro- and behavioural toxicity, carcinogenesis, pharmacokinetics, metabolism and reproductive effects currently being tested at Duke University (8).
Metabolism, toxicity and carcinogenicity of procarbazine derivatives reviewed (9).

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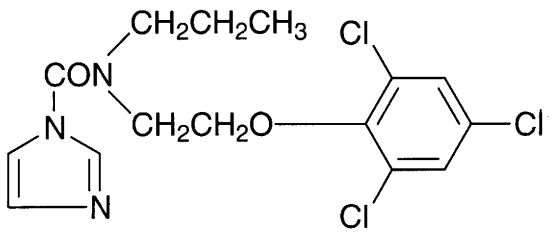
P275 prochloraz



$C_{15}H_{16}Cl_3N_3O_2$ **Mol. Wt.** 376.67 **CAS Registry No.** 67747-09-5

Synonyms *N*-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]-1*H*-imidazole-1-carboxamide; 1[*N*-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]carbamoyl]imidazole

EINECS No. 266-994-5 **RTECS No.** NI 4000400

Uses Fungicide; ergosterol biosynthesis inhibitor.

Physical properties

M. Pt. 46.5-49.3°C (>99% pure) **B. Pt.** 208-219°C at 0.2 mmHg (decomp.) **Specific gravity** 1.42 at 20°C
Partition coefficient log P_{ow} 4.38 **Volatility** v.p. 0.57×10^{-9} mmHg at 20°C
Solubility Water: 34.4 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, diethyl ether, toluene, xylene

Occupational exposure

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} (96 hr) rainbow trout, bluegill sunfish 1, 2.2 mg l^{-1}, respectively (1).

Invertebrate toxicity
Non-toxic to bees; LD_{50} oral 60 μg bee^{-1}, LD_{50} topical μg bee^{-1} (2).

Environmental fate

Degradation studies
Degradation in soil is not pH-dependent and leads to a range of mainly volatile metabolites; $t_{1/2}$ ~3 months; low toxicity to many soil microflora and fauna but inhibits soil fungi (1).

Adsorption and retention
Well absorbed onto soil particles and not readily leached (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 1600, 2400 mg kg^{-1}, respectively (1).
LD_{50} oral mallard duck 3132 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >2.16 mg l^{-1} (1).
LD_{50} dermal rabbit, rat >3000 and >5000 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects
No-effect level in 2-yr feeding trial in dogs 30 mg kg^{-1} diet (1).

Other effects

Any other adverse effects
Prochloraz inhibits cell-cell communication in rat liver epithelial cells determined by the scrape-loading/dye-transfer assay (3).

Legislation

WHO Toxicity Class III (4).
ADI (JMPR) 0.01 mg kg^{-1} body weight (2).
EC maximum residue limit for mushrooms 2 ppm, wheat and barley 0.05 ppm (1).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (6).

Other comments

Toxicity reviewed (7).
Hazards reviewed (8).

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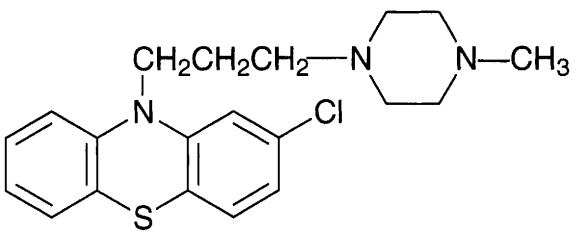
P276 prochlorperazine



$C_{20}H_{24}ClN_3S$ **Mol. Wt.** 373.95 **CAS Registry No.** 58-38-8

Synonyms 2-chloro-10-[3-(4-methyl-1-piperazinyl)propyl]-10*H*-phenothiazine; prochlorpromazine; prochlorpemazine

EINECS No. 200-379-4 **RTECS No.** SO 2700000

Uses A phenothiazine neuroleptic used to manage nausea, vomiting and vertigo.

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 400, 1800 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous mouse 400 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 120 mg kg^{-1} (3).

Teratogenicity and reproductive effects

Embryolethality but not teratogenicity was reported in mice following intraperitoneal injection of 100 mg kg^{-1} on day 10 of pregnancy (4).

Metabolism and toxicokinetics

Pharmacokinetics were studied in 8 humans following intravenous doses of 6.25-12.5 mg and 25 mg orally. Marked intra-individual variation was reported. $t_{1/2}$ 6.8-6.9 hr. Plasma clearance values above liver plasma flow suggested metabolism at other sites in addition to the liver. Peak plasma concentrations of 1.6-7.6 mg ml^{-1} occurred at 1.5-5 hr. Bioavailability estimated at 0-16% (5).

Other effects

Other adverse effects (human)

Severe dystonic reactions reported, particularly in children (6).
AIDS patients may be at greater risk of extrapyramidal reactions (6).
Hypertension and mouth ulceration have been reported (6).

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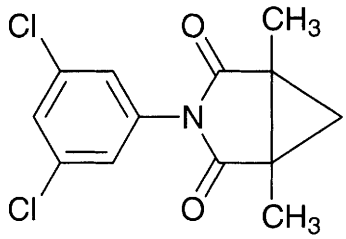
P277 procymidone



$C_{13}H_{11}Cl_2NO_2$ **Mol. Wt.** 284.14 **CAS Registry No.** 32809-16-8

Synonyms *N*-(3,5-dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboximide; 3-(3,5-dichlorophenyl)-1,5-dimethyl-3-azabicyclo[3.1.0]hexane-2,4-dione

EINECS No. 251-233-1 **RTECS No.** GZ 2150000

Uses Systemic fungicide; inhibitor of fungal triglyceride synthesis.

Physical properties

M. Pt. 166-166.5°C **Specific gravity** 1.452 at 25°C **Partition coefficient** log P_{ow} 3.14 (1)
Volatility v.p. 1.35×10^{-4} mmHg at 25°C
Solubility Water: 4.5 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, dimethylformamide, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish 3.6, 22.9 mg l^{-1}, respectively (1).
LC_{50} (48 hr) carp >10 mg l^{-1} (1).

Environmental fate

Degradation studies

Soil persistence ~4-12 wk, depending on humus content (1).
Procymidone added to vineyard soil underwent 90% degradation in 21 days (2).

Abiotic removal

Procymidone undergoes photolytic reactions in the presence of organic and inorganic soil constituents. Humic

and fulvic acids in aqueous solution lead to enhanced photodegradation of these chemicals. Iron oxide and TiO_2 contribute to the disappearance of the dicarboximide fungicides due to photocatalysis. Photolysis of these compounds leads to dechlorination and isomerisation (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 6800, 9100 mg kg^{-1}, respectively (1).
LD_{50} dermal mouse 7800 mg kg^{-1} (4).

Sub-acute and sub-chronic data

No-effect level in 90-day feeding trial in dog 3000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No-effect level in 2-yr feeding trial in ♀ and ♂ rat 300, 1000 mg kg^{-1}, respectively (1).

Teratogenicity and reproductive effects

Lowest-observable-effect levels for ovarian effects (ovarian stromal cell tumours, sex cord tumours, luteomas) in lifetime studies in rats 100 mg kg^{-1} day^{-1} (5).
Procymidone causes increases in LH and testosterone levels in the rat following binding to, and inhibition of, the androgen receptor (6).

Metabolism and toxicokinetics

An oral dose of 100 mg kg^{-1} was rapidly and almost completely excreted in urine of mice and rats within 7 days; major metabolic reactions were oxidation of one methyl group to carboxylic acid via pyroxymethyl and cleavage of the imide linkage (7).

Irritancy

Non-irritating to rabbit eyes and skin (dose and duration unspecified) (1).

Genotoxicity

Salmonella typhimurium (strain and metabolic activation unspecified) negative (8).
No increased incidence in chromosomal aberrations in Hungarian pesticide applicators exposed to procymidone and other pesticides (9).

Legislation

EC maximum residue limit for pome fruit, garlic, tomatoes, beans, melons and strawberries 2 ppm, for chicory, salads and grapes 5 ppm (1).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (11).
WHO Toxicity Class Table 5 (12).
ADI (JMPR) 0.1 mg kg^{-1} body weight (13).

Other comments

Considered an endocrine disruptor in the female (14).

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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. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
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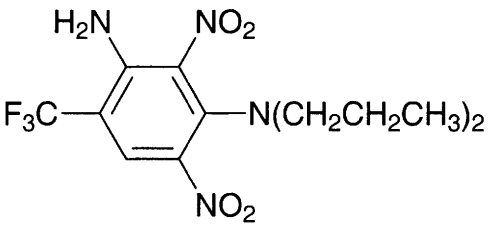
P278 prodiamine



$C_{13}H_{17}F_3N_4O_4$ **Mol. Wt.** 350.30 **CAS Registry No.** 29091-21-2

Synonyms 5-dipropylamino-α,α,α-trifluoro-4,6-dinitro-*o*-toluidine; 2,6-dinitro-N^1,N^1-dipropyl-4-(trifluoromethyl)-*m*-phenylenediamine; 2,4-dinitro-N^3,N^3-dipropyl-6-(trifluoromethyl)-1,3-benzenediamine

EINECS No. 249-421-3 **RTECS No.** ST 2200000

Uses Pre-emergence herbicide; inhibits sprouting grasses and broad-leaved weeds.

Physical properties

M. Pt. 124°C **Flash point** 196°C **Specific gravity** 1.47 at 25°C **Partition coefficient** log P_{ow} 4.017-4.174 (1)
Volatility v.p. 2.4×10^{-8} mmHg at 25°C
Solubility Water: 0.013 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, benzene, acetonitrile, hexane

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout 3.18, 47.3 mg l^{-1}, respectively (1).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* 5.4 mg l^{-1} (1).
LD_{50} topical bee >100 μg bee^{-1} (2).

Environmental fate

Abiotic removal
Photodegraded by reduction of nitro groups (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck, Japanese quail >10,000 mg kg^{-1} (1).
LD_{50} oral rat, mouse >5000, 15,380 mg kg^{-1}, respectively (1).
LD_{50} dermal rat >2000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
No-effect level in 2-yr feeding trials in rats 200 mg kg^{-1} (1).

Metabolism and toxicokinetics
After oral administration (dose unspecified) to rats 58.4% was excreted in faeces and 28.6% in urine after 48 hr (1).

Irritancy
Irritating to eyes but not skin of rabbits (dose and duration unspecified) (1).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (3).
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).
EPA Toxicity Class IV (2).

Other comments

Herbicidal activity reviewed (6).
Metabolic pathways reviewed (7).

References

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5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
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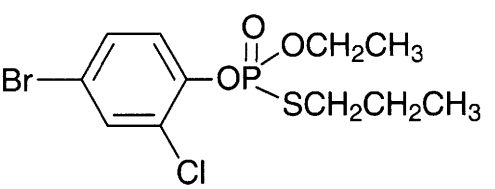
P279 profenofos



$C_{11}H_{15}BrClO_3PS$ **Mol. Wt.** 373.63 **CAS Registry No.** 41198-08-7

Synonyms *O*-(4-bromo-2-chlorophenyl) *O*-ethyl *S*-propyl phosphorothioate

EINECS No. 255-255-2 **RTECS No.** TE 6975000

Uses Contact and stomach-acting insecticide and acaricide, cholinesterase inhibitor.

Physical properties

B. Pt. 110°C at 0.001 mmHg **Specific gravity** 1.455 at 20°C **Partition coefficient** log P_{ow} 4.44
Volatility v.p. 9.75×10^{-6} mmHg at 20°C
Solubility Water: 28 mg l^{-1} at 25°C. Organic solvents: miscible with most organic solvents

Occupational exposure

Supply classification harmful
Risk phrases Harmful by inhalation, in contact with skin and if swallowed (R20/21/22)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S1/2, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, crucian carp, bluegill sunfish 0.08-0.3 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken 1900 μg kg^{-1} (2).
LD_{50} oral rat, rabbit 358, 700 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation rat 3 mg l^{-1} (1).
LD_{50} dermal rabbit 472 mg kg^{-1} (1).

Carcinogenicity and chronic effects
No-effect level in 2-yr feeding trial in rats 0.38 mg kg^{-1} diet (1).
No-effect level in 18-month feeding trials in mice 0.08 mg kg^{-1} diet (1).

Irritancy
Moderate eye and mild skin irritant in rabbits (dose and duration unspecified) (1).

Genotoxicity

Increased incidence of chromosomal aberrations in human lymphocytes *in vitro* (3).
Induced chromosomal aberrations, sister chromatid exchanges and micronuclei in somatic cells of mice *in vivo* (4).

Legislation

EC maximum residue limit in maize 0.05 ppm (1).
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 II (formulation) (8).
ADI 0.01 mg kg^{-1} body weight (8).

References

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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.
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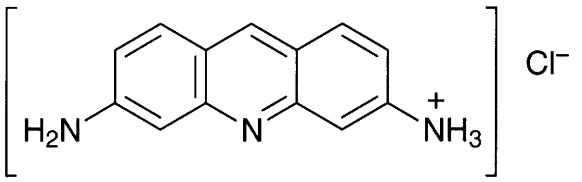
P280 proflavine hydrochloride



$C_{13}H_{12}ClN_3$ **Mol. Wt.** 245.71 **CAS Registry No.** 952-23-8

Synonyms proflavin hydrochloride; 3,6-acridinediamine, monohydrochloride; 3,6-diaminoacridinium chloride; 3,6-diaminoacridinium hydrochloride

EINECS No. 213-459-9 **RTECS No.** AR 9064000

Uses Slow acting antiseptic against Gram-positive bacteria, less active against Gram-negative bacteria. Acridine derivatives have been used to treat infected wounds or burns and for skin disinfection. Used in eye drops against superficial infections.

Physical properties

M. Pt. 270°C (decomp.)
Solubility Water: 10%. Organic solvents: chloroform, diethyl ether, liquid petroleum

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (1).
Increased incidence of hepatocellular carcinomas in ♀ mice fed 200-400 mg kg^{-1} diet (as the hemihydrate), although a positive control carcinogen tested in the same laboratory may have exerted an effect (2).
Increased incidence of intestinal tumours and hepatocellular carcinomas in rats fed 300-600 mg kg^{-1} diet (as the hemihydrate) (duration unspecified) (2).
The hemisulfate enhanced skin tumours in mice treated with an initiator, but had no promoting effect when applied dermally (duration and route unspecified) (2).

Genotoxicity

Salmonella typhimurium TA98, TA1537 without metabolic activation in the dark positive; TA98, TA1535, TA1537, TA1538 without metabolic activation in the light positive; TA1538 with metabolic activation positive (2).
Saccharomyces cerevisiae reverse mutations negative, mitotic gene conversion positive (metabolic activation unspecified) (2).
Drosophila melanogaster chromosome loss or nondisjunction negative (proflavine salt used in studies not specified) (2).
Salmonella typhimurium TA98, TA1537, TA1538 with and without metabolic activation positive, TA100 with metabolic activation positive (proflavin hydrochloride hemihydrate) (3).

Other effects

Other adverse effects (human)
Prolonged treatment may delay healing (4).

References

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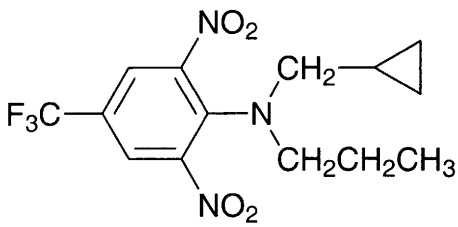
P281 profluralin



$C_{14}H_{16}F_3N_3O_4$ **Mol. Wt.** 347.29 **CAS Registry No.** 26399-36-0

Synonyms *N*-(cyclopropylmethyl)-α,α,α-trifluoro-2,6-dinitro-*N*-propyl-*p*-toluidine

EINECS No. 247-656-6 **RTECS No.** XU 5785000

Uses Superseded selective pre-planting herbicide.

Physical properties

M. Pt. 33-36°C

Solubility Water: 0.1 mg l^{-1} at 20°C

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) (S2)

Environmental fate

Degradation studies

Metabolised by soil microbes to: 2,6-dinitro-*N*-propyl-4-(trifluoromethyl)benzenamine, *N*-(cyclopropylmethyl)-*N*-propyl-2,6-dinitro-4-(trifluoromethyl)aniline, 2-amino-6-nitro-*N*-propyl-4-(trifluoromethyl)benzenamine and 2-amino-6-nitro-4-(trifluoromethyl)benzenamine. *Streptomyces* in soil can convert the dealkylated 2,6-dinitro-4-(trifluoromethyl)benzenamine into 2-amino-6-nitro-4-(trifluoromethyl)benzenamine and azoxy and azo compounds (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1808 mg kg^{-1} (1).

LC_{Lo} (duration unspecified) inhalation rat 3970 mg m^{-3} (2).

LD_{50} dermal rabbit 13,754 mg kg^{-1} (2).

Metabolism and toxicokinetics

In rats given 1 g kg^{-1} by intragastric intubation, urinary metabolites were: 2-amino-6-nitro-4-(trifluoromethyl)benzenamine, 2,6-dinitro-*N*-propyl-4-(trifluoromethyl)benzenamine, *N*-(cyclopropylmethyl)-2,6-dinitro-4-(trifluoromethyl)benzenamine, 2,6-dinitro-*N*-(3-hydroxypropyl)-4-trifluoromethyl)benzenamine, 2,6-dinitro-4-(trifluoromethyl)benzenamine, *N*-(cyclopropylmethyl)-2-(hydroxyamino)-6-nitro-*N*-propyl-4-(trifluoromethyl)benzenamine, 2-ethyl-7-nitro-5-(trifluoromethyl)benzimidazole, 6-dinitro-*N*-(cyclopropylmethyl)-*N*-(1-oxo-2-propenyl benzenamine and 2-(acetylamino)-6-nitro-4-(trifluoromethyl)benzenamine (1).

Irritancy

218 mg applied to abraded rabbit skin caused mild irritation and 44 mg instilled into rabbit eyes caused severe irritation (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).

References

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3. *Ciba Geigy Toxicological Data* 1977.
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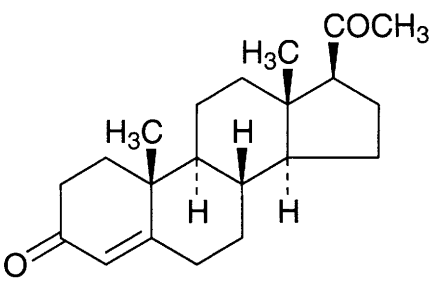
P282 progesterone



$C_{21}H_{30}O_2$ **Mol. Wt.** 314.47 **CAS Registry No.** 57-83-0

Synonyms pregn-4-ene-3,20-dione; corpus luteum hormone; luteal hormone; luteine; Syngesterone; Crinone

EINECS No. 200-350-6 **RTECS No.** TW 0175000

Uses Used to control dysfunctional uterine bleeding, to maintain pregnancy in women with histories of miscarriage and in contraceptives.

Occurrence Female sex hormone, secreted during latter half of the menstrual cycle and during pregnancy. Found in many tissues and biological fluids. It also occurs in some plant species.

Physical properties

M. Pt. α-form 127-131°C, β-form 121-122°C **Specific gravity** 1.166 α-form at 23°C, 1.171 β-form at 20°C
Solubility Organic solvents: acetone, 1,4-dioxane, ethanol

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal rat 327 mg kg^{-1} (1).
LD_{Lo} intravenous mouse 100 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Daily injection of 2-4 mg kg^{-1} to rats and mice increased the incidence and reduced the latent period of mammary tumours induced by 3-methylcholanthrene (MCA) or 7,12-dimethylbenz[*a*]anthracene (DMBA), if given after MCA or DMBA (3).
Increased incidence of mammary tumours and reduced latency reported in neonatal ♀ mice given 100 μg day^{-1} subcutaneously (3).

Teratogenicity and reproductive effects

In a model system in which genital tracts from human ♀ foetuses 7-18 wk old were grafted into castrated murine hosts, prenatal exposure of the developing human ♀ genital tract to progesterone was not associated with any obvious teratogenic effects (4).
Clinical use of progesterone during pregnancy was not associated with foetal developmental effects (5).
No abnormalities reported in rats after subcutaneous injection of 5-200 mg day^{-1} on days 15-20 of pregnancy, or in rhesus monkeys after intramuscular injection of 50 mg day^{-1}, 5 days wk^{-1} from days 24-28 until term. Some studies report a virilising and masculinising effect on foetuses exposed *in utero* (3).

Metabolism and toxicokinetics

Absorbed from the gastro-intestinal tract, and there is some controversy as to whether it is rapidly inactivated in the liver after oral administration or whether it is active. It is absorbed after buccal, rectal, vaginal or intramuscular injection. Blood $t_{1/2}$ is a few minutes. Metabolised in the liver, about 12% to pregnanediol which is excreted in urine conjugated with glucuronic acid (6).
Metabolised in humans and chimpanzees by reductases to pregnanediol; androsterone is the major metabolite in baboons and rhesus monkeys, indicating side-cleavage predominates in these species. Rabbits, guinea pigs, pigs and rats excrete acidic progesterone metabolites (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (7).
Escherichia coli WP2*uvr*A reverse mutation with and without metabolic activation negative (7).
Did not induce chromosomal aberrations in human lymphocytes, Chinese hamster cells or other animal bone marrow cells *in vitro* (cell type unspecified) (8).
Did not induce sister chromatid exchanges in human cells *in vitro* (8).
Studies on transformation of rodent cells *in vitro* were inconclusive; positive results were reported in rat embryo cells, weakly positive in mouse cells (9).
L5S1787 mouse lymphoma cell forward mutation assay negative (10).
Chromosomal aberrations induced in cultured human embryonic fibroblasts (3).
Did not induce lethal mutations in mice or chromosomal aberrations in rats treated *in vivo* (11).
Induced chromosomal aberrations, aneuploidy and polyploidy in ♂ dogs and ♀ hamsters after subcutaneous injection *in vivo* (3).

Other comments

Use as a contraceptive in women reviewed (12).
Role in embryo implantation and pregnancy maintenance reviewed (13).
Reproductive hazards in humans reviewed (5).

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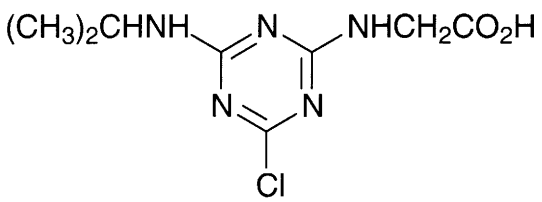
P283 proglinazine-ethyl



$C_8H_{12}ClN_5O_2$ **Mol. Wt.** 245.67 **CAS Registry No.** 68228-18-2

Synonyms *N*-(4-chloro-6-isopropylamino-1,3,5-triazin-2-yl)glycine; *N*-[4-chloro-6-[(1-methylethyl)amino]-1,3,5-triazin-2-yl]glycine

RTECS No. MB 9259000

Uses Superseded pre-emergence herbicide.

Physical properties

M. Pt. 110-112°C **Volatility** v.p. 2×10^{-6} mmHg at 20°C
Solubility Water: 750 mg l^{-1} at 25°C. Organic solvents: acetone, hexane, xylene

Environmental fate

Degradation studies
Degraded in soil, $t_{1/2}$ 56-70 days (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, rat, mouse >3000, >8000, >8000 mg kg^{-1}, respectively (1).
LD_{50} oral guinea pig 857-923 mg kg^{-1} (1).
LD_{50} dermal rat, rabbit >1500, >4000 mg kg^{-1}, respectively (1).
LD_{50} intraperitoneal mouse, rat 720, 1080 mg kg^{-1}, respectively (1).

Irritancy
Non-irritating to skin and eyes of rabbits (dose and duration unspecified) (1).

Sensitisation
Moderate skin sensitiser in guinea pig (1).

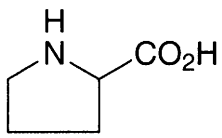
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, 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

P284 L-proline



$C_5H_9NO_2$ **Mol. Wt.** 115.13 **CAS Registry No.** 147-85-3

Synonyms 2-pyrrolidinecarboxylic acid

EINECS No. 205-702-2 **RTECS No.** TW 3584000

Uses Non-essential amino acid.

Occurrence Isolated from wheat gliadin and gelatin.

Physical properties

M. Pt. 220-222°C (decomp.)

Environmental fate

Degradation studies

Ratio of observed and theoretical COD of food industry wastewaters including L-proline was 66.3 and 89.2% respectively, with an average value of 21.1% (1).

Mammalian & avian toxicity

Metabolism and toxicokinetics

Homeostatic regulation of plasma proline concentrations in humans is partially mediated by reciprocal changes in rates of endogenous proline synthesis and its oxidation (2).

Other comments

Metabolism reviewed (3).

Proline is an effective inhibitor of mutagenicity (Ames test) due to Maillard-type reactions during cooking of meat and fish (4).

References

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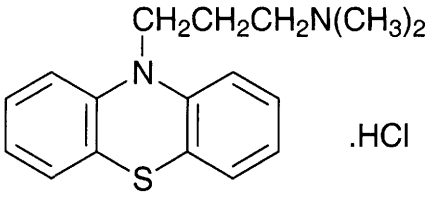
P285 promazine hydrochloride



$C_{17}H_{21}ClN_2S$ **Mol. Wt.** 320.89 **CAS Registry No.** 53-60-1

Synonyms 10-[γ-(dimethylamino)-*N*-propyl]phenothiazine hydrochloride; 10-[3-(dimethylamino)propyl]phenothiazine hydrochloride; Sparine

EINECS No. 200-179-7 **RTECS No.** SO 8575000

Uses Antipsychotic used for short-term management of agitated or disturbed behaviour, nausea or vomiting in labour or post operatively, and as a 'premed'.

Physical properties

M. Pt. 181°C (decomp.)

Solubility Water: 1 g 3 ml^{-1}. Organic solvents: chloroform, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 400 mg kg^{-1} (1).

LD_{50} intravenous rabbit, rat, mouse 21-38 mg kg^{-1} (2).

LD_{50} subcutaneous mouse, rat 300 mg kg^{-1} (2,3).

LD_{Lo} intraperitoneal mouse 225 mg kg^{-1} (4).

Teratogenicity and reproductive effects

Increased incidence of neonatal jaundice reported after use in human pregnancy (5).

Other effects

Other adverse effects (human)

Central nervous system effects reported in a human following an oral dose of 20 mg kg^{-1} (6).

References

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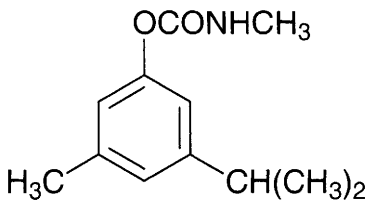
P286 promecarb



$C_{12}H_{17}NO_2$ **Mol. Wt.** 207.27 **CAS Registry No.** 2631-37-0

Synonyms 3-methyl-5-(1-methylethyl)phenol methylcarbamate; carbamic acid, methyl-, *m*-cym-5-yl ester; 3-isopropyl-5-methylphenyl methylcarbamate; 5-methyl-*m*-cumenyl methylcarbamate; Carbamult; ITC; Minacide

EINECS No. 220-113-0 **RTECS No.** FB 8050000

Uses Superseded insecticide.

Physical properties

M. Pt. 87.0-87.5°C **B. Pt.** 117°C at 0.01 mmHg **Partition coefficient** log P_{ow} 3.10 (1)
Volatility v.p. 3×10^{-4} mmHg at 25°C
Solubility Water: 91 mg l^{-1} at 25°C. Organic solvents: acetone, cyclohexanol, cyclohexanone, carbon tetrachloride, dimethylformamide, ethylene chloride, isobutanol, isopropanol, methanol, 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) – Avoid contact with the skin – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S24, S37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish, goldfish 0.31, 0.64, 8.6 mg l^{-1}, respectively (2,3).
LC_{50} (120 hr) European trout 1.2 mg l^{-1} (2).

Invertebrate toxicity
LD_{50} honeybee 1.1 μg bee^{-1} (2).

Bioaccumulation
Estimated bioconcentration factors of 49 and 134 indicate that environmental accumulation is likely to be moderate (4).

Environmental fate

Degradation studies
Soil $t_{1/2}$ 28 days; degradation products include carbon dioxide and methylamine (2,3).
Degraded by *Pseudomonas putida*, *Flurobactor* sp. and *Aeromonas liquifaciens* (5).

Abiotic removal
Hydrolysis $t_{1/2}$ 103 days at pH 7; 36 hr at pH 9 (2).
Reacts with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 5 hr (6).

Adsorption and retention

Calculated K_{ow} 365-1240 indicate that adsorption to soil and sediments is likely (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, mallard duck, bobwhite quail 4-120 mg kg^{-1} (2,3,7,8).
LC_{50} (4 hr) inhalation rat >160 mg m^{-3} (3).
LD_{50} dermal rat 450 mg kg^{-1} (9).
LD_{50} intraperitoneal rat 27 mg kg^{-1} (10).
LD_{50} intramuscular rat 44 mg kg^{-1} (11).
LD_{50} intravenous rat 5 mg kg^{-1} (11).

Carcinogenicity and chronic effects

Oral rat (18 month) 5 mg kg^{-1} day^{-1} 5 days wk^{-1} caused no adverse effects (3).

Metabolism and toxicokinetics

In mammals, the substituted phenol moiety is eliminated after condensation with glucuronic acid (3).

Other effects

Any other adverse effects

Cholinesterase inhibitor (2,3).

Legislation

The log P_{ow} value exceeds the European Communities recommended level of 3.0 (6th and 7th amendments) (12).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (13).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).
WHO Toxicity Class II (15).
EPA Toxicity Class II (formulation) (2).

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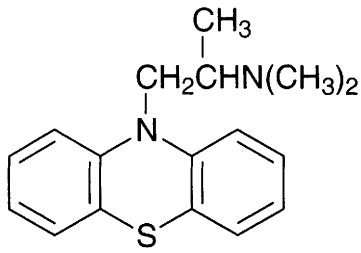
P287 promethazine



$C_{17}H_{20}N_2S$ **Mol. Wt.** 284.43 **CAS Registry No.** 60-87-7

Synonyms *N*-(2′-dimethylamino-2′-methyl)ethylphenothiazine; *N*,*N*,α-trimethyl-10*H*-phenothiazine-10-ethanamine; 10-[2-(dimethylamino)propyl]phenothiazine

EINECS No. 200-489-2 **RTECS No.** SO 6825000

Uses Histamine H_1-receptor antagonist used for symptomatic relief of hypersensitivity reactions, nausea, vomiting and as a sedative and hypnotic. Common ingredient in cold and cough preparations.

Physical properties

M. Pt. 60°C **B. Pt.** 190-192°C

Solubility Water: 1 in 0.6 parts (hydrochloride). Organic solvents: chloroform (hydrochloride), ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rabbit 326, 580 mg kg^{-1}, respectively (1,2).
LD_{50} intramuscular rat, mouse 170, 175 mg kg^{-1}, respectively (3).
LD_{50} intravenous mouse, rat 40, 45 mg kg^{-1}, respectively (3,4).
LD_{50} subcutaneous mouse, rat 225, 700 mg kg^{-1}, respectively (5,6).
LD_{50} intraperitoneal mouse 124 mg kg^{-1} (7).

Teratogenicity and reproductive effects

50 mg kg^{-1} day^{-1} on days 10-16 of pregnancy (route unspecified) was foetotoxic in rats, causing death of 40% of foetuses (8).

Metabolism and toxicokinetics

Well absorbed in humans after oral or intramuscular injection, peak plasma concentration occurring after 2-3 hr. It is widely distributed and enters the brain and crosses the placenta. Plasma-protein binding reported as 76-93%. Extensively metabolised, mainly to promethazine sulfoxide and *N*-desmethylpromethazine. Excreted slowly in urine and bile mainly as metabolites, $t_{1/2}$ 5-14 hr (9).

Irritancy

100 mg caused mild skin and severe eye irritation in rabbits (10).

Genotoxicity

Did not induce chromosomal aberrations in Chinese hamster ovary cells *in vitro* with or without metabolic activation; a slight increase in sister chromatid exchanges was reported with metabolic activation (11).

Other effects

Other adverse effects (human)

Side-effects include bradycardia, tachycardia, transient minor increases in blood pressure and hypotension (more commonly after injection), jaundice, blood dyscrasias and venous thrombosis at the injection site. Arteriospasm and gangrene may occur after inadvertent intra-arterial injection (9).

A toxic neurological syndrome has been reported in children after topical administration (12).

Findings indicated that a higher proportion of sudden infant death syndrome infants had been given phenothiazines, it was suggested that the victims may be excessively sensitive to these drugs. An EC study did not confirm a link between sudden death in infants and drug administration by national drug monitoring centres, but that the risk of apnoea was associated with all sedatives (9).

Other comments

Phenothiazines are not generally recommended in late pregnancy (9).

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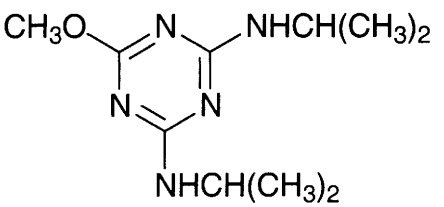
P288 prometon



$C_{10}H_{19}N_5O$ **Mol. Wt.** 225.29 **CAS Registry No.** 1610-18-0

Synonyms 2,4-bis(isopropylamino)-6-methoxy-s-triazine; 2,6-diisopropylamino-4-methoxytriazine; 2-methoxy-4,6-bis(isopropylamino)-s-triazine; prometone

EINECS No. 216-548-0 **RTECS No.** XY 4200000

Uses Non-systemic, non-selective herbicide, inhibits photosynthesis.

Physical properties

M. Pt. 91-92°C **Specific gravity** 1.088 at 20°C **Partition coefficient** log P_{ow} –1.06

Volatility v.p. 2.3×10^{-6} mmHg at 20°C

Solubility Water: 750 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, dichloromethane, methanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) goldfish, rainbow trout, bluegill sunfish 8.6, 20, >32 mg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} (10 day) *Phaeodactylum tricornutum* 0.1-0.25 mg l^{-1} (2).

EC_{50} (48, 24 hr) *Daphnia magna* 38, 78 mg l^{-1}, respectively (3).

Environmental fate

Degradation studies

Microbial degradation to hydroxy metabolites via hydrolytic cleavage of methoxy group and dealkylation of side-chains; persists in soil for up to 1 yr, depending on application rate, soil type and moisture (1).

Soil $t_{1/2}$ >459-1123 days (4).

Persistence was studied in 3-yr field trials in the semi-arid tropics; prometon was slightly phytotoxic in 2 out of 3 seasons at both the recommended and double the recommended application rate (5).

Abiotic removal

Stable to hydrolysis at pH 5, 7 and 9 at 25°C for 40 days, and stable in aqueous solution to natural sunlight for 2 wk (4).

Adsorption and retention

Results of adsorption/desorption tests suggest potential to leach through soil; 2.61 (sandy loam), 2.90 (silt loam), 2.40 (silty clay loam), 1.20 (silt loam) and 0.398 (sand); organic matter was 0.8-5% (4).

R_f values ranged from very mobile in Mississippi silt loam and Plainfield sand to low mobility in California sandy loam (4).

K_{oc} for Handford sandy loam and Tujunga loamy sand detected by mass balance 76 m^{-3} mg^{-1} (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 2160, 2980 mg kg^{-1}, respectively (1).

LC_{50} (4 hr) inhalation rat >3.26 mg kg^{-1} (1).

LD_{50} dermal rabbit >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

No-effect level in 90-day feeding trial in rats 5.4 mg kg^{-1} day^{-1} (1).

Rats fed 10-10,000 ppm for 4 wk showed reduced body weight at ≥3000 ppm; no pathological changes were reported at any dose (7).

No-observed-adverse-effect level 300 ppm and lowest-observed-adverse-effect level 1000 ppm in dogs fed prometon for 2 wk (7).

Teratogenicity and reproductive effects

No effects on implantation, litter size, foetal viability, resorption, foetal body weight or external soft tissue or skeletal malformation occurred in rats fed 0, 36, 120 or 360 mg kg^{-1} day^{-1} on days 6-15 gestation (4).

Reduced pregnancy rates but no malformations occurred in rabbits fed up to 24.5 mg kg^{-1} day^{-1} from days 6-30 of pregnancy (4).

Metabolism and toxicokinetics

Rapidly and completely absorbed by the gastro-intestinal tract in rats within 72 hr; no detectable levels of radioactivity in rat tissue 72 hr after gastric intubation of ^{14}C-prometon (8).

Urinary metabolites in rats included 2-methoxy-4,6-diamino-*s*-triazine (14%) and ammeline (31%); triazine ring cleavage does not appear to occur during metabolism (4).

After oral administration of ^{14}C-prometon to rats excretion was most rapid during the first 24 hr; after 72 hr excretion was mainly via urine (91%) with 9% via faeces (8).

Irritancy
Minimal dermal irritant in rabbits; 500 mg applied to intact skin for 24 hr caused barely perceptible erythema; mild oedema and slight desquamation occurred at 2000 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} (9).
WHO Toxicity Class Table 5 (10).
EPA Toxicity Class III (formulation) (11).

Other comments

Non-toxic to bees (1).
Drinking water equivalent level adjusted for children 0.2 mg l^{-1}; lifetime health advisory 0.1 mg l^{-1} (4).

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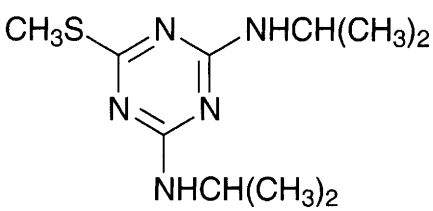
P289 prometryn



$C_{10}H_{19}N_5S$ **Mol. Wt.** 241.36 **CAS Registry No.** 7287-19-6

Synonyms 2,4-bis(isopropylamino)-6-(methylthio)-*s*-triazine; *N,N'*-diisopropyl-6-(methylthio)-1,3,5-triazine-2,4-diamine; N^2,N^4-diisopropyl-6-(methylthio)-1,3,5-triazine-2,4-diamine

EINECS No. 230-711-3 **RTECS No.** XY 4390000

Uses Selective systemic herbicide.

Physical properties

M. Pt. 118-120°C **Specific gravity** 1.157 at 20°C **Partition coefficient** log P_{ow} 3.1 at 25°C (1)
Volatility v.p. 1×10^{-6} mmHg at 20°C
Solubility Water: 48 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, methanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, carp, bluegill sunfish 2.5-10 mg l^{-1} (2,3).

Invertebrate toxicity

LC_{50} (duration unspecified) *Daphnia pulex* >40 mg l^{-1} (3).
EC_{50} (48, 24 hr) *Daphnia magna* 9.7, 23.5 mg l^{-1}, respectively (4).
Non-toxic to bees; LD_{50} contact >130, oral >99 μg bee^{-1} (2).

Toxicity to other species

LC_{50} (duration unspecified) *Rana brevipoda* tadpole <1 ppm (5).

Environmental fate

Nitrification inhibition

A mixture of 3 kg ha^{-1} yr^{-1} atrazine and 1 kg ha^{-1} yr^{-1} prometryn did not inhibit nitrification in soil sown to corn (6).
s-Triazines mostly inhibited ammonification and nitrification in soil; recommended tolerance limit using microbiological risk factor, 0.5-0.9 mg kg^{-1} soil (7).

Degradation studies

Microbial degradation in soil is by oxidation of the methylthio group to hydroxy metabolites, and dealkylation of the side chains; $t_{1/2}$ 40-70 days (1).

Abiotic removal

Decomposed by UV radiation (1).

Adsorption and retention

150 mg m^{-2} was applied to potatoes and carrots in sandy soils in lysimeters; percolate contained <1 μg l^{-1} hence there was no threat to groundwater under these conditions. Persistence is greater in soils with higher humus content (8).
Metabolites are more mobile than prometryn itself (9).
Classified as leachable according to an index based on soil $t_{1/2}$ and K_{oc}; K_{oc} 614 cm^{-3} g^{-1} (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 2000, 5235 mg kg^{-1}, respectively (11,1).
LD_{50} dermal rabbit >3100 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LC_{50} (5-7 days) oral bobwhite quail, mallard duck 16140, 38,736 mg kg^{-1}, in diet, respectively (1).
Dermal rabbit (21 days) no local or systemic toxicity observed at 1000 mg kg^{-1} day^{-1} (12).

Carcinogenicity and chronic effects

No-effect level in 2-yr feeding trials in dogs, rats 150, 1250 mg kg^{-1} diet, respectively (1).

Teratogenicity and reproductive effects

Reduced body, liver, kidney and spleen weight and raised serum aspartate aminotransferase activity reported in newborn rats following oral administration of 400 mg kg^{-1} day^{-1} to their dams on days 18-20 of pregnancy (13).

Irritancy

Not a skin irritant in rabbits (dose and duration unspecified) (1).
80 mg instilled into rabbit eyes caused mild irritation (14).

Sensitisation

Prometryn is not considered a sensitiser (12).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 negative (metabolic activation unspecified) (15).
Bacillus subtilis M45 negative (metabolic activation unspecified) (16,17).
Saccharomyces cerevisiae point mutation positive (metabolic activation unspecified) (18).
Non-mutagenic in chromosomal aberration, bacterial DNA repair and unscheduled DNA synthesis tests (12).

Legislation

EC maximum residue limit in vegetables 0.2 ppm (1).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (19).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (20).
WHO Toxicity Class Table 5 (21).
EPA Toxicity Class III or IV (formulation) (2).
ADI 0.01 mg kg^{-1} (2).

Other comments

Effect on *Rhizobium* sp. and *Azotobacterium* sp. reviewed (22).
Prometryn acts by inhibiting the electron transport in target broadleaves and grasses (12).

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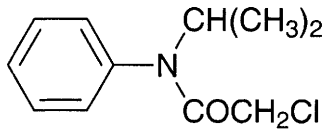
P290 propachlor



$C_{11}H_{14}ClNO$ **Mol. Wt.** 211.69 **CAS Registry No.** 1918-16-7

Synonyms 2-chloro-*N*-isopropylacetanilide; α-chloro-*N*-isopropylacetanilide; 2-chloro-*N*-(1-methylethyl)-*N*-phenylacetamide; propachlore

EINECS No. 217-638-2 **RTECS No.** AE 1575000

Uses Pre-emergence or early herbicide, inhibits cell elongation and protein synthesis.

Physical properties

M. Pt. 77°C **B. Pt.** 110°C at 0.03 mmHg **Specific gravity** 1.242 at 25°C **Partition coefficient** log P_{ow} 2.3
Volatility v.p. 7.9×10^{-5} mmHg at 25°C
Solubility Water: 613 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, chloroform, ethanol, toluene

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to the eyes – May cause sensitisation by skin contact (R22, R36, 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) rainbow trout, bluegill sunfish 0.17, >1.4 mg l^{-1}, respectively (1).
NOEC (duration unspecified) fathead minnow 0.17 mg l^{-1} (2).
LC_{50} (96 hr) guppy 0.75 mg l^{-1} (3).

Invertebrate toxicity
LC_{50} (duration unspecified) *Daphnia magna* 7 mg l^{-1} (4).
NOEC (duration unspecified) *Daphnia magna* 1 mg l^{-1} (2).
LC_{50} (96 hr) *Daphnia magna* 0.05 mg l^{-1} (3).
EC_{50} (96 hr) *Selenastrum capricornutum* 0.02 mg l^{-1} (5).
LC_{50} (48 hr) oral bee >1000 ppm, contact >25 μg bee^{-1} (1).

Environmental fate

Nitrification inhibition
In studies on soil microorganisms, nitrifying bacteria were most sensitive to inhibition by propachlor; application of 8-10 kg ha^{-1} reduced their population 3-4 fold (5).

Degradation studies
$t_{1/2}$ in anaerobic soil <4 days (6).
Microbial degradation in soil involves dechlorination (7).
Persists in soil 4-6 wk; negligible loss by photodecomposition or volatilisation (8).
At normal application rates $t_{1/2}$ 2-14 days in aerobic soils in the laboratory; at 500 ppm degradation was slower, 90% remaining after 21 days (6).

Degrades to [(1-methylethyl)phenylamino]oxoacetic acid and [(2-methylethyl)phenylamino]-2-oxoethanesulfonic acid in aerobic soils (6).
Rapid degradation suggests groundwater contamination is unlikely (6).
Microbial degradation is the major method of removal from soil and water; bacteria and fungi including *Penicillium, Aspergillus, Fusarium, Trichoderma, Moraxella* and *Xanthobacter* sp. are involved in degradation. *Moraxella* can use propachlor as its sole carbon source, releasing a metabolite 2-chloro-*N*-isopropylacetamide on which *Xanthobacter* grows. Major metabolites in soil are water-soluble oxanilic and sulfonic acids. Degradation in soil is almost complete within 6 months, unless soils are cold, dry and nutrient-poor. The conjugated *N*-isopropylaniline metabolite is more persistent than the parent substance (5).
Loss from water depends on microbial population; $t_{1/2}$ ~5 months in water with few bacteria; laboratory ecosystem studies showed almost complete degradation within 33 days (5).

Adsorption and retention
Moderately to very mobile in soils, mobility correlated with clay content and, to a lesser extent, organic matter and cation exchange capacity (6).
This leads to the potential for leaching into groundwater, although studies show this is unlikely to occur in practice; very high rainfall is required to transport residues 30 cm down the soil profile, and most studies report residues remain in the upper 4 cm (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral duck 512 mg kg^{-1} (4).
LD_{50} oral mouse, rat, rabbit 290-710 mg kg^{-1} (9-11).
LD_{50} dermal rabbit 380 mg kg^{-1} (12).

Sub-acute and sub-chronic data
No-observed-adverse-effect level in 90-day feeding trials in dogs 37.5-133.3 mg kg^{-1} day^{-1} (6).
No-observed-adverse-effect level in 90-day feeding trials in rats and mice 12 mg kg^{-1} day^{-1} and 58 mg kg^{-1} day^{-1}, respectively (6).

Carcinogenicity and chronic effects
No-effect level in rats and dogs in 2-yr feeding trials 50, 250 mg kg^{-1} diet, respectively (5).

Teratogenicity and reproductive effects
Reduced foetal viability but no maternal toxicity occurred in rabbits fed 15 and 50 mg kg^{-1} day^{-1} on days 7-19 of pregnancy (6).
No foetal or maternal toxicity reported in rats fed up to 250 mg kg^{-1} day^{-1} on days 6-19 of pregnancy (6).
No treatment-related gross necropsy findings reported in a two-generation rat reproduction study. The parental generation was fed up to 30 mg kg^{-1} day^{-1} for 100 days prior to mating and the F_1 generation similarly for 120 days (5).
Embryotoxicity and a low incidence of external tail malformations, skeletal abnormalities and hydrocephalus reported in rats fed 67.5-270 mg kg^{-1} on days 1-7 or 8-16 of pregnancy (5).
Hydrocephalus also reported in mice given 270 mg kg^{-1} day^{-1} on days 1-18 of pregnancy or 675 mg kg^{-1} on days 9, 10 or 11 (route unspecified) (5).

Metabolism and toxicokinetics
Excreted in urine within 72 hr after oral administration to mammals. Metabolised in liver and kidney, mainly via glutathione conjugation followed by conversion via the mercapturic acid pathway (13).
68% of a single oral 10 mg dose of ^{14}C-propachlor was recovered in rats urine after 56 hr (13,14).
56 hr after oral administration of 10 mg of ^{14}C-propachlor, radioactivity was not detected in tissue samples (6).
11 urinary metabolites were identified in rats; primary metabolic end products are mercapturic acid and glucuronic acid conjugates (20-25%), methyl sulfones (30-35%), phenols and alcohols (6,14).
Excreted as metabolites in urine (68%) and faeces (19%) of rats within 56 hr of an oral dose of 10 mg (6).

Irritancy
Erythematopapulous contact eczema reported after occupational exposure. 1 g ml^{-1} applied to abraded and intact skin for 24 hr produced erythema and slight oedema after 72 hr in rabbits (6).

0.1 cm^{-3} instilled into rabbit eyes for 30 sec caused corneal opacity, ulceration, slight iris irritation, conjunctival redness, chemosis, discharge and necrosis (6).
Severe eye and skin irritant; a 0.01% aqueous suspension caused strong conjunctivitis in rat eyes. Finely ground propachlor caused severe conjunctival irritation, ulceration and opacity in rabbit eyes. In addition, chemosis and necrosis were reported in the Draize test (5).

Sensitisation
May cause skin sensitisation in susceptible individuals (8).
Guinea pig maximisation test negative (15).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1538 with and without metabolic activation negative (16).
Saccharomyces cerevisiae D4 with and without metabolic activation negative (16).
Did not induce chromosomal aberrations and sister chromatid exchanges in Chinese hamster ovary cells (metabolic activation unspecified) (6).
Did not induce unscheduled DNA synthesis in primary rat hepatocytes (6).
Induced sister chromatid exchanges in Chinese hamster ovary cells with metabolic activation (5).
In vivo rat and mouse cytogenetic assay negative (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (17).
WHO Toxicity Class III (18).
EPA Toxicity Class III (formulation) (1).
Ten-day health advisory in drinking water for children is 0.5 $mg\ l^{-1}$; lifetime health advisory 0.092 $mg\ l^{-1}$ (6).

Other comments

Non-toxic to bees (8).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (19).
Aquatic ecotoxicological model for preliminary hazard assessment described (20).
Metabolic pathways reviewed (21).

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P291 propamocarb hydrochloride

$$(CH_3)_2N(CH_2)_3NHCO_2(CH_2)_2CH_3 \cdot HCl$$

$C_9H_{21}ClN_2O_2$ **Mol. Wt.** 224.73 **CAS Registry No.** 25606-41-1

Synonyms [3-(dimethylamino)propyl]carbamic acid, propyl ester, hydrochloride

EINECS No. 247-125-9 **RTECS No.** EZ 8860000

Uses Systemic fungicide used to control *Pythium* spp. and *Phytophthora* spp. on turf, outdoor woody and herbaceous ornamentals.

Physical properties

M. Pt. 45-55°C **Partition coefficient** log P_{ow} –2.745 (1) **Volatility** v.p. 6×10^{-3} mmHg at 25°C
Solubility Water: 1005 g l^{-1} at 20°C. Organic solvents: dichloromethane, ethyl acetate, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) carp, bluegill sunfish, trout 235-616 mg l^{-1} (1).

Invertebrate toxicity
LD_{50} >0.1 mg bee^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral pheasant, mallard duck 3050 and >6000 mg kg^{-1}, respectively (1).
LD_{50} oral mouse, rat 1600, 8600 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation rat >0.0057 mg l^{-1} (1).
LD_{50} dermal rat, rabbit >3900 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 763 mg kg^{-1} (1).

Carcinogenicity and chronic effects
No-effect level in 2-yr feeding trials in rats and mice 40, 50 mg kg^{-1} day^{-1}, respectively (1).
Beagle dogs (2 yr) LOEL 1000 ppm (33.3 mg kg^{-1} day^{-1}) in feed (2).

Irritancy
Practically non-irritating to eyes and skin (2).

Sensitisation
Not a dermal sensitiser (2).

Legislation

EC maximum residue limit in salads 5 ppm, cucumbers 2 ppm, tomatoes and strawberries 0.5 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 (2).
WHO Toxicity Class Table 5 (4).
EPA Toxicity Class IV (formulation) (5).
ADI (JMPR) 0.1 mg kg^{-1} body weight (5).

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P292 propane

$$CH_3CH_2CH_3$$

C_3H_8 **Mol. Wt.** 44.10 **CAS Registry No.** 74-98-6

Synonyms dimethylmethane; propyl hydride

EINECS No. 200-827-9 **RTECS No.** TX 2275000

Uses As a fuel gas. A refrigerant. Chemical intermediate. Aerosol propellant.
Occurrence Constituent of natural gas and crude petroleum.

Physical properties

M. Pt. –188°C **B. Pt.** –42.1°C **Flash point** –104°C **Specific gravity** 0.58 at –44°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.36 (1) **Volatility** v.p. 6460 mmHg at 20°C ; v.den. 1.6
Solubility Water: 65 ml l^{-1} at 17.8°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 1000 ppm (1800 mg m^{-3})
US-TWA 2500 ppm

UN No. 1978 **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
Utilised by *Microbacterium vaccae* and readily degraded by soil bacteria. *Mycobacterium phlei* is capable of growing on propane as the only carbon source (2).

Mammalian & avian toxicity

Acute data

Guinea-pigs were exposed to 24,000-29,000 ppm and 47,000-55,000 ppm for 5, 30, 60 and 120 min. At the lower concentration irregular breathing was observed and at higher concentration tremors were seen in the first 5 min of exposure. Stupor was observed in animals exposed for longer periods of time. All animals recovered and no pathological signs of organ toxicity were seen at necropsy. A narcotic effect was not seen until exposure levels were ~50,000 ppm (1).

Sub-acute and sub-chronic data

Monkeys exposed to 750 ppm for 90 days showed no signs of toxicity or any abnormalities (3).
Humans exposed to ≤1000 ppm 8 hr day^{-1} for 2 wk reported no adverse effects (4).

Metabolism and toxicokinetics

Dermal absorption is considered to be very low (1).

Irritancy

Moderately irritating to skin of rabbits but not to skin of mice (3).
Did not cause irritation when applied to human skin as an aerosol propellant in deodorant 2 × day^{-1} for 12 wk (5).

Genotoxicity

Salmonella typhimurium with and without metabolic activation negative (strains unspecified) (6).

Other effects

Other adverse effects (human)

Slight dizziness occurred after exposure to 100,000 ppm for a few min (6).
Application of liquified propane to skin may cause frostbite (1).

Any other adverse effects

In animals sensitises the myocardium to epinephrine-induced cardiac arrhythmias (1).

Other comments

Toxicity has been reviewed (3).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).
Propane is considered much less toxic than its next higher homologue, butane (1).
Odour threshold 20,000 ppm (1).
Autoignition temperature 450°C.

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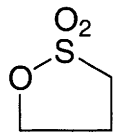
P293 1,3-propane sultone



$C_3H_6O_3S$ **Mol. Wt.** 122.14 **CAS Registry No.** 1120-71-4

Synonyms γ-propane sultone; 1,2-oxathiolane 2,2-dioxide; 3-hydroxy-1-propanesulfonic acid sultone

EINECS No. 214-317-9 **RTECS No.** RP 5425000

Uses Chemical intermediate.

Physical properties

M. Pt. 31-33°C **B. Pt.** 112°C **Flash point** >110°C **Specific gravity** 1.393 at 40°C with respect to water at 4°C
Solubility Water: 100 g l^{-1}. Organic solvents: esters, aromatic hydrocarbons, ketones

Occupational exposure

UN No. 2810
Supply classification toxic
Risk phrases May cause cancer – Harmful in contact with skin and if swallowed (R45, R21/22)
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)

Mammalian & avian toxicity

Acute data
LD_{50} subcutaneous rat 135 mg kg^{-1} (1).
LD_{Lo} skin mouse 1000 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 467 mg 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).
Gavage rat 30 mg kg^{-1} wk^{-1} as a 3% aqueous solution 4/10 survivors developed malignant tumours between days 248 and 377. The tumours were 1 glial-mesodermal mixed tumour and 1 adventitial cell sarcoma of the brain, 1 nephroblastoma and 1 subcutaneous spindle cell sarcoma (5).
Gavage rat 56 mg kg^{-1} 2 × wk^{-1} for 32 wk and 28 mg kg^{-1} 2 × wk^{-1} for 60 wk as an aqueous solution produced an incidence of gliomas of 29/52 and 27/52, respectively, in rats killed at 60 wk. The incidence of gliomas was similar in both ♂ and ♀ rats and, in addition, several rats had leukaemia, ear duct tumours and adenocarcinomas of the small intestine. One pituitary adenoma was found in 12 control rats killed at 61 wk; however, 1 ♀ control died at 33 wk with a cerebral glioma (5).
Intravenous rat 20 mg kg^{-1} wk^{-1} (total dose 570 mg kg^{-1}) 3/8 rats survived 381-492 days and 1 nephroblastoma, 1 carcinoma of the ileocaecal region and 1 mixed glial-mesodermal tumour of the brain together with a mammary carcinoma were observed (5).
Subcutaneous injection in mice and rats produced tumours at the injection site (5).
Intravenous rat (day 15 gestation) 20 mg kg^{-1} produced malignant neurogenic tumours in 3/25 offspring; 60 mg kg^{-1} produced malignant tumours in 4/14 offspring including 2 neurogenic tumours, 1 tumour of the pancreas and 1 tumour of the ovary (5).

Irritancy
Dermal rabbit 500 mg caused mild irritation (duration unspecified) (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102, TA1535, TA1537 with and without metabolic activation positive (7).
A CASE study reported 1,3-propane sultone to be mutagenic (8).
Escherichia coli Q13 with metabolic activation DNA damage positive (9).
Escherichia coli PQ37 SOS chromotest without metabolic activation positive (10).
In vitro Chinese hamster fibroblasts chromosomal aberrations positive (metabolic activation unspecified) (11).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).
The uses of 1,3-propane sultone have been reviewed (13).

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P294 1-propanethiol

$$CH_3CH_2CH_2SH$$

C_3H_8S **Mol. Wt.** 76.16 **CAS Registry No.** 107-03-9

Synonyms propyl mercaptan; propyl thiol

EINECS No. 203-455-5 **RTECS No.** TZ 7300000

Uses In synthesis. An odourant of odourless toxic gases.
Occurrence Identified in volatile products of freshly crushed onion and related plant bulbs (1).

Physical properties

M. Pt. –113°C **B. Pt.** 67-68°C **Flash point** <18°C **Specific gravity** 0.836 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.81 **Volatility** v.p. 40 mmHg at –3.2°C

Occupational exposure

UN No. 2402 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1790 mg kg^{-1} (2).

LC_{50} (4 hr) inhalation rat, mouse 7300, 4010 ppm, respectively (2).

LD_{50} intraperitoneal rat 515 mg kg^{-1} (2).

Metabolism and toxicokinetics

Does not appear to enter the mammalian metabolism, but may be directly oxidised and excreted as propane sulfate. Binds to microsomal cytochrome P_{450}, inhibits carbonic anhydrase and potentiates the action of bradykinin on rat blood pressure (1).

Irritancy

83 mg instilled into the eye of a rabbit caused severe irritation (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3,4).

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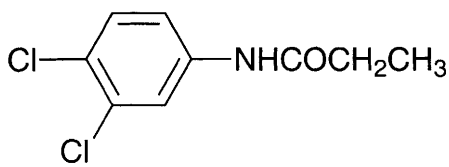
P295 propanil



$C_9H_9Cl_2NO$ **Mol. Wt.** 218.08 **CAS Registry No.** 709-98-8

Synonyms *N*-(3,4-dichlorophenyl)propanamide; 3,4'-dichloroanilinopropionaldehyde; dichloroanilinopropionaldehyde; propamide; 3',4'-dichloropropionanilide; 3,4-DCPA; Anilid; Elam; Propanex; Supernox

EINECS No. 211-914-6 **RTECS No.** UE 4900000

Uses Herbicide. Nematicide.

Physical properties

M. Pt. 92-93°C **Specific gravity** 1.25 at 25°C **Partition coefficient** log P_{ow} 3.3 at 20°C (1)

Volatility v.p. 9×10^{-5} mmHg at 60 °C

Solubility Water: 130 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, cyclohexane, ethanol, isophorone, methyl ethyl ketone, 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 dust (S2, S22)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) mosquito fish, carp, goldfish, Japanese killifish 11-14 mg l^{-1} (1,2).
LC_{50} (96 hr) channel catfish 4 mg l^{-1} (3).
LC_{50} (96 hr) guppy ~20 mg l^{-1} (4).

Invertebrate toxicity
LC_{50} (96 hr) *Daphnia magna* ~1.5 mg l^{-1} (4).
Scenedesmus quadricauda photosynthetic rate was reduced by 27% by 0.1 mg l^{-1} (5).
LC_{50} (96 hr) *Gammarus fasciatus* 16 mg l^{-1} (6).

Environmental fate

Degradation studies
Microbial degradation product in soil was identified as 3,4-dichloroaniline. Propanil was completely degraded in 155 hr (7).
Aspergillus nidulans and strains of *Pseudomonas* and *Alcaligenes* were found to degrade 3,4-dichloropropionanilide in soil (8,9).
Duration of activity in warm moist conditions in soil ~3 day (1).

Abiotic removal
Powdered activated carbon dose to reduce 5 mg l^{-1} to 0.1 mg l^{-1} was 136 mg l^{-1} carbon, and to reduce 1 mg l^{-1} to 0.1 mg l^{-1} was 25 mg l^{-1} carbon (10).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, dog 1300-4000 mg kg^{-1} (1,11,12).
LC_{50} (duration unspecified) inhalation rat >1250 mg m^{-3} (13).
LD_{50} dermal rabbit 4830-7080 mg kg^{-1} (1,14).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 400 mg kg^{-1} diet (1).

Metabolism and toxicokinetics
The major metabolic pathway in rat liver microsomes *in vitro* was acylamidase-catalysed hydrolysis to 3,4-dichloroaniline. The reaction did not require NADPH (15).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA104 with and without metabolic activation negative (16).
Escherichia coli WP2 *uvrA* with and without metabolic activation negative (16).
Bacillus subtilis DNA damage, without metabolic activation, positive (17).
In vitro Chinese hamster ovary cells, hypoxanthine guanine phosphoribosyl transferase assay negative (16).
In vitro primary rat hepatocytes, DNA repair assay negative (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Maximum admissible concentration 0.1 μg l^{-1} (18).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (19).

Log P_{ow} exceeds the European Communities recommended limit of 3.0 (20).
WHO guideline value for drinking water 20 μg l^{-1} (21).
WHO Toxicity Class III (22).
EPA Toxicity Class III (Propanox), II (Supernox) (13).

Other comments

Rice is reported to be resistant to 3,4-dichloropropionanilide because acylamidase activity detoxifies the herbicide (8).
Metabolic pathways reviewed (23).

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P296 1-propanol

$$CH_3CH_2CH_2OH$$

C_3H_8O **Mol. Wt.** 60.10 **CAS Registry No.** 71-23-8

Synonyms propyl alcohol; ethylcarbinol; 1-hydroxypropane; propylic alcohol; *n*-propanol; propan-1-ol

EINECS No. 200-746-9 **RTECS No.** UH 8225000

Uses Solvent for resins and cellulose esters. Chemical intermediate used in drugs, cosmetics, polishing compounds and brake fluid.

Occurrence In fusel oils. Metabolic product of microorganisms. Flavour volatile in foods.

Physical properties

M. Pt. –127°C **B. Pt.** 97.2°C **Flash point** 22°C **Specific gravity** 0.8053 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.25 **Volatility** v.p. 14.5 mmHg at 20°C ; v.den. 2.07
Solubility Water: miscible with water. Organic solvents: miscible with ethanol and diethyl ether

Occupational exposure

FR-VME 200 ppm (500 mg m^{-3})
SE-LEVL 150 ppm (350 mg m^{-3}) **SE-STEL** 250 ppm (600 mg m^{-3})
UK-LTEL 200 ppm (500 mg m^{-3}) **UK-STEL** 250 ppm (625 mg m^{-3})
US-TWA 200 ppm (492 mg m^{-3}) **US-STEL** 250 ppm (614 mg m^{-3})

UN No. 1274 **HAZCHEM Code** 2[redacted]E (flash point <23°C, initial boiling point >35°C) **HAZCHEM Code** 2[redacted] (flash point ≥23°C, ≤61°C, initial boiling point >35°C) **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} (48 hr) rainbow trout 3200 mg l^{-1} (1).
LC_{50} (48 hr) fathead minnow 5000 mg l^{-1} (1).
LC_{50} (48 hr) paddy fish 5900 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia pulex, Daphnia cucullata, Daphnia magna* 3025-7080 mg l^{-1} (2).
EC_{50} (30 min) *Photobacterium phosphoreum* 9308 ppm Microtox test (3).
NOEC (96 hr) *Selenastrum capricornutum* 2000 mg l^{-1} (1).
Cell multiplication inhibition test *Pseudomonas putida, Scenedesmus quadricauda, Entosiphon sulcatum* 2700, 3100, 38 mg l^{-1}, respectively (4).

Toxicity to other species
LC_{50} (48 hr) Mexican axolotl, South African clawed toad 4000 mg l^{-1} (5).

Bioaccumulation
As the compound is biodegradable and has a bioconcentration factor of 0.7, no bioaccumulation is expected (6).

Environmental fate

Nitrification inhibition
50% inhibition of NH_3 oxidation-pure culture *Nitrosomonas europaea* at 20 mg l^{-1} (7).

Degradation studies
COD is 91% of ThOD (2.4 g O_2 g^{-1} of 1-propanol) (6).
Activated sludge with compound as sole carbon source COD 98.8%; 71 mg COD g dry inoculum^{-1} hr^{-1} (8).
Degradation by activated sludge 13.9% of ThOD after 6 hr, 26.8% of ThOD after 12 hr and 36.9% of ThOD after 24 hr (9).

Abiotic removal
In the atmosphere the compound is degraded by hydroxyl radicals. Photodegradation is not expected, nor is hydrolysis or light-induced degradation in water (6).
Adsorption capacity on activated carbon 38 mg g^{-1} carbon; influent 1000 mg l^{-1}, effluent 811 mg l^{-1} 18.9% reduction (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1870 mg kg^{-1}; LC_{Lo} 4000 ppm (11).
LD_{50} oral mouse 6800 mg kg^{-1} (12).
LC_{50} inhalation mouse 48 g m^{-3} (duration unspecified) (13).
LD_{50} intravenous rat 590 mg kg^{-1} (14).
Inhalation mouse (2 hr) 50 mg l^{-1} caused deep narcosis (6).
Oral rat 150-3000 mg kg^{-1}. The animals that died showed hyperaemia, vacuolation and dilated sinusoids in the liver, and hyperaemia, tubular cloudy swelling and tubular necrosis in the kidneys (6).
9/9 rats exposed to 160 mg died within 165 min with 6 dying immediately from respiratory arrest (6).

Teratogenicity and reproductive effects

Inhalation ♂ and pregnant ♀ rats (6 wk) 3500 or 7000 ppm 7 hr day^{-1}. The higher concentration was minimally toxic to maternal rats and produced a low incidence of teratogenicity; the lower concentration was not toxic and produced no teratogenicity. Exposure to high concentrations affected fertility in ♂ rats with only 2/17 producing litters but no consistent effects were seen in the behavioural or neurochemical tests measured (15).
Inhalation rat (1-19 day gestation) 3500, 7000 and 10,000 ppm. The highest concentration produced only minimal maternal toxicity. Following exposure to 7000 and 10,000 ppm foetal weight reduced significantly and more litters had malformations. With 10,000 ppm there was also an increase in resorptions (16).

Metabolism and toxicokinetics

Rapidly absorbed and distributed throughout the body following ingestion. Metabolised to propionic acid by alcohol dehydrogenase via the aldehyde. In rat, $t_{1/2}$ after an oral dose of 1000 mg kg^{-1} was 45 min. In both animals and humans, eliminated in expired air or urine (6).

Irritancy

Dermal rabbit 500 mg caused mild irritation (duration unspecified) (17).
4 mg instilled into the eye of a rabbit caused severe irritation (duration unspecified) (18).
20 mg instilled into the eye of a rabbit (24 hr) caused moderate irritation (19).

Sensitisation

In an ear-swelling test on CF1 mice no sensitisation was observed (6).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (20).
Escherichia coli PQ37 with and without metabolic activation negative (21).
In vitro Chinese hamster ovary cells sister chromatid exchanges negative (6).
In vitro V79 Chinese hamster lung fibroblasts sister chromatid exchanges with and without metabolic activation negative (6).
In vitro V79 Chinese hamster lung fibroblasts no increase in the number of micronuclei (metabolic activation unspecified) (6).

Other effects

Other adverse effects (human)

Filter paper moistened with aqueous 75% 1-propanol was placed on the arms of volunteers; 9/12 people showed erythema for at least 1 hr following exposure. The reaction was blocked following pretreatment with 40% 4-methylpyrazole (an inhibitor of alcohol dehydrogenase activity) in hydrophilic ointment before exposure (6).
Repeated skin contact may lead to dermatitis. Vapours are irritating to the mucous membranes of the upper respiratory tract and to eyes. Severe intoxication by inhalation, swallowing or skin absorption may result in central nervous system depression (headache, nausea, vomiting and dizziness), hypotension, anaemia and respiratory depression (22).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (24).
Autoignition temperature 370°C.

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P297 2-propanol

$$CH_3CH(OH)CH_3$$

C_3H_8O **Mol. Wt.** 60.10 **CAS Registry No.** 67-63-0

Synonyms isopropanol; isopropyl alcohol; *sec*-propyl alcohol; Avantin; Propol; IPA; Alcosolve 2

EINECS No. 200-661-7 **RTECS No.** NT 8050000

Uses Solvents. Cosmetics and pharmaceutical aid (1).
Acetone manufacture (2).
Occurrence Plant volatile, animal waste and emissions from volcanoes and microbes (3).

Physical properties

M. Pt. −88.5 to −89.5°C **B. Pt.** 82.5°C **Flash point** 11°C (closed cup) **Specific gravity** 0.7854 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.05 (4) **Volatility** v.p. 33 mmHg at 20°C ; v.den. 2.07
Solubility Water: freely soluble. Organic solvents: miscible with chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 200 ppm (500 mg m^{-3})
FR-VLE 400 ppm (980 mg m^{-3})
JP-OEL ceiling limit 400 ppm (980 mg m^{-3})
SE-LEVL 150 ppm (350 mg m^{-3}) **SE-STEL** 250 ppm (600 mg m^{-3})
UK-LTEL 400 ppm (999 mg m^{-3}) **UK-STEL** 500 ppm (1250 mg m^{-3})
US-TWA 400 ppm (983 mg m^{-3}) **US-STEL** 500 ppm (1230 mg m^{-3})

UN No. 1219 **HAZCHEM Code** 2[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 tightly closed – Keep away from sources of ignition – No smoking (S2, S7, S16)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 10,400 mg l^{-1} (5).
LC_{50} (7 day) guppy 7060 ppm (5).

Invertebrate toxicity
LC_{50} (5 min) *Photobacterium phosphoreum* 35,390 ppm Microtox test (6).
Semi-chronic LOEC *Microcystis aeruginosa* 1000 mg l^{-1}.
Cell multiplication inhibition test, toxicity threshold, *Pseudomonas putida* 1050 mg l^{-1}, *Microcystis aeruginosa* 1000 mg l^{-1}, *Entosiphon sulcatum* 4930 mg l^{-1} (7,8).

Environmental fate

Degradation studies
Degradation with sewage at 20°C for 5 days resulted in 58% ThOD (9).
Filtered sewage seed resulted in 49% ThOD (10).
It was 99% degraded with acclimated activated sludge at 20°C (52 mg COD g-hr rate) (11).
BOD_5 at 1000 ppm, warburg/sewage (12).
ThOD in fresh dilution water 28% and in salt dilution water 13% (13).

Abiotic removal
Reacts with hydroxyl ions in the atmosphere. The estimated $t_{1/2}$ ranges from 33 hr to 3.5 days, depending on the hydroxyl ion concentration (3,14).

Mammalian & avian toxicity

Acute data
LD_{50} oral dog 4797 mg kg^{-1} (15).
LD_{50} oral mouse 3600 mg kg^{-1} (16).
LD_{50} oral rat 5045 mg kg^{-1} (16).
LD_{50} intraperitoneal rat 2735 mg kg^{-1} (17).
LD_{50} intraperitoneal mouse 4477 mg kg^{-1} (17).
LD_{Lo} oral man 250 ml (18).

Sub-acute and sub-chronic data
Inhalation ♂ and ♀ rat (6 hr) 0, 500, 1500, 5000 or 10,000 ppm. Transient sedation of the central nervous system was observed at 5000 and 10,000 ppm in both sexes. A slight decrease in motor activity was recorded for ♂ rats at 1500 ppm. The no-observed-effect level was 500 ppm (19).
Oral humans (6 wk) daily dose of 2.6-6.4 mg kg^{-1}, no adverse effects (20).
Combined exposure to organic solvents including isopropyl alcohol caused liver injury and hospitalisation in 3 workers within 2-4 months of starting work in a chemical plant (21).

Carcinogenicity and chronic effects

Insufficient evidence for carcinogenicity to humans or animals, IARC classification group 3 (22).

Inhalation C3H, ABC or C57BL mice (5-8 month) 7700 mg m^{-3}. Animals were killed at 8-12 months of age. The incidence of lung tumours was not increased, compared with that in controls (23).

Teratogenicity and reproductive effects

Inhalation rats (1-19 day gestation) 5000 ppm 7 hr day^{-1}, congenital malformations were reported at maternally toxic levels (24).

Increased incidence of malformations, resorptions and reduced foetal weight were reported following inhalation exposure of pregnant rats to maternally toxic levels of 10,000 ppm (duration unspecified) (24).

Metabolism and toxicokinetics

It is readily absorbed from the gastro-intestinal tract but there is little absorption through intact skin. Lungs may absorb the vapour. 15% of an ingested dose is metabolised to acetone. Isopropyl alcohol is metabolised slower than ethanol (18).

Some of the compound conjugates with glucuronic acid. Acetone is excreted in expired air and urine (25).

Irritancy

Dermal (duration unspecified) rabbit 500 mg caused mild irritation, and 10 mg instilled into rabbit eye caused moderate irritation (26,27).

Application to human skin may cause dryness and irritation (28).

Sensitisation

Following two cases of contact dermitis in laboratory workers handling pre-injection swabs (70% isopropyl alcohol, 1% propylene oxide), one was found to be allergic to isopropyl alcohol (29).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with or without metabolic activation negative (30).

In vitro V79 Chinese hamster lung fibroblasts with or without metabolic activation, no increase in sister chromatid exchange frequencies (31).

Other effects

Other adverse effects (human)

Ingestion or inhalation of large quantities of the vapour may cause flushing, headache, dizziness, nausea, mental depression, narcosis and coma (24).

Isopropyl alcohol is more toxic than ethyl alcohol. Due to the presence of the main metabolite, acetone, in the circulation, keto-acidosis and ketonuria commonly occur (18).

Second and third degree chemical skin burns have been reported, caused by topical application in two premature infants of very low birth weight (32).

Cases of acute hepatitis, renal failure and pulmonary oedema in colour printing factory workers were attributed to combined use of carbon tetrachloride and isopropyl alcohol in cleaning operations (33).

Several lethal cases have been described as a result of lethal ingestion of 0.47 l of 70% isopropyl alcohol. Death was preceded by deep coma and shock and resulted from respiratory arrest (34).

Any other adverse effects

High levels of vapour inhalation cause ataxia, prostration and deep narcosis in mice (35).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (36).

Other comments

Leachate from landfills and emissions from petroleum storage, car exhaust and plastics combustion (3,37).

Reviews on ecotoxicology, environmental effects, epidemology, experimental toxicology, exposure, exposure levels, human health effects, physico-chemical properties and workplace experience listed (38).

Volatilisation and leeching into groundwater are important in the removal from soil. It is not expected to absorb onto aquatic sediments (35).
Metabolism has been reviewed (25).
Carcinogenicity has been reviewed (39).
Early reports associated excess incidence of paranasal cancer with isopropyl alcohol manufacture. This has since been attributed to the intermediate 'isopropyl oil' (22,40).

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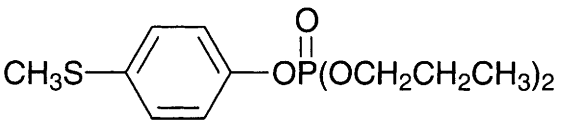
P298 propaphos



$C_{13}H_{21}O_4PS$ **Mol. Wt.** 304.35 **CAS Registry No.** 7292-16-2

Synonyms phosphoric acid, 4-(methylthio)phenyl dipropyl ester; phosphoric acid, *p*-(methylthio)phenyl dipropyl ester; Kayaphos

RTECS No. TC 6586000

Uses Systemic insecticide.

Physical properties

B. Pt. 175-177°C at 0.85 mmHg **Specific gravity** 1.1504 at 20°C **Partition coefficient** log P_{ow} 3.67
Volatility v.p. 0.9×10^{-6} mmHg at 25°C
Solubility Water: 125 mg l^{-1} at 25°C. Organic solvents: soluble in most organic solvents

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 4.8 mg l^{-1} (1).
In vitro cytotoxicity to goldfish GF-scale cells using 24 hr neutral red assay. NR_{50} 44.1 mg l^{-1}, indicating moderate cytotoxicity (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit 70-90 mg kg^{-1} (1).
LD_{50} percutaneous mouse 156 mg kg^{-1} (1).

Sub-acute and sub-chronic data
In 90-day feeding trials, no-effect level was 100 mg kg^{-1} for rats and 5 mg kg^{-1} for mice (1).

Other effects

Other adverse effects (human)
6/18 workers exposed to propaphos and diazinon showed abnormal values in serum cholinesterase activity compared with 3/45 workers occasionally exposed to the pesticides and 0/90 non-exposed workers. There was no decrease in the value of erythrocyte acetylcholinesterase activity in any of the 3 groups (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).
Log P_{ow} exceeds the European Union recommended limit of 3.0 (6).
WHO Toxicity Class Ib (7).

Other comments

Toxic to bees (8).

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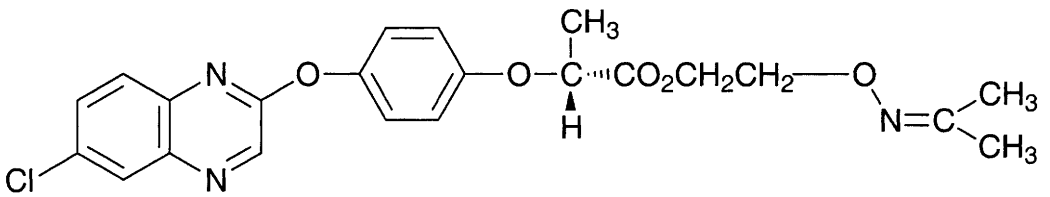
P299 propaquizafop



$C_{22}H_{22}ClN_3O_5$ **Mol. Wt.** 443.89 **CAS Registry No.** 111479-05-1

Synonyms 2-isopropylideneamino-oxyethyl (*R*)-2-[4-(6-chloroquinoxalin-2-yloxy)phenoxy]propionate; (*R*)-2-[[(1-methylethylidene)amino]oxy]ethyl 2-[4-[(6-chloro-2-quinoxalinyl)oxy]phenoxy]propanoate

RTECS No. UA 2458258

Uses Herbicide.

Physical properties

M. Pt. 66.3°C **Specific gravity** 1.30 (20°C) **Partition coefficient** log P_{ow} 4.78 (25°C) (1)
Volatility v.p. 3.3×10^{-12} mmHg (25°C)
Solubility Water: 630 μg l^{-1} (25°C). Organic solvents: acetone, ethanol, hexane, *n*-octanol, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, carp, bluegill sunfish 1.2, 0.19, 0.34 mg l^{-1}, respectively (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* >2 mg l^{-1} (1).
Contact LD_{50} >200 μg bee^{-1} (1).

Bioaccumulation
No tendency for bioaccumulation (1).

Environmental fate

Degradation studies
In soil and water, fast degradation to the free acid (DT_{50} 3 days) and to further metabolites (DT_{90} 2-4 weeks) (1).

Abiotic removal
Stable to UV light (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >5000 mg kg^{-1} (1).
LD_{50} oral mouse 3009 mg kg^{-1} (1).
LD_{50} percutaneous rat >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LD_{50} (5 days) oral mallard duck, bobwhite quail >6593 mg kg^{-1} feed (1).
No-observable-effect level (13 weeks) rats, dogs 6.25, 15 mg kg^{-1} body weight day^{-1}, respectively (1).

Teratogenicity and reproductive effects

No teratogenic or embryotoxic effects in rats or rabbits (1).

Metabolism and toxicokinetics

Rapidly eliminated in the rat via urine and faeces following oral administration (1).

Irritancy

Non-irritant to skin, moderate eye irritation in rabbits (1).

Sensitisation

No allergic sensitisation in guinea pigs (route not specified) (1).

Genotoxicity

Considered non-mutagenic (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 870/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (3).
WHO Toxicity Class III (4).
ADI 0.015 mg kg^{-1} body weight (1).

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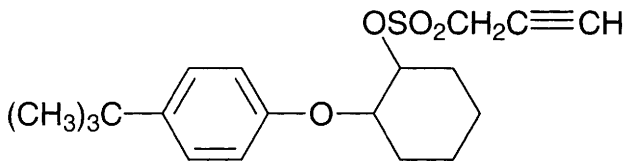
P300 propargite



$C_{19}H_{26}O_4S$ **Mol. Wt.** 350.48 **CAS Registry No.** 2312-35-8

Synonyms sulfurous acid, 2-[4-(1,1-dimethylethyl)phenoxy]cyclohexyl 2-propynyl ester; sulfurous acid, 2-(*p-tert*-butylphenoxy)cyclohexyl 2-propynyl ester; 2-[4-(1,1-dimethylethyl)phenoxy]cyclohexyl 2-propynyl sulfite; Omite; Propargil; Ornamite; Acarion; Artrol; Chemit; Comite; Kelaran

EINECS No. 219-006-1 **RTECS No.** WT 2900000

Uses Non-systemic acaricide.

Physical properties

Flash point 71.4°C (closed cup) **Specific gravity** 1.113 at 20°C **Partition coefficient** log P_{ow} 3.73 (1)
Volatility v.p. 4.5×10^{-8} mmHg (25°C)
Solubility Water: 632 mg l^{-1} (25°C). Organic solvents: miscible with acetone, benzene, ethanol, hexane, heptane, methanol

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 (S2, S24)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 0.1-0.12 mg l^{-1} (1).

Invertebrate toxicity
LD_{50} (48 hr) contact, 15 μg bee^{-1} (2).

Environmental fate

Degradation studies
$t_{1/2}$ in most soils 2-4 wk but in sand/loam soils 18 wk (1).

Mammalian & avian toxicity

Acute data
LC_{50} (8 day) oral Japanese quail, mallard duck 3401, >4640 mg kg^{-1} diet, respectively (1).
LD_{50} oral redwinged blackbird >100 mg kg^{-1} (3).
LD_{50} oral rat 2200 mg kg^{-1} (1).
LD_{50} percutaneous rabbit 10,300 mg kg^{-1} (1).
LC_{50} inhalation rat 2.5 mg l^{-1} (duration unspecified) (1).
LD_{50} intraperitoneal ♂, ♀ rat 172, 260 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials, no-effect level for rats and dogs was 900 mg kg^{-1}, and for mice was 1000 mg kg^{-1} (1).

Metabolism and toxicokinetics

Five urinary metabolites have been identified in a lactating goat: 1-[4-(2,*x*-dihydroxycyclohexyloxy)phenyl]-2,2-dimethylacetic acid, 1-[4-(2-hydroxycyclohexyloxy)phenyl]-2,2-dimethylacetic acid, 1-[4-(1,1-dimethyl-2-hydroxyethyl)phenoxy]-2,*x*-cyclohexanediol, 1-[4-(1,1-dimethyl-2-hydroxyethyl)phenoxy]-2-cyclohexanol and 1-[4-(2,*x*-dihydroxycyclohexyloxy)phenyl]- 2,2-dimethyl sodium sulfate. The metabolites resulted from the hydrolysis of propynyl sulfite and subsequent hydroxylation of the *tert*-butyl portion of the molecule; additional metabolites were formed by further oxidation or sulfation of the *tert*-butyl portion of the molecule and oxidation of the cyclohexyl moiety (4).

Irritancy

Slight skin irritation with rabbits (1).

Genotoxicity

No increase in chromosomal aberrations was seen in workers spraying pesticides including propargite in closed spaces, but there was a slight increase in chromosomal aberrations in workers exposed to the pesticides in open fields (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
Log P_{ow} exceeds the European Union recommended limit of 3.0 (8).
WHO Toxicity Class III (9).
EPA Toxicity Class I (formulation) (2).
EEC maximum residue level apples, grapes 5 ppm (1).

Other comments

Not dangerous to bees and less harmful to predatory mites than other acaricides (1).
The hazardous effects associated with propargite have been reviewed (10).

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P301 propargyl alcohol

$$HC{\equiv}CCH_2OH$$

C_3H_4O **Mol. Wt.** 56.06 **CAS Registry No.** 107-19-7

Synonyms prop-2-yn-1-ol; 2-propyn-1-ol; ethynylcarbinol; 3-propynol; propynyl alcohol; 3-hydroxy-1-propyne

EINECS No. 203-471-2 **RTECS No.** UK 5075000

Uses Intermediate in chemical synthesis.

Physical properties

M. Pt. –48 to –52°C **B. Pt.** 114-115°C **Flash point** 36°C (closed cup) **Specific gravity** 0.9715 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.38 **Volatility** v.p. 11.6 mmHg at 20°C ; v.den. 1.9 **Solubility** Water: miscible. Organic solvents: acetone, benzene, chloroform, 1,2-dichloroethane, diethyl ether, dioxane, ethanol, tetrahydrofuran, pyridine

Occupational exposure

DE-MAK 2 ppm (4.7 mg m^{-3})
FR-VME 1 ppm (2 mg m^{-3})
UK-LTEL 1 ppm (2.3 mg m^{-3}) **UK-STEL** 3 ppm (7.0 mg m^{-3})
US-TWA 1 ppm (2.3 mg m^{-3})
Supply classification toxic
Risk phrases Flammable – Toxic by inhalation, in contact with skin and if swallowed – Causes burns (R10, R23/24/25, 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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S28, S36, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 1.53 mg l^{-1} (1).

Invertebrate toxicity
Cell multiplication inhibition test *Pseudomonas putida* 150 mg l^{-1} (2).
Cell multiplication inhibition test *Scenedesmus quadricauda, Entosiphon sulcatum* 17-18 mg l^{-1} (2).
Cell multiplication inhibition test *Uronema parduczi* 18->800 mg l^{-1} (3).

Environmental fate

Degradation studies
BOD_5 2% ThOD, COD 97% ThOD (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, guinea pig, rat 50-70 mg kg^{-1} (4-6).
LC_{50} (2 hr) inhalation rat 850 ppm (6).
LC_{50} (2 hr) inhalation mouse 2000 mg m^{-3} (7).
LD_{50} dermal rabbit 88 mg kg^{-1} (4,8).

Metabolism and toxicokinetics

Inhibited aldehyde dehydrogenase in rats but did not effect enzymes *in vitro*. Metabolised to propionaldehyde by alcohol dehydrogenase (9).

Other effects

Any other adverse effects

Hepatic microsomes from phenobarbital-induced Wistar rats showed slight binding of propanyl alcohol to cytochrome P_{450} and stimulation of CO-inhibition NADPH oxidation. Substances binding in this way were more effective in degrading the haem moiety of cytochrome P_{450}. The study suggested metabolic activation may be required, possibly of the cytochrome P_{450} mixed function oxidase system (10).

Rats had moderate multifocal medullary haemorrhages in the thymus, interstitial haemorrhage with atrophy of the surrounding acinar cells in the pancreas, mild centrilobular congestion and mild vascular degeneration of the hepatocytes in the liver, and mild congestion of the pulmonary vessels and interalveolar septa in the lungs (4).

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4. Archer, T. E. *J. Environ. Sci. Health, Part B* 1985, **B20**, 593.
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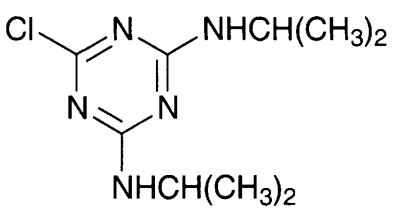
P302 propazine



$C_9H_{16}ClN_5$ **Mol. Wt.** 229.71 **CAS Registry No.** 139-40-2

Synonyms 1,3,5-triazine-2,4-diamine, 6-chloro-*N*,*N*′-bis(1-methylethyl)-; *s*-triazine, 2-chloro-4,6-bis(isopropylamino)-; Milo-Pro; Gesamil; Milogard; Prozinex; Primatol P

EINECS No. 205-359-9 **RTECS No.** XY 5300000

Uses Selective systemic herbicide.

Physical properties

M. Pt. 212-214°C **Specific gravity** 1.162 at 20°C **Volatility** v.p. 3×10^{-8} mmHg at 20°C

Solubility Water: 5 mg l^{-1} at 20°C. Organic solvents: benzene, carbon tetrachloride, diethyl ether, toluene

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)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, goldfish, bluegill sunfish 17.5, >32 and >100 mg l^{-1}, respectively (1).

Invertebrate toxicity
Not toxic to bees (2).

Environmental fate

Degradation studies
In soil microbial degradation occurs with hydrolysis of the chlorine atom to give hydroxypropazine, dealkylation of both substituted amino groups, presumably followed by ring opening and decomposition (1).

Mammalian & avian toxicity

Acute data
LC_{50} (8 day) oral bobwhite quail, mallard duck >10,000 mg kg^{-1} diet (1).
LD_{50} oral rat >7000 mg kg^{-1} (1).
LD_{50} oral guinea pig, mouse 1200, 3180 mg kg^{-1}, respectively (3).
LC_{50} (4 hr) inhalation rabbit >2.04 mg l^{-1} (1).
LD_{50} dermal rat, rabbit >3100 and >10,200 mg kg^{-1}, respectively (1).

Sub-acute and sub-chronic data
In a 130-day feeding trial, ♂ and ♀ rats receiving 250 mg kg^{-1} diet showed no ill-effects (1).

Genotoxicity

Salmonella typhimurium TA97a, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (4).
Escherichia coli PQ37 with and without metabolic activation negative (5).
Aspergillus nidulans mitotic recombination 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} (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 IV (formulation) (2).

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1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
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8. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

P303 propene

$$CH_3CH{=}CH_2$$

C_3H_6 **Mol. Wt.** 42.08 **CAS Registry No.** 115-07-1

Synonyms 1-propene; methylethylene; propylene; 1-propylene; methylethene

EINECS No. 204-062-1 **RTECS No.** UC 6740000

Uses Chemical intermediate. Used in manufacture of lubricating oil additives, PVC resins and hydroquinone and aluminium alkyls.

Occurrence Produced as a by-product of ethylene manufacture and by steam cracking natural gas liquids, naphtha and gas oil (1).

Physical properties

M. Pt. –185°C **B. Pt.** –48°C **Flash point** –108°C **Specific gravity** 0.5193 (liquid) at 20°C with respect to water at 4°C **Volatility** v.p. 7600 mmHg at 19.8°C ; v.den. 1.5

Solubility Organic solvents: acetic acid, diethyl ether, ethanol

Occupational exposure

SE-LEVL 500 ppm (900 mg m^{-3})

UN No. 1077 **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)

Ecotoxicity

Bioaccumulation

Using regression-derived equations the bioconcentration range and K_{oc} range are estimated to be 13-31 and 219-237, respectively (2).

Environmental fate

Degradation studies

Readily degraded by microorganisms and so not expected to bioaccumulate or bioconcentrate in organisms and food chain (3).

Abiotic removal

Water vapour (<11,000 ppm) had no effect on the photooxidation rate of propene by nitrogen oxides or on the yield of nitrogen dioxide and ozone. Carbon monoxide (<200 ppm) increased the rate of photooxidation and product formation (3).

Atmospheric $t_{1/2}$ 7.7 hr (calculated) (3).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

National Toxicology Program tested mice and rats via inhalation. No evidence of carcinogenicity in either species (5).

Inhalation rat (24 months) and mouse (18 months) 200, 1000 and 5000 ppm 7 hr day^{-1}, 5 day wk^{-1}. No evidence of carcinogenicity was seen. A similar study carried out for 104 wk failed to produce brain tumours (6).

Metabolism and toxicokinetics

Propene is metabolised by the cytochrome P_{450}-dependent mixed-function oxidase system to propene oxide. This metabolite is much more toxic than the parent compound and is considered mutagenic; its carcinogenicity, however, is questionable (6).

Irritancy

Not a skin irritant but may cause burns by direct contact with liquified form (species unspecified) (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).
A CASE study predicted propene would not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells (8).
Escherichia coli with and without metabolic activation negative (6).

Other effects

Other adverse effects (human)

Mild intoxication, paresthesias and failure to concentrate were reported after exposure to 6.4% for 2-25 min; these symptoms were greater after 1 min exposure to 12.8%; unconsciousness occurred in 3 min at 24 and 33%. Vomiting and vertigo occurred at 35 and 40% and reddening of eyelids, flushed face, lachrymation, cough and flexing of the legs were observed at 40, 50 and 70%. 50% was anaesthetic in 2 min; recovery was complete (1).

Other comments

Human health effects, experimental toxicology, physico-chemical properties reviewed (5,9,10).
Odour threshold: 17.3 mg m^{-3} (1).
Autoignition temperature 455°C.

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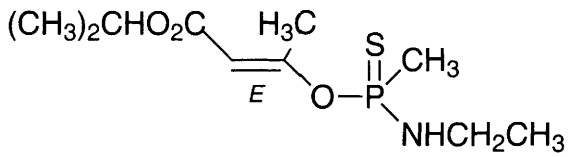
P304 propetamphos



$C_{10}H_{20}NO_4PS$ **Mol. Wt.** 281.31 **CAS Registry No.** 31218-83-4

Synonyms 2-butenoic acid, 3[[(ethylamino)methoxyphosphinothioyl]oxy]-, 1-methylethyl ester; crotonic acid, 3-hydroxy-, isopropyl ester, *O*-ester with *O*-methyl *N*-ethyl phosphoramidothioate, (*E*)-; Blotic; Safrotin

EINECS No. 250-517-2 **RTECS No.** GQ 4750000

Uses Insecticide with contact and stomach action.

Physical properties

B. Pt. 87-89°C at 0.005 mmHg **Specific gravity** 1.1294 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.82 **Volatility** v.p. 14.3×10^{-6} mmHg at 20°C
Solubility Water: 110 mg l^{-1} at 24°C. Organic solvents: soluble in most organic solvents

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) – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) carp 8.8 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck 197 mg kg^{-1} (1).
LD_{50} oral ♂ rat 119 mg kg^{-1} (1).
LD_{50} percutaneous ♂ rat 2300 mg kg^{-1} (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials, no-effect level for rats was 6 mg kg^{-1} (1).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (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).
Log P_{ow} exceeds European Union recommended limit of 3.0 (5).
WHO Toxicity Class Ib (6).
EPA Toxicity Class II (formulation) (7).

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4. *S. I. 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; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
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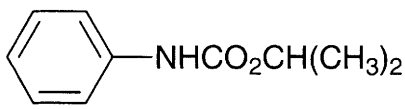
P305 propham



$C_{10}H_{13}NO_2$ **Mol. Wt.** 179.22 **CAS Registry No.** 122-42-9

Synonyms phenylcarbamic acid, 1-methylethyl ester; carbanilic acid, isopropyl ester; isopropyl carbanilate; isopropyl phenylcarbamate; isopropylphenyl urethane; Agermin; Birgin; Collarin; Tixit; Tuberite; Antigermina; Batalex; Bikartol; Hostafume

EINECS No. 204-542-0 **RTECS No.** FD 9100000

Uses Herbicide, plant growth regulator.

Physical properties

M. Pt. 87.0-87.6°C **B. Pt.** sublimes on heating **Specific gravity** 1.09 at 20°C
Partition coefficient log P_{ow} 1.22 (calc.) (1)
Solubility Water: 250 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, cyclohexane, ethanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) bluegill sunfish, guppy 32-35 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (96 hr) *Gammarus lacustris* 10 mg l^{-1} (3).
LC_{50} (48 hr) *Daphnia pulex, Simocephalus serrulatus* 10 mg l^{-1} (4).

Environmental fate

Degradation studies
Ring labelled ^{14}C-propham incubated in silt loam soil in the dark at ~25°C and 60% water holding capacity declined from 8.5 to <5% of applied radioactivity during 60 days (1).
^{14}C-propham incubated with loamy soil for 61 days and sandy loam soil for 63 days at 25°C and 60% of water holding capacity decreased from 0.08 to 0.04 ppm and from 0.06 to 0.03 ppm, respectively (1).
Readily degraded by soil microorganisms, $t_{1/2}$ 15 days at 16°C, 5 days at 29°C, by enzymic hydrolysis of ester bond and degradation of the *N*-phenylcarbamic acid to aniline and carbon dioxide, with further microbial degradation of aniline (2).
2 ppm degraded under aerobic conditions when incubated in dark at 25°C and 60% water holding capacity in silt loam, loam and sandy loam soils, $t_{1/2}$ 2-7 days, 4-7 days, 7-14 days, respectively (1).

Abiotic removal

4 ppm ^{14}C-propham declined to 2.4 ppm in unbuffered distilled water in 14 days of irradiation with a Pyrex filtered light at 25°C. Degradation products included: isopropyl 4-hydroxycarbanilate; isopropyl 4-aminobenzoate; 1-hydroxy-2-propyl carbanilate and polymeric materials (1).

Adsorption and retention

Freundlich K values for adsorption to two silt loams, a silty clay loam, a sandy clay loam, two sandy loams 0.74 and 2.72, 1.77, 0.65 and 0.27 and 1.58, respectively (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >2000 mg kg^{-1} (2).
LD_{50} oral rat, mouse 1000, 2160 mg kg^{-1}, respectively (5,6).
LD_{50} intraperitoneal mouse, rat 200, 600 mg kg^{-1}, respectively (7,8).
LD_{Lo} oral human 714 mg kg^{-1} (7).

Sub-acute and sub-chronic data

In 30-day feeding trials rats receiving 10,000 mg kg^{-1} diet showed no ill-effects (2).
Wistar rats fed 0, 200, 1000 or 5000 ppm for 13 wk showed decreased body weight gain in ♂ at 5000 ppm; decreased erythrocyte cell counts, haemoglobin, haematocrit and mean cell haemoglobin concentration and increased mean cell volume in ♂ at 1000 and 5000 ppm and ♀ at 5000 ppm; increased adrenal weight at 1000, 5000 ppm in ♂, increased liver and spleen weight in ♂ at 5000 ppm, increased relative liver weight at 1000 ppm in ♀ and relative liver and kidney weight at 5000 ppm in ♀; and a dose-dependent increase in haemosiderin content of the spleen in ♀ and ♂ at 1000 and 5000 ppm (9).
Sprague-Dawley rats fed 0, 250, 1000 or 2000 ppm in diet for 91 days showed increased spleen weight and spleen-to-body weight ratio at 2000 ppm in ♂ and 70% inhibition of plasma cholinesterase activity in ♀ at 2000 ppm on day 45 (1).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (10).
Gavage mouse (C57BL/6XC3H/Anf) 215 mg kg body weight^{-1} day^{-1} from day 7 to wk 4 of age then 560 mg kg^{-1} (diet) until wk 78 or subcutaneously injected with 215 mg kg^{-1} body weight on day 28 of life and observed until wk 78, showed no increased tumour frequency compared with controls (11,12).
No tumours were found in rats receiving 10 mg in diet day^{-1} for 18 months or 15 mg as a 5% mixture with kaolin powder in diet for 15 months (13).
No increased tumour incidence was seen in hamsters fed 2 g propham kg diet^{-1} for 33 months, compared with controls (14).
♀ Osborne-Mendel rats injected in the right femoral muscle with 400 mg kg^{-1} body weight month^{-1} for 6 months then observed for a yr. 4/10 rats necropsied had tumours: 1 adenofibroma of the groin, 2 adenomyomas of the uterus and 1 adenocarcinoma of the breast. One mammary adenoma was found in controls (15).

Teratogenicity and reproductive effects

Wistar rats were fed 0, 200, 1000 or 5000 ppm in diet in a two-generation two litter per generation study. At >200 ppm, breakdown of erythrocytes, indicated by increased incidence of siderosis in the spleen and liver, was seen in F_0 and F_{1b} parents. At 5000 ppm, reduced litter size decreased rate of body weight gain and decreased lactation index were seen. No-adverse-effect level was 1000 ppm or 80 mg kg^{-1} body weight day^{-1} (16).
Sprague-Dawley rats were administered 0, 37.6, 376 or 1879 mg kg^{-1} day^{-1} on days 6 to 15 of gestation. The only effects recorded were reduced maternal and foetal body weights and higher resorption rates at 1879 mg kg^{-1} and incomplete ossification of the parietal and frontal bones of the skull at 376 and 1879 mg kg^{-1} (1).

Metabolism and toxicokinetics

Metabolised in mammals by *N*-oxidation to hydroxyisopropyl carbanilate (2).
Oral rat 4-200 mg kg^{-1} body weight [isopropyl-^{14}C]- and [ring-^{14}C]-labelled propham. 80-85% was excreted within 3 days. Herbicide material was distributed throughout body, with highest concentrations in the kidney. 5% of the isopropyl-labelled compound was excreted as carbon dioxide via the lungs (17,18).

Irritancy

3% aqueous solution was slightly irritating to the skin and eyes of albino rabbits (duration unspecified) (1).

Genotoxicity

Salmonella typhimurium (strain unspecified) with and without metabolic activation negative (1).
In vitro human lymphocytes without metabolic activation sister chromatid exchanges negative (19).
In vitro S49 mouse lymphoma cells gene mutation without metabolic activation negative (20).
In vivo mouse micronucleus test negative (1).

Other effects

Any other adverse effects

A single oral dose of 2000 mg kg^{-1} to ♂ and ♀ rats produced loss of righting reflex, ptosis, piloerection, decreased locomotor activity, chronic pulmonary disease and rugae and irregular thickening of the stomach (1).
Sprague-Dawley rats administered 1136 mg kg^{-1} orally showed no adverse effects, 2174 mg kg^{-1} resulted in light anaesthesia, while 3348 mg kg^{-1} resulted in light anaesthesia and death in 1/6 of animals tested (duration unspecified) (1).

Legislation

WHO Toxicity Class Table 5 (21).
EPA toxicity Class IV formulation) (22).
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).

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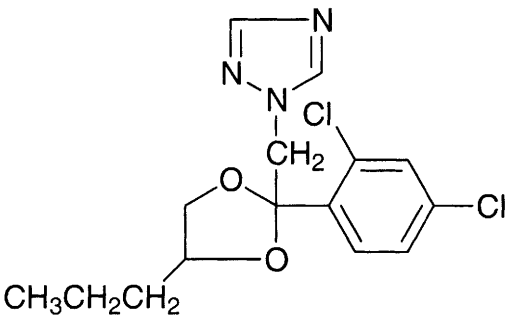
P306 propiconazole



$C_{15}H_{17}Cl_2N_3O_2$ **Mol. Wt.** 342.22 **CAS Registry No.** 60207-90-1

Synonyms 1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]1*H*-1,2,4-triazole; Desmel; proconazole; Alamo; Bumper; Fidis; Mantis; Tilt

EINECS No. 262-104-4 **RTECS No.** XZ 4620000

Uses Agricultural fungicide.

Physical properties

B. Pt. 180°C at 0.1 mmHg **Specific gravity** 1.27 at 20°C **Partition coefficient** log P_{ow} 3.72 at pH 6.6 and 25°C
Volatility v.p. $<3 \times 10^{-6}$ mmHg at 20°C
Solubility Water: 110 mg l^{-1} at 20°C. Organic solvents: *n*-hexane, miscible with ethanol, acetone, isopropanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) brown trout, carp 20, >100 mg l^{-1}, respectively (1).

Invertebrate toxicity
Not toxic to bees; LD_{50} (contact and oral) >100 μg bee^{-1} (2).

Environmental fate

Degradation studies
Degraded in aerobic soils and aquatic systems by hydroxylation of the propyl side-chain and the dioxolane ring followed by formation of the 1,2,4-triazole, $t_{1/2}$ soil 40-70 days; aquatic 25-85 days at 25°C (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1517 mg kg^{-1} (1).
LD_{50} dermal rat >4000 mg kg^{-1} (1).

Metabolism and toxicokinetics
Metabolised in rats by enzymic attack of the propyl side-chain and cleavage of the dioxolane ring with some attack of the 2,4-dichlorophenyl and 1,2,4-triazole rings. Metabolised in mice via cleavage of the dioxolane ring (3).

Irritancy
Skin and eye irritant in rabbits (duration unspecified) (1).

Sensitisation
No sensitisation reported in guinea pigs (1).

Legislation

WHO Toxicity Class II (4).
ADI 0.02 mg kg^{-1} body weight (5).
EEC maximum residue levels bananas 0.1 ppm, wheat 0.2 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).
Log P_{ow} exceeds the European Community recommended limit of 3.0 (5).

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P307 propineb

$C_5H_8N_2S_4Zn$ (theoretical monomer) **Mol. Wt.** 289.79 **CAS Registry No.** 12071-83-9

Synonyms zinc, [[(1-methyl-1,2-ethanediyl)bis[carbamodithioato]](2–)]-; zinc, [propylenebis (dithiocarbamato)]-; Antracol; Cypromate; methyl zineb; mezineb; zinc 1,2-propylene bisdithiocarbamate

EINECS No. 235-134-0 **RTECS No.** ZH 4950000

Uses Agricultural fungicide.

Physical properties

M. Pt. >150°C (decomp.) **Specific gravity** 1.813 at 23°C **Partition coefficient** log P_{ow} –0.260 (calc.) (1)
Volatility v.p. $<1.33 \times 10^{-7}$ mmHg at 20°C
Solubility Water: 10 mg l^{-1} at 20°C. Organic solvents: dichloromethane, hexane, toluene

Occupational exposure

UN No. 2757

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, golden orfe 1.9, 133 mg l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, Japanese quail 100, >5000 mg kg^{-1}, respectively (1,2).
LD_{50} oral rabbit, rat 2500, 8500 mg kg^{-1}, respectively (3,4).
LC_{50} (4 hr) inhalation rat >0.693 mg l^{-1} (1).
LD_{50} dermal rat (7 hr) >1000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Wistar rats fed 0, 100 or 500 ppm in diet for 6 months had enlarged thyroid at 500 ppm (5).

10 ♂ and 10 ♀ Wistar rats exposed to 0, 5, 8, 29 or 44 mg m^{-3} 5 × wk^{-1} for 6 hr for 3 wk. Rats exposed to 44 mg m^{-3} exhibited severely disturbed behaviour, including paralysis of the extremeties and sharp loss of body weight; all were cachetic and all ♀ and 1 ♂ died by the 13th day exposure. Animals that died had small spleens and livers, enlarged adrenals, inflamed lungs, and acute vasculature congestion of the lungs, liver, kidneys and bronchial lymph nodes. No difference was seen between surviving animals and controls (5).

♂ Wistar rats administered 0, 2, 10, 50, 250 ppm in feed for 62 days were sacrificed at 7, 21, or 62 days. Mean body weight at 250 ppm was slightly lower than controls although food intake was unaffected. Total serum thyroxin decreased at 50 and 250 ppm at 21 and 62 days. Thyroid weights decreased at 250 ppm at 21 and 62 days. Thyroid weights decreased at 250 ppm at 7 days but increased at 50 and 250 ppm at 62 days. No treatment-related changes were seen in the thyroid (5).

Dermal rabbit 0, 50, 250 mg kg^{-1} day^{-1} 5 × wk^{-1} for 7 hr for 3 wk showed no skin reactions attributable to the material but 3 rabbits died of severe pneumonitis. A slight increase in liver weight of ♀ rabbits treated with 250 mg kg^{-1} day^{-1} was the only difference from controls (5).

Carcinogenicity and chronic effects

In 2-yr feeding trials, rats receiving 50 mg kg^{-1} diet showed no ill-effects (1).

In a 2-yr feeding study beagle dogs receiving 0, 100, 300, 1000 or 3000 ppm in diet showed no treatment-related effects (5).

NMRI mice were administered 0, 50, 200 or 800 ppm in feed for 104 wk. ♂ mice had an increased incidence in hepatocellular adenomas, possibly treatment-related but there were no other differences observed compared with controls (5).

Wistar rats fed diets containing 0, 10, 100, 1000, 2000 or 8000 ppm for 2 yr had increased mortality rates at >1000 ppm, dose-related weight gain and food intake at >1000 ppm, apparent muscular weakness leading to paralysis at >1000 ppm and increased kidney, liver and thyroid weights at >100 ppm and degeneration of skeletal muscle at >1000 ppm (5).

No carcinogenic effects were seen in Wistar rats administered 0, 5, 10, 25, 50 or 100 ppm in diet for 2 yr (5).

Teratogenicity and reproductive effects

In a three-generation study Long Evans rats received 0, 20, 60, 200, 600 ppm in feed. Slight paralysis in parents and lower gestation rates and decreased number of pups per litter were seen at 200 ppm, with increased mortality, decreased weight gain, severe hind limb paralysis in parents and substantially lower gestation rates, lower birth weights and decreased numbers of pups per litter at 600 ppm (5).

Mated ♀ rats given 0, 3, 10, 30, 100 mg kg^{-1} day^{-1} on days 6-15 of gestation showed slight maternal toxicity at 30 mg kg^{-1} day and paralysis of extremities, ataxia, dyspnoea, tremors, depressed foetal growth and teratogenic effects (dysplasia of extremities) at 100 mg kg^{-1} day^{-1} (5).

Mated ♀ rabbits given 0, 10, 30, 100 mg kg^{-1} day^{-1} by gavage on days 6-18 of gestation showed severe maternal toxicity, including reduced weight gain and food intake, dyspnoea, and ventral-lateral recumbency and signs of abortion at 100 mg kg^{-1}. Weight gain and food intake were also reduced at 30 mg kg^{-1} No embryotoxic or foetotoxic effects were observed at 100 mg kg^{-1} day^{-1} (5).

Metabolism and toxicokinetics

♂ Sprague-Dawley rats orally dosed with 5 or 50 mg ^{14}C-propineb kg^{-1} absorbed 60-70% of radioactivity in 48 hr. 50% of radioactivity was excreted in urine and 40% in faeces with 3% in bile. Maximum thyroid concentrations occurred at 24 hr compared with 3-5 hr for most other organs. $t_{1/2}$ from tissues 5-20 days. Metabolites in urine included propylene diamine, propylene urea and 4-methylimidazoline (5).

Irritancy

No human irritancy reported despite regular skin contact during cleaning (5).

Sensitisation

Guinea pigs challenged with 25% propineb after intradermal induction with 0.1% and topic induction with 25% gave a positive response against no positive response in controls. A second challenge with 2.5% caused positive reactions in 18/20 treated animals compared with 4/10 controls (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 (metabolic activation unspecified) negative (5).
Escherichia coli WP2 (metabolic activation unspecified) negative (5).
In vitro Chinese hamster ovary cells HGPRT forward mutation assay negative (5).
In vitro mouse micronucleus test negative (5).

Legislation

WHO Toxicity Class Table 5 (6).
EPA Toxicity Class IV (formulation) (7).
ADI 0.007 mg kg^{-1} body weight (7).
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).

Other comments

Not toxic to bees (1).

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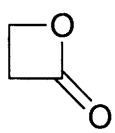
P308 β-propiolactone



$C_3H_4O_2$ **Mol. Wt.** 72.06 **CAS Registry No.** 57-57-8

Synonyms 2-oxetanone; hydracrylic acid, β-lactone; 3-hydroxypropionic acid lactone; 3-propanolide; 1,3-propiolactone; Betaprone

EINECS No. 200-340-1 **RTECS No.** RQ 7350000

Uses Intermediate in organic synthesis. Veterinary viral disinfectant. Intermediate sterilisation of human grafts. Sporicide to sterilise water, milk, nutrient broths and vaccines. To inactivate influenza virus for use as a vaccine.

Physical properties

M. Pt. –33.4°C **B. Pt.** 162°C (decomp.) **Flash point** 70°C **Specific gravity** 1.146 at 20°C with respect to water at 4°C **Volatility** v.p. 3.4 mmHg at 25°C ; v.den. 2.5
Solubility Water: 37% v/v at 25°C. Organic solvents: miscible with acetone, chloroform, diethyl ether, ethanol

Occupational exposure

US-TWA 0.5 ppm (1.5 mg m^{-3})
Supply classification very toxic
Risk phrases May cause cancer – Very toxic by inhalation – Irritating to eyes and skin (R45, R26, R36/38)
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

Bioaccumulation
Bioconcentration is unlikely due to rapid hydrolysis (1).

Environmental fate

Degradation studies
Confirmed to be biodegradable (2).

Abiotic removal
Reacts with photochemically produced hydroxyl radicals in the atmosphere $t_{1/2}$ 45 days (1).
Aqueous hydrolysis to 3-hydroxypropionic acid $t_{1/2}$ 3.5 hr (1).
In saline waters acts with chloride to form 3-chloropropionic acid (1).

Mammalian & avian toxicity

Acute data
TD_{Lo} oral rat 2870 mg kg^{-1} (3).
TC_{Lo} (6 hr) inhalation rat 5 ppm (4).
LD_{50} intraperitoneal mouse 405 mg kg^{-1} (5).

Carcinogenicity and chronic effects
Oral ♀ Sprague-Dawley rat 10 mg wk^{-1} for 487 days, 3/5 rats developed squamous cell carcinomas in the forestomach compared with 0/5 controls (6).
Dermal mouse 0.3 ml of 2.5% solution in acetone for 52 wk produced papillomas in 5/9 mice surviving for 55 wk. Two tumours became malignant squamous-cell carcinomas at 40 wk and 2 were probably malignant (7).
Dermal hamster 0.5 ml of 2.5% solution 2 × wk^{-1} produced papillomas in 4/13, melanomas in 4/13, keratoacanthomas in 4/13, and squamous-cell carcinomas in 2/13 hamsters surviving 32-100 wk (8).
♀ ICR/Ha Swiss mice receiving 0.73 mg subcutaneously wk^{-1} 3/30 developed squamous papillomas at the injection site and 18/30 developed malignant tumours (9 fibrosarcomas, 3 adenocarcinomas and 6 squamous cell carcinomas) at the injection site. No local tumours developed in controls (6).
Subcutaneous rat 2 mg 2 × wk^{-1} for 38 wk produced local sarcomas in 10/12 rats. No tumours were seen in controls (9).

Metabolism and toxicokinetics
Hydrolysed to β-hydroxypropionic acid (species unspecified) (10).
Can react with chloride ion to form 3-chloropropionic acid, especially in blood plasma (11).

Irritancy
Caused irritation, lachrymation and permanent corneal opacitication when undiluted in rabbits (dose and duration unspecified) (12).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation positive; TA1538 with and without metabolic activation negative (13).
Induced sister chromatid exchanges in Chinese hamster Don (lung) cells and CHO (ovary) cells without metabolic activation positive (14).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, workplace experience and epidemiology listed (15).

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P309 propionaldehyde

$$CH_3CH_2CHO$$

C_3H_6O **Mol. Wt.** 58.08 **CAS Registry No.** 123-38-6

Synonyms propanal; methylacetaldehyde; propaldehyde; *n*-propanal; propionic aldehyde; propylaldehyde; propylic aldehyde

EINECS No. 204-623-0 **RTECS No.** UE 0350000

Physical properties

M. Pt. -81°C **B. Pt.** 49°C **Flash point** <-6°C (open cup) **Specific gravity** 0.807 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.59 **Volatility** v.p. 235 mmHg at 20°C ; v.den. 2.0
Solubility Water: 200 g l^{-1} at 20°C. Organic solvents: miscible with ethanol, diethyl ether

Occupational exposure

UN No. 1275 **HAZCHEM Code** 2YE **Conveyance classification** flammable liquid
Supply classification highly flammable, irritant
Risk phrases Highly flammable – Irritating to eyes, respiratory system and skin (R11, R36/37/38)

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 (S2, S9, S16, S29)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) Mississippi silverside, bluegill sunfish 100, 130 mg kg^{-1}, respectively (1).
Rainbow trout exposed to 5000 μg l^{-1} at pH 7.5-8.2 suffered stress (duration unspecified) (2).

Environmental fate

Degradation studies

BOD_5 38% of ThOD; COD 97% of ThOD; $KMnO_4$, acid 7% of ThOD, alkaline 8% of ThOD (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1410 mg kg^{-1} (4).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (4).
LD_{50} dermal rabbit 5040 mg kg^{-1} (4).
LD_{50} subcutaneous mouse, rat 680, 820 mg kg^{-1}, respectively (5).

Teratogenicity and reproductive effects

Rat foetuses were injected intra-amniotically with 10, 100 and 1000 μg propionaldehyde on day 13 of gestation. Examination of embryos on day 20 of gestation showed a dose-dependent increase in resorbed foetuses with significance at 1000 μg $foetus^{-1}$. One foetus was malformed, with a shortened tail (6).

Irritancy

Dermal rabbit 500 mg open (72 hr) caused mild irritation and 41 mg instilled into rabbit eye (72 hr) caused severe irritation (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (8).
Non-mutagenic at 58 μg l^{-1} in V79 cells, toxic at 116 μg l^{-1} (9).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

Reviews on human health effects, experimental toxicology, workplace experience and physico-chemical properties listed (11).

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P310 propionic acid

$$CH_3CH_2CO_2H$$

$C_3H_6O_2$ **Mol. Wt.** 74.08 **CAS Registry No.** 79-09-4

Synonyms propanoic acid; carboxyethane; ethanecarboxylic acid; ethylformic acid; metacetonic acid; pseudoacetic acid; methylacetic acid

EINECS No. 201-176-3 **RTECS No.** UE 5950000

Uses Esterifying agent. Used in the production of cellulose propionate and other propionates and in the manufacturing of fruit flavours and perfume bases.

Physical properties

M. Pt. -21.5°C **B. Pt.** 141°C **Flash point** 51°C **Specific gravity** 0.782 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.33 **Volatility** v.p. 10 mmHg at 37°C ; v.den. 2.56
Solubility Water: miscible with water. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 10 ppm (31 mg m^{-3})
FR-VME 10 ppm (30 mg m^{-3})
SE-LEVL 10 ppm (30 mg m^{-3}) **SE-STEL** 15 ppm (45 mg m^{-3})
UK-LTEL 10 ppm (31 mg m^{-3}) **UK-STEL** 15 ppm (46 mg m^{-3})
US-TWA 10 ppm (30 mg m^{-3})

UN No. 1848 **HAZCHEM Code** 2W **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) – Do not breathe vapour – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S36, S45)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) bluegill sunfish 188 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* 50 mg l^{-1} (1).

Environmental fate

Degradation studies
ThOD 1.513 g O_2 g^{-1} (2).
COD 99% of ThOD; BOD_5 37% of ThOD (3).
Degradation by activated sludge 18.6% of ThOD after 6 hr, 30.8% of ThOD after 12 hr and 40.4% of ThOD after 24 hr (4).

Abiotic removal
Adsorption capacity on activated carbon 65 mg g^{-1} carbon; influent 1000 mg l^{-1}, effluent 674 mg l^{-1} 32.6% reduction (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3500 mg kg^{-1} (6).
LD_{50} intraperitoneal rat 200 mg kg^{-1} (6).
LD_{50} intravenous mouse 625 mg kg^{-1} (7).

Irritancy

Dermal rabbit 495 mg caused severe irritation (duration unspecified) (8).
990 µg instilled into the eye of rabbit caused severe irritation (duration unspecified) (8).
Moderate human skin irritant (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (10).
Escherichia coli WP67 and CM87 DNA repair test positive (11).
Escherichia coli PQ37 SOS Chromotest with and without metabolic activation negative (11).
In vitro Chinese hamster V79 cells with and without metabolic activation sister chromatid exchange negative (11).
In vivo did not increase the number of micronucleated polychromatic erythrocytes in Chinese hamsters (11).

Other effects

Other adverse effects (human)

Mild coughs, asthmatic responses, mild eye redness and mild to moderate skin burns have been reported following occupational exposure (12).

Other comments

Human health effects, experimental toxicology, physico-chemical properties reviewed (13,14).
Autoignition temperature 485°C.

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P311 propionic anhydride

$$CH_3CH_2C(O)O(O)CCH_2CH_3$$

$C_6H_{10}O_3$ **Mol. Wt.** 130.14 **CAS Registry No.** 123-62-6

Synonyms propanoic acid, anhydride; methylacetic anhydride; propanoic anhydride; propionic acid anhydride; propionyl oxide

EINECS No. 204-638-2 **RTECS No.** UF 9100000

Uses Esterification agent for perfume oils, fats, oils, cellulose. Dehydration agent for some sulfonations and nitration reactions. Production of alkyl resins, dyes and drugs.

Physical properties

M. Pt. –45°C **B. Pt.** 167°C **Specific gravity** 1.0125 at 20°C with respect to water at 4°C
Solubility Water: (decomp.). Organic solvents: chloroform, diethyl ether, ethanol, methanol

Occupational exposure

UN No. 2496 **HAZCHEM Code** 3X **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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2360 mg kg^{-1} (1).
LD_{50} dermal rabbit 10 g kg^{-1} (1).

Irritancy
Dermal rabbit 10 mg (24 hr) caused mild irritation and 750 μg instilled into rabbit eye (72 hr) caused severe irritation (1).

Other comments

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

References

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P312 propionitrile

CH_3CH_2CN

C_3H_5N **Mol. Wt.** 55.08 **CAS Registry No.** 107-12-0

Synonyms cyanoethane; ether cyanatus; ethyl cyanide; hydrocyanic ether; propanenitrile; *n*-propanenitrile; propionic nitrile

EINECS No. 203-464-4 **RTECS No.** UF 9625000

Physical properties

M. Pt. –91.8°C **B. Pt.** 97.2°C **Flash point** 2.2°C **Specific gravity** 0.782 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.16 **Volatility** v.p. 44.6 mmHg at 25°C
Solubility Water: 11.9 g 100 g^{-1} at 40°C. Organic solvents: miscible with diethyl ether, dimethylformamide, ethanol

Occupational exposure

UN No. 2404 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid
Conveyance classification toxic

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 5260 ppm Microtox test (1).

Toxicity to other species
LD_{Lo} subcutaneous frog 8000 mg kg^{-1} (2).

Bioaccumulation
Calculated bioconcentration factor 0.78 indicates that environmental accumulation is unlikely (3).

Environmental fate

Degradation studies
Degraded by activated sludge by hydrolysis to the amide followed by hydrolysis of the amino group resulting in propionic acid and the nitrogen released as ammonia nitrogen (4).

Abiotic removal
Degraded by atmosphere hydroxyl radicals $t_{1/2}$ 83 days (5).
Volatilises in water $t_{1/2}$ 13.3 hr in model river (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 35, 39 mg kg^{-1}, respectively (6,7).
LC_{50} (1 hr) inhalation mouse 163 ppm (8).
LD_{50} dermal rabbit 210 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 28 mg kg^{-1} (9).

Teratogenicity and reproductive effects
A single intraperitoneal injection 30-83 mg kg^{-1} to pregnant hamsters on day 8 of gestation caused cranioschisis occulta with encephalocoele, cranioschisis aperta with exencephaly and fusions and bifurcations of the ribs (10).

Metabolism and toxicokinetics
Metabolised by rat nasal tissue *in vitro* to release hydrogen cyanide (11).

Irritancy
Dermal rabbit 500 mg (24 hr) caused mild irritation and 100 mg instilled into rabbit eye (24 hr) caused moderate irritation (12).

Genotoxicity

Saccharomyces cerevisiae BR1669 induced high levels of mitotic chromosome gain but no response for hyperploidy and Type II reversion (13).
Drosophila melanogaster induced aneuploidy with equal amounts of chromosome loss and gain (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Cyanides: maximum admissible concentration 50 $\mu g\ l^{-1}$ (15).

Other comments

Detected in drinking water and in shale-oil wastewater.
Reviews on human health effects, experimental toxicology, environmental effects and exposure listed (16).

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P313 propionyl chloride

$$CH_3CH_2C(O)Cl$$

C_3H_5ClO **Mol. Wt.** 92.52 **CAS Registry No.** 79-03-8
Synonyms propanoyl chloride; propionic acid chloride; propionic chloride
EINECS No. 201-170-0 **RTECS No.** UG 6657000

Physical properties

M. Pt. –94°C **B. Pt.** 77-79°C **Flash point** 53.6°C **Specific gravity** 1.065 at 20°C with respect to water at 4°C
Volatility v.den. 3.2
Solubility Water: vigorously decomp. Organic solvents: ethanol

Occupational exposure

UN No. 1815 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive
Supply classification highly flammable, corrosive
Risk phrases Highly flammable – Reacts violently with water – Causes burns (R11, R14, 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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S16, S26, S45)

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (1).

Other comments

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

References

1. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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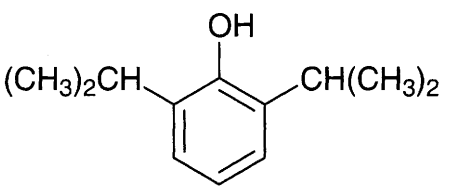
P314 propofol



$C_{12}H_{18}O$ **Mol. Wt.** 178.27 **CAS Registry No.** 2078-54-8
Synonyms 2,6-diisopropylphenol; 2,6-bis(1-methylethyl)phenol; Dipriran; disoprofol; ICI 35868
EINECS No. 218-206-6 **RTECS No.** SL 0810000
Uses Anaesthetic. Catalyst.

Physical properties

M. Pt. 19°C **B. Pt.** 242°C **Flash point** 113°C (closed cup) **Specific gravity** 0.955 at 20°C with respect to water at 4°C

Ecotoxicity

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 14 mg l^{-1} Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 170 mg kg^{-1} (2).

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

Metabolism and toxicokinetics

Following intravenous administration of 9 mg kg^{-1} ^{14}C-propofol to ♀ rats, there was rapid decline in blood concentration ($t_{1/2}$ 4 min) associated with distribution into highly perfused tissues and muscle. A second decline ($t_{1/2}$ 33 min) was associated with metabolism, and a third decline was associated with a slow depletion of the drug from deep tissue compartments ($t_{1/2}$ 6.4 hr). Blood and brain propofol concentrations on waking (at 7 min post-dose) were 4 μg ml^{-1} and 9 μg g^{-1}, respectively (4).

Following intravenous administration of 2-3 mg kg^{-1} to human surgical patients, the elimination $t_{1/2}$ was 55.6 hr (5).

Following intravenous administration of 0.5 mg kg^{-1} to ♂ volunteers, 88% was recovered in the urine and <2% in faeces. The major metabolites were the gluconuric acid conjugate and the gluconuric acid and sulfate conjugate of its hydrosulfated derivative 2,6-diisopropyl-1,4-quinol. <0.3% was excreted as unchanged propofol (6).

Other effects

Other adverse effects (human)

Among ~2 million patients anaesthetised in the UK, 268 adverse reactions were reported. Among those there were 37 reports of seizures (13 of these were known to be epileptics), 16 involuntary movements, 10 opisthotonus, 32 anaphylactic reactions and 13 cardiac arrests (7).

Fatalities have been reported among anaesthetised children (8).

Anaphylactic-like reactions have been reported among patients (9).

Any other adverse effects

In vitro rat liver mitochondria, 18 mg affected the generation and maintenance of the transmembrane electrode potential while leaving unchanged the coupling between the electron flow in the respiratory chain and ATP synthesis (10).

Inhalation pig, did not trigger malignant hyperthermia in an anaesthetic screening assay (dose and duration unspecified) (11).

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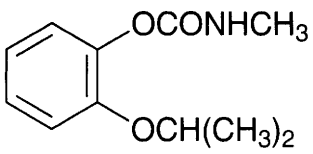
P315 propoxur



$C_{11}H_{15}NO_3$ **Mol. Wt.** 209.25 **CAS Registry No.** 114-26-1

Synonyms 2-(1-methylethoxy)phenol methylcarbamate; methylcarbamic acid, *o*-isopropoxyphenyl ester; 2-isopropoxyphenyl methylcarbamate; Baigon; Baygon; Blattanex; Pilargon; Propogon; Undene

EINECS No. 204-043-8 **RTECS No.** FC 3150000

Uses Domestic insecticide to control flies, fleas, ants etc. Aphid control.

Physical properties

M. Pt. 91.5°C **B. Pt.** Decomp. on distillation. **Specific gravity** 1.12 at 20°C
Partition coefficient log P_{ow} 0.14 (1) **Volatility** v.p. 0.01 mmHg at 120°C
Solubility Water: 2 g l^{-1} at 20°C. Organic solvents: acetone, methanol and many organic solvents. Only slightly soluble in cold hydrocarbons

Occupational exposure

DE-MAK 2 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.5 mg m^{-3}
UK-LTEL 0.5 mg m^{-3} **UK-STEL** 2 mg m^{-3}
US-TWA 0.5 mg m^{-3}
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) – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish, 3.7, 6.6 mg l^{-1}, respectively (2).
LC_{50} (96 hr) red swamp clawfish 1.43 ppm (3).

Invertebrate toxicity
LC_{50} (96 hr) *Gammarus lacustris* 34 μg l^{-1} (4).
LC_{50} (96 hr) *Gammarus fasciatus* 50 μg l^{-1} (5).
LC_{50} (96 hr) stonefly 13 μg l^{-1} (6).
LC_{50} (72 hr) *Culex salinarius, Psorophora columbiae, Anopheles quadrimaculatus* larvae 0.18-0.45 ppm (3).
The inhibitory effects of insecticides on bacterial enzyme activity in soil decreased in the order: dithiophosphoric acid >thiophosphoric acid >phosphoric acid >propoxur (7).
Two 1 hr exposures of propoxur caused significantly fewer symptoms of intoxication than a 2 hr continuous exposure in the midge *Chironomus riparius* if at least 2 to 6 hr in clean water was provided between doses (8).
Highly toxic to bees (9).

Environmental fate

Degradation studies
5 ppm has a half life of >28 days in irradiated and non-irradiated dry sandy loam soil (1).

First step of degradation is hydrolysis of the carbamate and it is dependent on soil type as well as the aromatic moiety structure (10).

Abiotic removal

Half lifes in non-chlorinated and chlorinated water were: at pH 7, 290 and 9.2 days, respectively; and at pH 8, 9.2 and 0.29 days, respectively (11).

Persistence in river water in sealed jar under sunlight and artificial light, initial concentration 10 $\mu g\ l^{-1}$, 50% remained after 1 wk and 5% by 8 wk (12).

Relatively stable in (laboratory) abiotic conditions (13).

Adsorption and retention

^{14}C-propoxur 0.94-98.6 $\mu g\ l^{-1}$ very mobile in sandy loam, silt loam and silty clay: distilled water slurries (1:5 soil solution ratio) (1).

Unaged propoxur very mobile (70-79% of applied was leached from sandy loam and silt-loam columns), aged propoxur (30 day) only slightly mobile with 72-75% remaining on the column (1).

Mean K_{oc} 47 in Japanese soils (14).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 3.83 mg kg^{-1}, starling 13.3-17.0 mg kg^{-1}, coturnix 42.2 mg kg^{-1} (15-18).

LD_{50} oral house finch, house sparrow, yellow-headed blackbird, red-necked pheasant, common grackle, rock dove, mallard duck 4.22-17.8 mg kg^{-1} (15-18).

LD_{50} oral rat ♂ ♀ 83, 86 mg kg^{-1}, respectively (19).

LC_{50} (1 hr) inhalation rat 1440 mg m^{-3} (20).

LD_{50} dermal rat 800 mg kg^{-1} (21).

LD_{50} intravenous, intraperitoneal, intramuscular rat 11-53 mg kg^{-1} (22,23).

Inhalation (5 min) rat 5 ml in spray, no effect on learning processes but produced memory loss (24).

Rats (4 hr) inhalation of spray containing 2% propoxur, 26, 38 mg (spc) l^{-1} (air) (spc = spray can contents) tolerated with no symptoms, 80 mg (spc) l^{-1} air slight cholinergic symptoms on day of exposure, 86 mg (spc) l^{-1} air displayed staggering gait and pilo-erection on day of exposure. All rats had recovered by 1st post-observation day (25).

Sub-acute and sub-chronic data

Oral ♂ rat (9 wk) 0-8000 ppm daily no-observed-effect level 4000 ppm, ♀ rat (9 wk) only 4000 ppm tested and this was toxic (1).

Inhalation (3 wk) rat 5 ml spray daily caused a delay in learning and memory, acetylcholinesterase activity in the brain decreased initially but regained normal levels after 24 hr (24).

Inhalation rats (4 wk, dose not specified) caused decrease in hepatic phosphatase and aminotransferase activities and increase in blood urea levels (26).

Carcinogenicity and chronic effects

Oral rat (2 yr) 0-6000 ppm, major adverse effects were low food consumption and body weight in animals on 6000 ppm dose (1).

Oral dog (2 yr) 0-2000 ppm. At 2000 ppm dogs of both sexes appeared to be weak and sick. All the ♀ dogs and 25% of ♂ dogs died before the study period was completed (1).

Oral rat (2 yr) 0-5000 ppm daily, increased numbers of uncommon bladder tumours (carcinomas and papillomas) at 5000 ppm 34/57 ♂, 33/48 ♀. Similar study oral mice (2 yr) 0-6000 ppm showed no evidence of increased tumour frequency (1).

Teratogenicity and reproductive effects

Gavage rabbit (length of exposure not stated) 0-10 mg kg^{-1} no adverse effects observed in dams or foetuses (1).

Logistic regression and discriminant analysis were used to predict propoxur's developmental toxicity in mice, rats and humans. Designated negative for mice and positive for rats. The developmental toxicity towards humans was predicted to be negative (27).

Metabolism and toxicokinetics

Human ♂ oral 50 or 92.2 mg, the metabolite 2-isopropoxyphenol was detected in urine (28).

A study conducted on human volunteers, under controlled conditions of temperature (30°C) and humidity, indicated that the level of skin moisture influences the absorption of propoxur via the dermal route, ranging from, on average, 13, 33, and 63% of the "potentially absorbed dose" which is excreted in the urine as the primary metabolite 2-isopropoxyphenol at relative humidity levels, an average, of 50, 70, and 90%. (The "potentially absorbed dose" is defined as the difference between the applied dose and the dislodged dose after 4 hr.) (29).

Pathway derived from rat studies. Depropylation to 2-hydroxyphenol-*N*-methyl carbamate followed by hydrolysis of this to isopropoxyphenol. Minor pathways include: ring hydroxylation at the 5 or 6 position, secondary hydroxylation of the 2'-carbon of the isopropoxy group, and *N*-methyl hydroxylation (1).

Oral intravenous rat ♂ isopropoxyphenol detected in tissues 10 min after dosing with maximum levels being reached by 30-60 min (30).

Irritancy

Skin rabbit (72 hr) no irritation on abraded or unabraded skin. 100 mg instilled into rabbit eye caused no irritation (1).

Eyes rabbit, monkey (in household aerosol insecticide spray) maximum pupillary constriction (pinpoint pupil) 10-30 min exposure, complete recovery within 4 hr. Topical application to eyes of rabbits (0.1-1%) caused dose-related response symptoms, mild conjuctival hyperaemia, chemosis and discharge (ocular irritation). Accidental human exposure will result in pupillary constriction and ocular irritation (31).

Sensitisation

Shown not to be a skin sensitiser in guinea pigs (1).

Genotoxicity

Salmonella typhimurium with and without metabolic activation negative (32,33).

Escherichia coli without metabolic activation negative (34).

In vitro human lymphocytes induced sister chromatid exchanges and micronuclei (metabolic activation unspecified) (35).

In vitro Chinese hamster ovary cells induction of micronuclei dose and sample time dependent (36).

In vivo mouse bone marrow erythrocytes induction of micronuclei dose and sample time dependent (36).

Intraperitoneal Swiss mice single dose 25 mg kg^{-1} (maximum tolerated dose) significant micronucleus formation in bone marrow cells after 24- and 48-hr exposure. Intraperitoneal doses of 12.5 and 6.25 mg kg^{-1} did not induce micronuclei (37).

Oral Swiss mice single dose 50 mg kg^{-1} (maximum tolerated dose) and 25 mg kg^{-1} significant micronucleus formation in bone marrow cells after 24- and 48-hr exposure. 12.5 mg kg^{-1} single dose negative (37).

Other effects

Other adverse effects (human)

♂ oral 1.5 mg kg^{-1} caused vomiting after 23 min (38).

Inhabitants from villages that had been sprayed at a rate of 2 g m^{-2} daily for 18 days. Selected inhabitants examined 2, 8 and 18 days after spraying were found to have depressed cholinesterase activity (39).

26% of workers spraying the insecticide experienced symptoms of headache, vomiting and nausea (1).

A 17-yr-old ♂ who ingested tick and flea insecticide containing propoxur at an unspecified dose level was admitted unconscious to hospital. He made a full recovery after treatment; clinical treatment is discussed (40).

Any other adverse effects

Oral dog (3 wk study, single dose) 5, 10, 20 mg kg^{-1} (1% powder formulation). Changes in blood composition and blood chemical levels occurred initially, but returned to normal levels within 7 days (41).

Intragastric dose rat, 0.2 LD_{50} examined after 24 hr and 4 wk chronic treatment showed disorder of phosphorus metabolism in kidney (42).

Rats and mice exposed to 0.25 LD_{50} suffered depression of central nervous system (43).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (44).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (45).
WHO Toxicity Class II (46).
ADI (JMPR) 0.02 mg kg^{-1} body weight (9).

Other comments

Cholinesterase activity inhibitor (32).
Pollutant detected in Polish river waters (47).
Recommended maximum pesticide levels for bees reviewed (48).
Hazards reviewed (49).
Calculated upper maximum lifetime cancer risks reviewed (50).
Maximum dose calculations and risk assessment and possible regulation to human infants reviewed (51).
Does not represent a significant hazard to humans immediately after use in an apartment (52).
Dermal and respiratory exposure to propoxur of glasshouse workers, estimated dermal and respiratory exposure levels were 0.2-46 mg and 3-278 µg, respectively. Measurement of the major metabolite 2-isopropoxyphenol excreted in urine (24 hr) indicated that >80% of propoxur was excreted via this route. On the basis of this rate of excretion it was concluded that there is no reason to suspect increased health risks for workers during harvesting (53).

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P316 2-propoxyethanol

$$CH_3CH_2CH_2OCH_2CH_2OH$$

$C_5H_{12}O_2$ **Mol. Wt.** 104.15 **CAS Registry No.** 2807-30-9

Synonyms ethylene glycol monopropyl ether; ethylene glycol mono-*n*-propyl ether; propyl cellosolve; propyl glycol; 2-(propyloxy)ethanol; Ektasolve EP

EINECS No. 220-548-6 **RTECS No.** KM 2800000

Physical properties

M. Pt. –75°C **B. Pt.** 150-153°C **Flash point** 48°C **Specific gravity** 0.913 at 20°C
Volatility v.p. 51.2 mmHg at 77°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 20 ppm (86 mg m^{-3})
SE-LEVL 10 ppm (45 mg m^{-3}) **SE-STEL** 20 ppm (90 mg m^{-3})
Supply classification harmful
Risk phrases Flammable – Harmful in contact with skin – Irritating to the eyes (R10, R21, R36)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes – Wear suitable protective clothing and gloves (S2, S24/25, S36/37)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3090 mg kg^{-1} (1).

LC_{50} (7 hr) inhalation mouse 1530 ppm (2).

LD_{50} dermal rabbit, guinea pig 960, 1000 mg kg^{-1}, respectively (1,3).

Teratogenicity and reproductive effects

Oral mouse administered 2000 mg kg^{-1} day^{-1} on days 6-13 of gestation then allowed to deliver litters showed no significant difference in litter size, birth weight, neonatal growth or survival to postnatal day 3 compared with controls (4).

Irritancy

Dermal guinea pig 500 mg (72 hr) caused mild irritation and 100 mg instilled into rabbit eye (72 hr) caused severe irritation (1).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

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P317 2-propoxyethanol acetate

$$CH_3CH_2CH_2OCH_2CH_2OC(O)CH_3$$

$C_7H_{14}O_3$ **Mol. Wt.** 146.19 **CAS Registry No.** 20706-25-6

Synonyms 2-propoxyethyl acetate

RTECS No. AJ 3345000

Physical properties

B. Pt. 57-58°C at 3 mmHg

Occupational exposure

DE-MAK 20 ppm (120 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 9460 mg kg^{-1} (1).

Irritancy

Dermal guinea pig (72 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye (72 hr) caused mild irritation (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (2).

References

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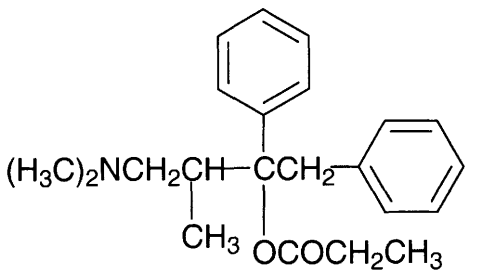
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985, Luxembourg

P318 propoxyphene



$C_{22}H_{29}NO_2$ **Mol. Wt.** 339.48 **CAS Registry No.** 469-62-5

Synonyms dextropropoxyphene; α-[2-(dimethylamino)-1-methylethyl]-α-phenyl benzeneethanol propanoate ester, (2*S*,3*R*)-form; 4-dimethylamino-3-methyl-1,2-diphenyl-2-propionyloxybutene, (2*S*,3*R*)-form; propoxyphene-(+)-α-form; propoxyphene, (2*S*,3*R*)-form; Darvon

EINECS No. 207-420-5 **RTECS No.** EL 2900000

Uses Analgesic.

Physical properties

M. Pt. 75-76°C

Environmental fate

Degradation studies

Non-biodegradable (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 270 mg kg^{-1} (2).
LD_{50} oral rat 135 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 50 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 110 mg kg^{-1} (3).
LD_{50} intravenous mouse 25 mg kg^{-1} (3).

Teratogenicity and reproductive effects

No teratogenic effect was observed in rats and rabbits (4).

Metabolism and toxicokinetics

Metabolised mainly in the liver; ~25% is metabolised by *N*-demethylation to norpropoxyphene. Distributed into the milk (5).

$t_{1/2}$ in plasma ~23 hr (6).

Other effects

Other adverse effects (human)

Causes intrahepatic cholestasis. Acute overdose, as for any narcotic drug, may result in respiratory arrest and coma, with an initial clinical presentation of pinpoint pupils, hypertension, brachycardia and respiratory depression, urinary retention, muscle spasm and itching (7).

In humans, overdose has been associated with convulsions. May have prolonged or protracted clinical course lasting 24-48 hr or more (8).

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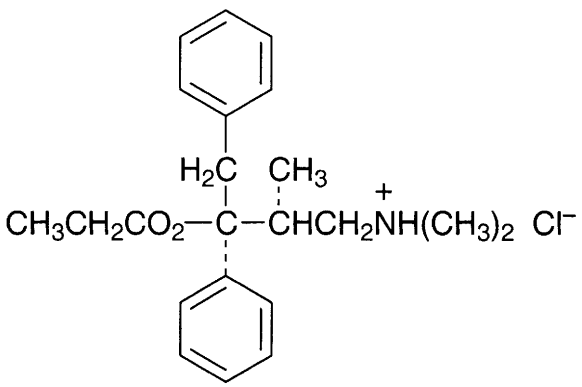
P319 propoxyphene hydrochloride



$C_{22}H_{30}NO_2Cl$ **Mol. Wt.** 375.94 **CAS Registry No.** 1639-60-7

Synonyms benzeneethanol, α-[2-(dimethylamino)-1-methylethyl]-α-phenyl-, propanoate (ester), hydrochloride, [*S*-(*R**,*S**)]-; Darvon; dextropropoxyphene hydrochloride; Doloxene; Evantin; (+)-propoxyphene hydrochloride; D-propoxyphene hydrochloride; α-propoxyphene hydrochloride

EINECS No. 216-683-5 **RTECS No.** EL 3000000

Uses Analgesic.

Physical properties

M. Pt. 163-168.5°C

Solubility Water: soluble. Organic solvents: acetone, chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 84 mg kg^{-1} (1).

LD_{50} intraperitoneal rat, mouse, 58, 111 mg kg^{-1}, respectively (2).

LD_{50} intravenous rat, mouse 15, 25 mg kg^{-1}, respectively (2,3).

LD_{50} subcutaneous rat 134 mg kg^{-1} (2).

Teratogenicity and reproductive effects

Lowest teratogenic dose oral rat 1050 mg kg^{-1} (4).

Metabolism and toxicokinetics

Readily absorbed from the gastro-intestinal tract and distributed and concentrated in the liver, lungs and brain. 80% of dextropropoxyphene and its metabolites bound to plasma proteins. Crosses the placenta and has been detected in breast milk. *N*-demethylated to nordextropropoxyphene in the liver and excreted in urine within 5 days, mainly as metabolites (5).

Other effects

Other adverse effects (human)

Adverse effects include gastro-intestinal effects, dizziness and drowsiness (5).

Three patients taking coproxamol containing propoxyphene hydrochloride had relapsing jaundice mimicking biliary disease (6).

No long-term adverse effects were observed in human volunteers administered 65 mg $4 \times day^{-1}$ for 6 months (7).

Chronic abuse of coproxamol containing dextropropoxyphene and paracetamol caused haemolysis and haemolytic anaemia in an elderly woman and complete nerve deafness in another patient (8,9).

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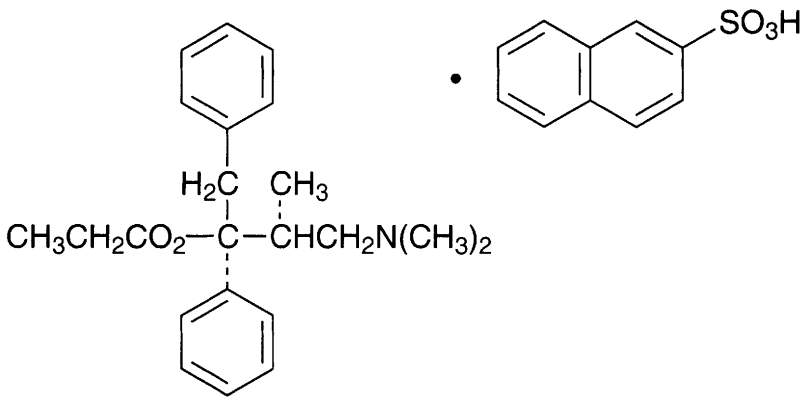
P320 propoxyphene napsylate



$C_{32}H_{37}NO_5S$ **Mol. Wt.** 547.72 **CAS Registry No.** 17140-78-2

Synonyms 2-naphthalenesulfonic acid, compound with [*S*-(*R**,*S**)]-3-(dimethylamino)-2-methyl-1-phenyl-1-(phenylmethyl)propyl propanoate (1:1); dextropropoxyphene napsylate; (+)-propoxyphene napsylate; D-propoxyphene napsylate; Darvon N

EINECS No. 241-205-7 **RTECS No.** QK 1600000

Uses Analgesic.

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, rat, mouse 183, 647, 915 mg kg^{-1}, respectively (1).

Teratogenicity and reproductive effects

Daily dietary doses of 200 and 400 mg kg^{-1} adversely affected reproductive capacity and resulted in 20% maternal death rate in rats (2).

No teratogenic effects were observed in rats administered ≤400 mg kg^{-1} day^{-1} or rabbits administered 80 mg kg^{-1} day^{-1} (2).

Other effects

Other adverse effects (human)

No adverse long-term effects were seen in human volunteers administered 100 mg 4 × day^{-1} for 6 months (3).

Other comments

See also propoxyphene hydrochloride.

References

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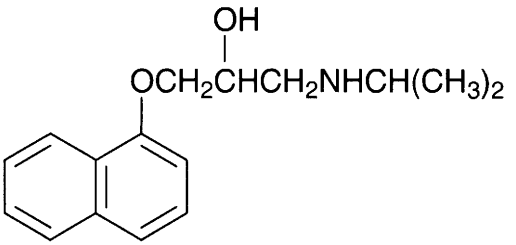
P321 propranolol



$C_{16}H_{21}NO_2$ **Mol. Wt.** 259.35 **CAS Registry No.** 525-66-6

Synonyms 1-[(1-methylethyl)amino]-3-(1-naphthalenyloxy)-2-propanol; 1-(isopropylamino)-3-(1-naphthyloxy)-2-propanol; β-propranolol; Proprasylyt; Reducor; Arlocardyl

EINECS No. 208-378-0 **RTECS No.** UB 7500000

Uses Antihypertensive. Antianginal. Antiarrhythmic. Beta-blocker.

Physical properties

M. Pt. Crystals from cyclohexane 96°C

Solubility Water: soluble. Organic solvents: chloroform, ethanol

Occupational exposure

UK-LTEL 2 mg m^{-3} **UK-STEL** 6 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat, 289, 660 mg kg^{-1}, respectively (1,2).

LD_{50} intravenous rat, mouse, guinea pig 1.9, 23, 26 mg kg^{-1}, respectively (2-4).

LD_{Lo} intravenous human 71 μg kg^{-1} (5).

Metabolism and toxicokinetics

Rapidly metabolised by isolated rat hepatocytes *in vitro* to a range of metabolites, reflecting the *in vivo* metabolic fate, including: propranolol glycol, 1-naphthol, 1, 4-dihydroxynaphthalene and naphthoxylactic acid (6).

Almost completely absorbed from the gastro-intestinal tract, metabolised in the liver, with metabolites including 4-hydroxypropanolol excreted in the urine with little unchanged compound. Plasma $t_{1/2}$ 3-6 hr. Crosses the blood brain barrier and placenta in humans (7).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation positive; TA100 with and without metabolic activation negative (8).

Induced DNA strand breaks in human fibroblasts *in vitro* (8).

Other effects

Other adverse effects (human)

Associated with retroperitoneal fibrosis in the gastro-intestinal tract of one patient (9).

8/44 patients receiving 0.6-5 g day^{-1} developed a paradoxical rise in blood pressure within 24 hr (10).

The most serious adverse effects include heart failure, heart block and bronchospasm with fatigue and coldness of the extremities being troublesome side-effects (7).

11/63 hypertensive patients being treated with propranolol suffered from visual hallucinations, some of which were recurring (11).

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P322 propyl acetate

$$CH_3CO_2CH_2CH_2CH_3$$

$C_5H_{10}O_2$ **Mol. Wt.** 102.13 **CAS Registry No.** 109-60-4

Synonyms propyl methanoate

EINECS No. 203-686-1 **RTECS No.** AJ 3675000

Uses Used in the manufacture of flavours and perfumes, and as a solvent for resins, cellulose derivatives and plastics.

Physical properties

M. Pt. -92°C **B. Pt.** 99-102°C **Flash point** 14°C (closed cup) **Specific gravity** 0.887 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.23 **Volatility** v.p. 40 mmHg at 29°C ; v.den. 3.52
Solubility Water: 16 ml l^{-1} at 16°C. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

DE-MAK 200 ppm (850 mg m^{-3})
FR-VME 200 ppm (840 mg m^{-3})
JP-OEL 200 ppm (830 mg m^{-3})
SE-LEVL 100 ppm (420 mg m^{-3}) **SE-STEL** 200 ppm (800 mg m^{-3})
UK-LTEL 200 ppm (849 mg m^{-3}) **UK-STEL** 250 ppm (1060 mg m^{-3})
US-TWA 200 ppm (835 mg m^{-3}) **US-STEL** 250 ppm (1040 mg m^{-3})

UN No. 1276 **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) fathead minnow 60 mg l^{-1} (1).
In fish, propyl acetate was metabolised by *in vivo* hydrolysis of carboxylic acid esters. Lethality properties of this class of compounds cannot be compared unless carboxylase esterase activities for the species are known (2).

Invertebrate toxicity

Cell multiplication inhibition test, *Pseudomonas putida* 1700 mg l^{-1}, *Entosiphon sulcatum* 97 mg l^{-1} (3).

Bioaccumulation

Calculated bioconcentration factors of 2-5 indicate that environmental bioaccumulation will be insignificant (4).

Environmental fate

Degradation studies

BOD_5 62% reduction in dissolved oxygen using a settled domestic wastewater seed (5).
High mobility in soil reported (6).

Abiotic removal

Evaporation was significant in the removal of propyl acetate from dry and wet soil (7).
Hydrolysed rapidly to alcohol and acid (7).

Adsorption and retention

Activated sludge 0.149 g g^{-1} carbon (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit 6630-9370 mg kg^{-1} (9).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (9).

Metabolism and toxicokinetics

Esters, used as industrial solvents and of interest as occupational exposure hazards, were incubated for 1-8 hr in water or in blood. No hydrolysis occurred in the pure aqueous solution, but progressive hydrolysis occurred in blood (10).

Other effects

Other adverse effects (human)

Reported to be narcotic in high concentrations in humans (11).

Other comments

Reviews on experimental toxicology, epidemiology and human health effects listed (12).

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P323 propylamine

$$CH_3CH_2CH_2NH_2$$

C_3H_9N **Mol. Wt.** 59.11 **CAS Registry No.** 107-10-8

Synonyms aminopropane; 1-aminopropane; 1-propanamine; monopropylamine

EINECS No. 203-462-3 **RTECS No.** UH 9100000

Uses Chemical intermediate.

Occurrence Occurs naturally in various species of marine algae (1).

Physical properties

M. Pt. –83°C **B. Pt.** 48-49°C **Flash point** –12°C (closed cup) **Specific gravity** 0.7191 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 0.48 **Volatility** v.p. 248 mmHg at 20°C

Solubility Water: miscible. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1277 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) creek chub 40-60 mg l^{-1} (2).

Environmental fate

Nitrification inhibition

No inhibition of NH_3 oxidation *Nitrosomonas* sp. at 100 mg l^{-1} (3).

Degradation studies

Degradation by *Aerobacter* spp. 200 mg l^{-1} 30°C. Parent 100% degradation in 31 hr while mutant strains 100% degradation in 9 hr (2).

Arthrobacter P1 metabolised aminopropane via primary amine oxidase activity and utilised both carbon and nitrogen as sources of growth (4).

BOD_{13} of 102% was measured using a non-activated sludge inoculum (5).

Abiotic removal

Reacts photochemically with hydroxyl radicals in the atmosphere (6).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 250-570 mg kg^{-1} (7,8).

LC_{50} (2 hr) inhalation mouse 2500 mg m^{-3} (7).

LC_{50} (4 hr) inhalation rat 2310 ppm (9).

LD_{50} dermal rabbit 560 mg kg^{-1} (10).

Irritancy

Dermal rabbit (24 hr) 100 µg caused irritation, while 720 µg instilled into rabbit eye caused severe irritation (10,11).

Other comments

Reviews on human health effects, experimental toxicology, environmental effects and ecotoxicology listed (12).

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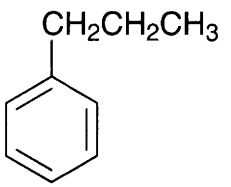
P324 propylbenzene



C_9H_{12} **Mol. Wt.** 120.19 **CAS Registry No.** 103-65-1

Synonyms isocumene; 1-phenylpropane; *n*-propylbenzene

EINECS No. 203-132-9 **RTECS No.** DA 8750000

Uses In textile dyeing and printing. Solvent for cellulose acetate.

Physical properties

M. Pt. –99.2°C **B. Pt.** 159°C **Flash point** 30°C (closed cup) **Specific gravity** 0.862 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.72 **Volatility** v.p. 10 mmHg at 43.4°C ; v.den. 4.14
Solubility Water: 0.06 g l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2364 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification irritant
Risk phrases Flammable – Irritating to the respiratory system (R10, R37)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Bioaccumulation
Estimated bioconcentration factor 66 (1)

Environmental fate

Carbonaceous inhibition

Inhibited methanogenesis by bacteria in methanogenic granular sludge by 50% at 0.2 g l^{-1} and by 80% by 0.43 g l^{-1} (2).

Degradation studies

Log K_{oc} (adsorption coefficient) 2.86 (3).

Readily oxidised in Warburg respirometer studies using an activated sludge acclimated to aniline, 8-day theoretical BOD 34.4% (4).

Abiotic removal

Volatilisation $t_{1/2}$ 3.3 and 39 hr estimated for a model river and pond (1,5).

Degraded in the atmosphere by photochemically produced hydroxyl radicals $t_{1/2}$ 2.7 day (6)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6040 mg kg^{-1} (7).

LC_{Lo} inhalation mouse 20 g m^{-3} (duration unspecified) (8).

Metabolism and toxicokinetics

In humans, converted into benzoic acid, conjugated with glycine and excreted in the urine as hippuric acid (9).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (10).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (11).

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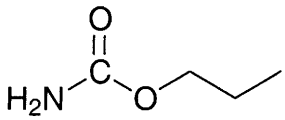
P325 *n*-propyl carbamate



$C_4H_9NO_2$ **Mol. Wt.** 103.12 **CAS Registry No.** 627-12-3

Synonyms carbamic acid, propyl ester; propyl urethane; propyl carbamate

RTECS No. FD 0875000

Uses As an intermediate in the manufacture of dimethylol propyl carbamate-based resins, which are used in the textile industry as durable-press fabric finishes.

Physical properties

M. Pt. 61-63°C **B. Pt.** 196°C

Solubility Water: very soluble. Organic solvents: acetone, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_5 oral redwinged blackbird, starling >100 mg kg^{-1} (1).

LD_{50} subcutaneous mouse 1300 mg kg^{-1} (2).

Sub-acute and sub-chronic data

In three-day feeding trials with white wheat seeds, more than 50% of deer mice were killed by a dose of 1225 mg *n*-propyl carbamate kg^{-1} (3).

Carcinogenicity and chronic effects

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

Tested in 32 strain A mice (10-12 wk old) by intraperitoneal injection of 0.5 mg per mouse weekly, for 13 weeks. At six months of age, 19 mice had developed lung tumours, with an average of 0.9 tumours per mouse. Another group of 46 mice were tested using recrystallised *n*-propyl carbamate; 30/46 mice developed lung tumours, with an average of 1.0 tumour per mouse. Of 141 untreated controls, 24 developed lung tumours, with an average of 0.18 tumours per mouse (5).

Tests in mice found that *n*-propyl carbamate is a possible carcinogen for the epidermis, liver and lung (6).

Teratogenicity and reproductive effects

Intraperitoneal injection in Syrian hamsters (day 8 of gestation) of 248 mg kg^{-1} had teratogenic effects (7).

Metabolism and toxicokinetics

In rats, intraperitoneally injected *n*-propyl carbamate is excreted in the urine (8).

Genotoxicity

Escherichia coli (2 pph, 3 hr) positive (9).

Escherichia coli WP2 uvrA without metabolic activation negative (10).

Bacillus subtilis without metabolic activation, reverse mutation assay negative (11).

Other comments

Physico-chemical properties, human health effects, exposure levels, experimental toxicology, workplace experience and epidemiology reviewed (12).

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P326 propyl chloroformate

$$ClCO_2CH_2CH_2CH_3$$

$C_4H_7ClO_2$ **Mol. Wt.** 122.55 **CAS Registry No.** 109-61-5

Synonyms propyl chlorocarbonate

EINECS No. 203-687-7 **RTECS No.** LQ 6830000

Physical properties

B. Pt. 105-106°C (1) **Flash point** 28°C **Specific gravity** 1.0901 at 20°C with respect to water at 4°C
Volatility v.p. 26 mmHg at 20°C ; v.den. 4.2
Solubility Organic solvents: chloroform, diethyl ether, ethyl ether; miscible with benzene

Occupational exposure

UN No. 2740 **Conveyance classification** toxic substance, danger of fire (flammable liquid), corrosive
Supply classification toxic
Risk phrases Flammable – Toxic by inhalation – Causes burns (R10, R23, 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 – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 650 mg kg^{-1} (2).
LC_{50} (1 hr) inhalation mouse 319 ppm (2).
LD_{50} dermal mouse 10 mg kg^{-1} (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (3).

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P327 propylene glycol

$$CH_3CH(OH)CH_2OH$$

$C_3H_8O_2$ **Mol. Wt.** 76.10 **CAS Registry No.** 57-55-6

Synonyms 1,2-propanediol; 1,2-dihydroxypropane; 2-hydroxypropanol; isopropylene glycol; methylethyl glycol; monopropylene glycol

EINECS No. 200-338-0 **RTECS No.** TY 2000000

Uses A preservative. A plasticiser. Used in pharmaceutical manufacturing as a solvent and as a stabiliser in vitamin preparations. Humectant. Used as a non-toxic antifreeze in breweries and dairy establishments.

Physical properties

M. Pt. –60°C **B. Pt.** 187°C **Flash point** 107°C **Specific gravity** 1.0362
Partition coefficient log P_{ow} –0.92 (1) **Volatility** v.p. 0.08 mmHg at 20°C ; v.den. 2.6
Solubility Water: miscible. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UK-LTEL 150 ppm (474 mg m^{-3}) (total vapour and particulates); 10 mg m^{-3} (particulates)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish >5000 mg l^{-1} (2).
LC_{50} (48 hr) guppy >10 g l^{-1} (3).
Fingerling trout exposed to 50 g l^{-1} for 24 hr at 10°C showed no signs of stress and no mortality (4).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 710 ppm Microtox test (5).
EC_{50} (24 and 48 hr) *Daphnia magna* >10 g l^{-1} (6).

Bioaccumulation
The bioconcentration factor has been estimated to be <1 (1).

Environmental fate

Degradation studies
ThOD 1.685 g O_2 g^{-1}; BOD_5 0.955 g O_2 g^{-1} (7).

Abiotic removal
Activated carbon adsorbability 0.024 g g^{-1} C; 1000 mg l^{-1} influent, 835 mg l^{-1} effluent, 11.6% reduction (8).

Adsorption and retention
The miscibility in water and low P_{ow} is indicative of high mobility in soil (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 20, 22 g kg^{-1}, respectively (9,10).
LD_{50} intravenous rat, mouse 6423, 6630 mg kg^{-1}, respectively (11).
LD_{50} intraperitoneal rat, mouse 6660, 9718 mg kg^{-1}, respectively (12,13).
LD_{50} subcutaneous mouse 17,370 mg kg^{-1} (14).

Sub-acute and sub-chronic data

Oral rat no-effect level 13.2 g kg^{-1} day^{-1} for 69 days and 30 ml kg^{-1} day^{-1} for 6 months (15).
♂, ♀ Sprague-Dawley rats were exposed by nose-only inhalation to 0.0, 0.16, 1.0 or 2.2 mg l^{-1} air, 6 hr day^{-1}, 5 day wk^{-1} for 90 days. The mean body weights of ♀ rats exposed to 2.2 mg l^{-1} were significantly less than controls from day 50 onward; this effect was consistent with a decrease in feed consumption from day 43 onwards. ♂ rats showed no difference in body weight compared with controls. Exposure caused nasal haemorrhage and ocular discharge in a high proportion of animals, possibly as a result of dehydration of the nose and eyes (16).
Oral rat (15 wk) 50,000 ppm. Serum and urine analysis and organ weights were comparable to controls (17).

Carcinogenicity and chronic effects

Repeated application to the skin of mice throughout their life did not increase the tumour incidence and mortality as compared with controls. Skin lesions, slight inflammation and ulceration were seen, but no persistent abnormalities occurred (18).
No carcinogenic potential was observed in rats fed up to 50,000 ppm (equivalent to 2.5 g kg^{-1} day^{-1}) (17).
Oral rat (2 yr) 0, 6250, 12,500, 25,000 or 50,000 ppm. No effects on body weight, mortality, food consumption, organ weight or pathological findings, including tumour incidence, were seen (17).

Teratogenicity and reproductive effects

♀ rats were treated orally with 0.2 ml of 10% propylene glycol in water before mating and/or during pregnancy. No significant results indicative of maternal toxicity, embryotoxicity or teratogenicity were obtained (19).
Injection of 20% propylene glycol into the yolk sac of 3-day-old chicken embryos caused 100% mortality; controls suffered 6.6% mortality (20).
Pregnant CD-1 mice were treated by oral gavage on days 8-12 of gestation. No effects on early postnatal growth or viability were seen (21).

Metabolism and toxicokinetics

Readily absorbed from the gastro-intestinal tract; some evidence of topical absorption when applied to damaged skin. Metabolised in the liver, by oxidation, to lactic and pyruvic acid and is also excreted in the liver unchanged (22).
Using the Michaelis-Menten rate equation the maximum metabolising capacity was found to be 8.33 mmol propylene glycol kg^{-1} hr^{-1} in rats, which is equivalent to 1.06 kg day^{-1} for a 70 kg human. The low threshold level and significant rate of metabolism suggest that reported central nervous system toxicity may be due to metabolites such as lactaldehyde and other oxo compounds (23).
Following intravenous injection plasma pharmacokinetics were non-linear. The apparent 1st-order $t_{1/2}$ was 2.3 hr and there was no evidence of lactic acidosis, haemolysis or an increase in osmolality at 3-15 g m^{-2} infused over 4 hr (24).

Irritancy

May cause local irritation of the skin and mucous membranes (22).
Dermal human (7 days) 500 mg caused mild irritation (25).
Dermal human (3 days) 104 mg caused moderate irritation (26).
500 mg instilled into rabbit eye (24 hr) caused mild irritation (27).

Sensitisation

Did not increase the ear thickness in the mouse ear sensitisation assay, therefore classed as non-sensitising (28).
Hypersensitivity reactions have been reported in humans (22).

Genotoxicity

Salmonella typhimurium TA98, TA100 negative (metabolic activation not specified) (29).
Bacillus subtilis rec assay negative without metabolic activation (29).
In vitro hamster lung fibroblast cells sister chromatid exchanges negative, chromosomal aberrations without metabolic activation positive (29).
Silk worm mutations negative (29).

Other effects

Other adverse effects (human)

Hyperosmolality, lactic acidosis, and central nervous system depression have occurred in patients treated with preparations containing the compound, particularly in patients with renal impairment (22).
Reversible symptoms of central nervous system depression have occurred in subjects ingesting as little as 60 ml (30).
Children who had ingested 7.5 ml day^{-1} for 8 days developed symptoms including stupor, seizures, sweating and rapid respiratory and heart rates (31).

Other comments

Concentrations of 0.5-1.0% inhibit natural cytotoxicity and neutrophil chemiluminescence. These potential immunosuppressive effects should be taken into account when evaluating drug formulations (32). Experimental toxicology, human health effects and environmental effects reviewed (33,34).
Toxicity has been reviewed (35).
Skin toxicity has been evaluated (36).
Autoignition temperature, 371°C.

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P328 propylene glycol allyl ether

$$CH_3CH(OH)CH_2OCH_2CH{=}CH_2$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 1331-17-5

Synonyms propylene glycol monoallyl ether; (2-propenyloxy)propanol; (allyloxy)propanol; 1-(2-propenyloxy)propanol

RTECS No. UA 4900000

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 510 mg kg^{-1} (1).

LD_{50} dermal rabbit 1100 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 10 mg produced mild irritation; 2 mg instilled into rabbit eye caused severe irritation (1).

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P329 propylene glycol dinitrate

$$CH_3CH(ONO_2)CH_2ONO_2$$

$C_3H_6N_2O_6$ **Mol. Wt.** 166.09 **CAS Registry No.** 6423-43-4

Synonyms propylene nitrate; propylene dinitrate; isopropylene nitrate; PGDN; 1,2-propylene glycol dinitrate; 1,2-propanediol dinitrate

EINECS No. 229-180-0 **RTECS No.** TY 6300000

Uses Explosive propellant.

Physical properties

M. Pt. –27.7°C **B. Pt.** 92°C **Volatility** v.p. 0.07 mmHg at 22.5°C

Solubility Water: 1.3 g l^{-1}

Occupational exposure

DE-MAK 0.05 ppm (0.34 mg m^{-3})
FR-VME 0.05 ppm (0.3 mg m^{-3})
SE-LEVL 0.1 ppm (0.7 mg m^{-3})
SE-STEL 0.3 ppm (2 mg m^{-3})
UK-LTEL 0.2 ppm (1.4 mg m^{-3})
UK-STEL 0.2 ppm (1.4 mg m^{-3})
US-TWA 0.05 ppm (0.34 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral ♀ rat 1190 mg kg^{-1} (1).
LD_{50} oral rat 250 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse, guinea pig 402-1047 mg kg^{-1} (2).
LD_{Lo} intravenous monkey 410 mg kg^{-1} (3).
LD_{Lo} subcutaneous cat 200 mg kg^{-1} (1).
LD_{50} subcutaneous ♀ rat, ♀ mouse 463 and 1208 mg kg^{-1}, respectively (1).

Sub-acute and sub-chronic data

Dermal rabbit (20 day) 1, 2 and 4 mg kg^{-1}. At 1 mg kg^{-1} there were no signs of systemic effects and only reversible erythema. At 2 mg kg^{-1} the animals were weak, cyanotic and had rapid, shallow breathing. At 4 mg kg^{-1} 13/14 animals were dead by the 5th application (4).
Inhalation ♂, ♀ rats, ♂, ♀ guinea pigs, ♂ squirrel monkeys, ♂ beagle dogs (90 days) 67, 108 and 236 mg m^{-3} 24 hr day^{-1}. At 67 mg m^{-3} dogs had hepatic haemosiderin deposition in sinusoids, bile canaliculi and Kupffer cells. At 108 mg m^{-3} guinea pigs showed foci of pulmonary haemorrhage. Dogs, ♀ rats and monkeys exposed to 236 mg m^{-3} showed heavy iron-positive deposits, vacuolar change and focal necrosis. Monkeys had increased serum urea nitrogen level and decreased alkaline phosphatase activity at the two higher doses, suggesting renal damage. Dogs showed decreases in haemoglobin levels and haematocrit (4).

Carcinogenicity and chronic effects

♂, ♀ dogs, rats, mice were exposed 6 hr day^{-1} 5 day $week^{-1}$ for 1 yr to the torpedo fuel Otto Fuel II; exposure levels of 1.4 and 240 mg m^{-3} were based on propylene glycol dinitrate, the major component. Dogs, which were only exposed to the lower concentration were the most sensitive species with measurable reductions in erythrocytes, haematocrit and Hb levels. Slightly increased metHb was seen in the dogs and also in rats exposed to the higher concentration. No other significant effects were seen in rats exposed to either concentration. Examination of tissues from the three species showed no exposure-related non-neoplastic changes and no increase in the incidence of neoplastic changes was seen. Primary bone tumours were seen in 4 rats exposed to propylene glycol dinitrate, but the incidence of these tumours did not increase in a dose-related fashion (5).

Teratogenicity and reproductive effects

From 1980 to 1983, spontaneous abortions among ♀ naval munitions workers were the same or lower when compared with hospital employees and all other Navy women; no spontaneous abortions were seen among a few pregnant women exposed to the compound (4).

Metabolism and toxicokinetics

In vivo propylene glycol 2-mononitrate was the predominant metabolite, with inorganic nitrate as the major metabolite in 24-hr urinary excretion, accounting for 56% of the original dose (4).

Irritancy

100 mg instilled in rabbit eye caused mild irritation (3).

Genotoxicity

Otto Fuel II (containing 75% propylene glycol dinitrate) produced negative results in the Ames *Salmonella typhimurium* assay with and without metabolic activation, sister chromatid exchange in L5178Y mouse lymphoma cells, mouse bone marrow cytogenetic analysis, and mouse-dominant lethal assay. The material was mutagenic in the mouse lymphoma forward mutation assay (4).

Other effects

Other adverse effects (human)

Human volunteers were exposed to 0.2, 0.65, 1.3, 2.3, 3.25 and 9.75 mg m^{-3} as a one-off or on a daily basis over various periods of time. The incidence of headaches increased with increasing dosage from 2 subjects with mild headaches at 0.65 mg m^{-3} to all 8 subjects suffering from severe headaches at 9.75 mg m^{-3}. At 9.75 mg m^{-3} all subjects had eye irritations by 40 min of exposure (4).

Naval employees chronically exposed to the compound in the form of Otto Fuel II reported acute headaches and nasal congestion, but no cardiovascular or neurotoxicity disorders (4).

Elevated rates and significantly elevated relative risks of myocardial infarction and angina pectoris were seen in Navy munition workers exposed to the compound from 1966 to 1979 (4).

Any other adverse effects

Subcutaneous injection can cause a decrease in arterial blood pressure, with the maximum drop occurring within 30 min of injection. This is attributed to arteriolar and venous dilation (4).

Other comments

Reviews on human health effects, workplace experience, epidemology and experimental toxicity listed (6).

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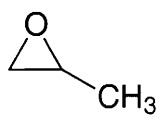
P330 propylene oxide



C_3H_6O **Mol. Wt.** 58.08 **CAS Registry No.** 75-56-9

Synonyms 1,2-epoxypropane; 1,2-propylene oxide; methyloxirane; methylethylene oxide; propene oxide; PO; NCI-C5099

EINECS No. 200-879-2 **RTECS No.** TZ 2975000

Uses Solvent. Chemical intermediate, principally in the production of polyols used in polyurethane and in the manufacture of propylene glycol. Used as a food reagent, as an etherifying agent in the production of modified starch and as a fumigant of packaged food.

Physical properties

M. Pt. –112°C **B. Pt.** 34.2°C **Flash point** –37°C (closed cup) **Specific gravity** 0.8304 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 0.03 **Volatility** v.p. 445 mmHg at 20°C ; v.den. 2.0
Solubility Water: 40.5%. Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol, methanol

Occupational exposure

FR-VME 20 ppm (50 mg m^{-3})
SE-LEVL 2 ppm (5 mg m^{-3}) **SE-STEL** 10 ppm (25 mg m^{-3})
UK-LTEL MEL 5 ppm (12 mg m^{-3})
US-TWA 20 ppm (48 mg m^{-3})

UN No. 1280 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid
Supply classification extremely flammable, toxic
Risk phrases May cause cancer – Extremely flammable – Harmful by inhalation, in contact with skin and if swallowed – Irritating to eyes, respiratory system and skin (R45, R12, R20/21/22, 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} (96 hr) bluegill sunfish, mosquito fish 140-215 mg l^{-1} static bioassay (1).

Bioaccumulation
Calculated bioconcentration factors of –0.2 and –0.4 indicate that environmental accumulation is unlikely (2).

Environmental fate

Degradation studies
8-9% degradation by filtered effluent seed and adapted effluent seed in 5 days (3).

Abiotic removal
Estimated $t_{1/2}$ for hydrolysis 11.6 days at pH 7-9 and 6 days at pH 5, in freshwater. In sea water, $t_{1/2}$ for hydrolysis 4 days at pH 7-9 and 36 hr at pH 5 with the formation of chloropropanols (4).
Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in water ~9 yr, and in the atmosphere 19 days (5-7).
Calculated $t_{1/2}$ for volatilisation from model river water 3 days and from oligotrophic lake 18 days (8).

Adsorption and retention
Calculated K_{oc} values of 4-30 indicate that 1,2-epoxypropane is expected to be very mobile in soil (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, guinea pig 380-1140 mg kg^{-1} (10-12).
LC_{50} (4 hr) inhalation rat, mouse 4100, 9500 mg m^{-3}, respectively (13).
LD_{50} dermal rabbit 1250 mg kg^{-1} (14).

Sub-acute and sub-chronic data
Inhalation rat, no organ injury was observed following exposure to 9500 mg m^{-3} for 0.5 hr, 4750 mg m^{-3} for 2 hr, or 2400 mg m^{-3} for 7 hr (15).
Inhalation rat, rabbit, guinea pig, monkey, 240 or 460 mg m^{-3} 5 days wk^{-1} for 7 months. The high dose induced an increase in average lung weight in ♀ guinea pigs but not in other species. All species tolerated the lowest dose without adverse effects (15).
Gavage rat (24 day) 200 mg kg^{-1} day^{-1} produced no toxic effect (15).
Inhalation rat, mouse (13 wk) 475, 950 or 1200 mg m^{-3} 6 hr day^{-1} on 5 days wk^{-1} caused no compound-related gross or pathological effects (16).
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 electroenecephalograms 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 years. No treatment-related effects were detected (17).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (18).

National Toxicology Program tested rats and mice via inhalation. Some evidence of carcinogenic activity (increased incidence of chemically related neoplasms, malignant, benign or combined) in ♂ and ♀ rats. Clear evidence of carcinogenic activity (dose-related increase of malignant neoplasms, increase of a combination of malignant and benign neoplasms or marked increase of benign neoplasms with indication of progression to malignancy) in ♂ and ♀ mice (16).

Inhalation rat (2 yr) 0, 100 or 300 ppm 7 hrs day^{-1} 5 days wk^{-1} for 104 wk. Increased mortality, incidence of inflammatory lesions of the respiratory system, and dose-related complex epithelial hyperplasia in the nasal cavity were observed in treated animals. In addition, 2 rats in the high-dose group developed nasal cavity adenomas which were not seen in controls. Adrenal phaeochromocytomas developed in 8/78 controls, 25/78 of the low-dose group and 22/80 rats in the high-dose group. Peritoneal mesotheliomas were observed in 3/78 control, 8/78 low-dose and 9/80 high-dose animals (19).

Gavage rat, 0, 15 or 60 mg kg^{-1} 2 × wk^{-1} for 109 wk. Survival rates of treated and control animals were comparable. A dose-dependent increase in the incidence of local tumours (mainly squamous-cell carcinomas of the forestomach) and papillomas, hyperplasia or hyperkeratosis of the forestomach were observed in treated rats (20).

Subcutaneous mouse, 0, 0.1, 0.3, 1.0 or 2.5 mg kg^{-1} wk^{-1} for 95 wk. Survival rates were comparable for controls and treated groups. A dose-related increase in the incidences of local sarcomas (fibrosarcomas and pleomorphic sarcomas) was reported (21).

Teratogenicity and reproductive effects

Inhalation rabbit, 1200 mg m^{-3} 7 hr day^{-1} on either days 7-19 or 1-19 of gestation. Resorption rate was increased (4.3%) compared with controls (1.5%) in the group exposed on days 1-19 of gestation. Food consumption, but not maternal body weight, was reduced in exposed animals (22).

Inhalation rat, 120 mg m^{-3} 7 hr day^{-1} either 3 wk prior to gestation to day 16 of gestation, or days 7-16, or days 1-16 of gestation. The number of corpora lutea and implantation sites dam^{-1}, and consequently the number of live foetuses $litter^{-1}$, were lower in rats receiving pregestational exposure. Foetal growth was also reduced in this group. No treatment-related major malformation was seen, but the incidence of primary wavy ribs was increased in all treated groups. Food consumption was reduced in dams that received pregestational exposure, and maternal weight gain was lower in all treated groups (22).

Metabolism and toxicokinetics

In vitro reaction products have been reported with deoxyadenosine, deoxyguanosine, deoxycytidine and thymidine (23-25).

N^7-(2-hydroxypropyl)histidine has been detected in the haemoglobin of exposed workers (26).

Irritancy

Inhalation rat and guinea pig (7 hr) 1100 mg m^{-3} caused irritation of the eyes and respiratory passages (15).

Dermal rabbit (6 min) 50 mg caused severe irritation and 5 mg instilled into rabbit eye (exposure unspecified) caused severe irritation (15).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (23-25).

Escherichia coli PQ37, SOS-Chromotest with and without metabolic activation negative (25).

Klebsiella pneumoniae without metabolic activation induction of mutations positive (26).

Drosophila melanogaster sex-linked recessive lethal assay positive (27).

In vitro Chinese hamster V79 lung cells, sister chromatid exchanges positive (28).

In vitro human lymphocytes and rat liver epithelial-type cells (RL_1) with and without metabolic activation chromosomal aberrations positive (29,30).

In vitro primary rat hepatocytes, DNA single-strand breaks positive (31).

In vitro human diploid fibroblasts (VH-10) DNA strand breaks positive (32).

In vivo mouse bone marrow, induction of micronuclei positive (30).

In vivo mouse, dominant lethal assay and sperm abnormalities negative (27).

Other effects

Other adverse effects (human)

A mortality study of 602 exposed workers was reported. The men had also been exposed to benzene, ethylene oxide and ethylene chlorohydrin. The study included workers from 1928 although production of propylene oxide began only in 1959. The observed and expected number of cancer deaths did not differ significantly (33).

Legislation

Organic solvents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (34).

Other comments

Product of combustion of fossil fuels. Trace impurity in poly(propylene oxide) (35).
Physical properties, use, occurrence, carcinogenicity, mammalian toxicity, teratogenicity and mutagenicity reviewed (35).
Environmental fate reviewed (2).
Reviews on toxicity and human health effects are listed (36).
Propylene oxide reacts *in vitro* with DNA at neutral pH to yield two principal products, *N*-7-(2-hydroxypropyl)guanine and *N*-3-(2-hydroxypropyl)adenine (37).
In vitro reaction products have been reported with deoxyadenosine, deoxyguanosine, deoxycytidine and, thymidine (38-40).
Mutagenic and carcinogenic properties are reviewed (41).

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P331 propyl formate

$$HCO_2CH_2CH_2CH_3$$

$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 110-74-7

Synonyms formic acid, propyl ester; propyl methanoate

EINECS No. 203-798-0 **RTECS No.** LR 0175000

Physical properties

M. Pt. –93°C **B. Pt.** 81-82°C **Flash point** –3°C (closed cup) **Specific gravity** 0.904 at 20°C
Partition coefficient log P_{ow} 0.83 **Volatility** v.p. 100 mmHg at 29.5°C ; v.den. 3.03
Solubility Water: soluble in 45 parts water. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1281 **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 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 mouse, rat 3400, 3980 mg kg^{-1}, respectively (1).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3).

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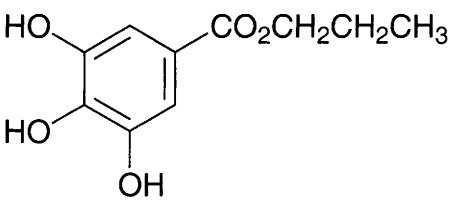
P332 propyl gallate



$C_{10}H_{12}O_5$ **Mol. Wt.** 212.20 **CAS Registry No.** 121-79-9

Synonyms benzoic acid, 3,4,5-trihydroxypropyl ester; gallic acid, propyl ester; propyl 3,4,5-trihydroxybenzoate; Embanox; Nipa; Nipagallin; Progallin; Sustane PG; Tenox PG

EINECS No. 204-498-2 **RTECS No.** LW 8400000

Uses Antioxidant for foods, fats, oils, emulsions, waxes, transformer oils.

Physical properties

M. Pt. 148-150°C **Partition coefficient** log P_{ow} 0.967 (1)
Solubility Water: 0.35 g 100 ml^{-1} at 25°C. Organic solvents: cottonseed oil, diethyl ether, ethanol, lard

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 the skin – Wear suitable gloves (S2, S24, S37)

Mammalian & avian toxicity

Acute data
LD_{50} oral cat, mouse, rat 400, 1700, 2100 mg kg^{-1}, respectively (2-4).
LD_{50} intraperitoneal rat 380 mg kg^{-1} (5).

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice in feed. No evidence for carcinogenicity in ♀ rats, mice, equivocal evidence for carcinogenicity in ♂ rats, mice (6).

Irritancy
Skin sensitiser and irritant in some humans (7).

Sensitisation
Alkyl gallates reported to cause contact sensitisation in humans (8,9).
May only cause sensitisation on damaged skin, similar to hydroxybenzoates (10).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (11).
In vitro Chinese hamster ovary cells sister chromatid exchanges positive with and without metabolic activation, chromosomal aberrations positive without metabolic activation, negative with metabolic activation (12).
In vivo mouse B6C3F_1 bone marrow cells did not induce micronuclei (13).

Other effects

Other adverse effects (human)
Methaemoglobinaemia in infants associated with antioxidants used to preserve oil in a soyabean infant feed, including propyl gallate, which was suspected as the cause as the structure is similar to pyrogallol, a methaemoglobin inducer (14).

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P333 propyl isocyanate

$$CH_3CH_2CH_2NCO$$

C_4H_7NO **Mol. Wt.** 85.11 **CAS Registry No.** 110-78-1
Synonyms isocyanatopropane; isocyanic acid, propyl ester; 1-isocyanatopropane; 1-propyl isocyanate
EINECS No. 203-803-6 **RTECS No.** NR 0190000

Physical properties

B. Pt. 83-84°C **Flash point** 0°C **Specific gravity** 0.908

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. 2482 **HAZCHEM Code** 3WE **Conveyance classification** toxic substance, danger of fire (flammable liquid)

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 56 mg kg^{-1} (1).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

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P334 propyl nitrate

$$CH_3CH_2CH_2NO_3$$

$C_3H_7NO_3$ **Mol. Wt.** 105.09 **CAS Registry No.** 627-13-4

Synonyms nitric acid, propyl ester

EINECS No. 210-985-0 **RTECS No.** UK 0350000

Uses Fuel ignition promoter. In rocket fuel. Organic intermediate.

Physical properties

M. Pt. −100°C **B. Pt.** 84.8°C **Flash point** 20°C **Specific gravity** 1.053 at 20°C with respect to water at 4°C
Volatility v.p. ~16 mmHg at 25°C ; v.den. 3.62
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 25 ppm (110 mg m^{-3})
FR-VME 25 ppm (105 mg m^{-3})
US-TWA 25 ppm (107 mg m^{-3}) **US-STEL** 40 ppm (172 mg m^{-3})

UN No. 1865 **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{50} intravenous rabbit 200 mg kg^{-1} (1).
LD_{Lo} intravenous dog, cat 100 mg kg^{-1} (1).
Oral rat 5000 mg kg^{-1} body weight was fatal; at 1000 mg kg^{-1} body weight produced weakness, incoordination and cyanosis (2).

Inhalation rat (4 hr) 10,000 ppm caused cyanosis and methaemoglobinaemia before death (3).
Inhalation (4 hr) mouse 7134 or 5816 ppm caused cyanosis and convulsions before death in 15/20 and 2/10 animals, respectively (3).
Intravenous dog 5 mg kg^{-1} caused reduced blood pressure, 30 mg kg^{-1} showed heart rate and 50 mg kg^{-1} reduced contractile force of the heart and ceased muscular contractions of the gut. Dogs stopped breathing temporarily then started at an abnormally fast rate, with cyanosis at all doses, with full recovery within 2 hr. 200 mg kg^{-1} caused a drop in blood pressure, respiratory paralysis and death within 1 minute (1).

Sub-acute and sub-chronic data
Oral rat 1500 mg kg^{-1} 5 day wk^{-1} for 2 wk showed temporary weakness, cyanosis, methaemoglobinaemia, weight loss and spleen swelling becoming less severe as treatment continued (2).
Inhalation rat, mouse, guinea pig, hamster 3235 ppm 6 hr day^{-1}, 5 day wk^{-1} for 8 wk. Rats had cyanosis, lethargy and, in the first wk, weight loss. 5/20 died. Mice showed moderate excitement and cyanosis, 6/29 died. No overt toxicity was seen in hamsters and guinea pigs and ten of each all survived treatment (3).
Three dogs exposed to 2000 ppm all died after suffering cyanosis, methaemoglobinaemia, vomiting and convulsions. Two dogs which died after exposure to 900 or 560 ppm for 6 hr day^{-1}, 5 day wk^{-1} died after day 6, and 1 animal exposed to 560 ppm survived for 6 wk. Three dogs survived 26 wk exposure to 260 ppm, but suffered mild anaemia, red blood cell damage, and a slight depression of the nervous system (3).
Intravenous injection of 40 mg kg^{-1} day^{-1} to a dog caused no lesions in the intestine, spleen, pancreas, kidneys, liver, lungs and heart after 8 days (1).

Irritancy
Caused mild, temporary inflammation but no corneal damage when instilled into rabbit eye (dose and duration unspecified). Caused staining, swelling and thickening of the skin of rabbits treated for 10 days (dose unspecified) (4).

Genotoxicity

A very slight mutagenic potential was reported in the bacteriophage T4B virus (5).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Reviews on human health effects, epidermiology, workplace experience, and experimental toxicology listed (7).

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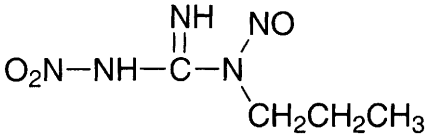
P335 1-propyl-3-nitro-3-nitrosoguanidine



$C_4H_9N_5O_3$ **Mol. Wt.** 175.15 **CAS Registry No.** 13010-07-6

Synonyms *N*-propyl-*N'*-nitro-*N*-nitrosoguanidine; *N'*-nitro-*N*-nitroso-*N*-propylguanidine; 3-nitro-1-nitroso-1-propylguanidine

EINECS No. 235-856-6 **RTECS No.** MF 4643000

Physical properties

M. Pt. 108-110°C (decomp.)

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Oral ♂ F344 rat. The compound induced an increase in ornithine decarboxylase activity and an increase in DNA synthesis in the pyloric mucosa of the stomach. These inductions are thought to be markers of promotive activities of complete carcinogens and tumour promoters in the glandular stomach (1).

Genotoxicity

Salmonella typhimurium positive (strains and metabolic activation activation unspecified) (2).
Enhanced the transposition frequency in MudI (Ap^R *lac*) in *Escherichia coli* (3).

Other comments

All *N*-alkyl homologues of *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine show DNA modifying and mutagenic activity (4).

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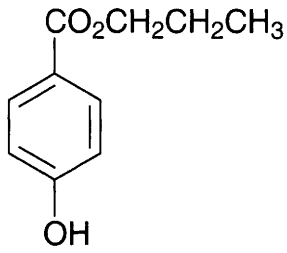
P336 propylparaben



$C_{10}H_{12}O_3$ **Mol. Wt.** 180.20 **CAS Registry No.** 94-13-3

Synonyms propyl *p*-hydroxybenzoate; propyl 4-hydroxybenzoate; 4-hydroxybenzoic acid, propyl ester; Nipasol; Paridol Propyl

EINECS No. 202-307-7 **RTECS No.** DH 2800000

Uses Preservative in food, cosmetics and pharmaceuticals. Used for treatment of moniliasis.

Physical properties

M. Pt. 96-97°C **Flash point** <66°C **Specific gravity** 1.0634

Solubility Water: 1 part in 2000 parts water. Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral dog, rabbit 6000 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 1650 mg kg^{-1} (3).

LD_{50} oral mouse 6000-8000 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Dogs fed 700 mg kg^{-1} day^{-1} for 90 days suffered no ill-effects (5).

Rats fed 140 mg kg^{-1} showed no ill-effects, but some growth stimulation occurred after 18 months. Growth retardation occurred when rats were fed 1600 mg kg^{-1} day^{-1} (4).

Carcinogenicity and chronic effects

Six-wk-old Syrian golden hamsters were given a diet containing 3% for 20 wk. The compound had no carcinogenic effect (6).

Metabolism and toxicokinetics

Oral dog 1 g kg^{-1}. The compound was readily hydrolysed with peak tissue concentration 6 hr after administration; after 48 hr the compound was completely eliminated. The compound is hydrolysed in the liver, kidney and muscle, but not in other tissues. When administered to mice, rats, rabbits and dogs is excreted in the urine as the unchanged compound, 4-hydroxybenzoic acid, 4-hydroxyhippuric acid, ester glucuronides, ether glucuronides and ether sulfates (7).

Sensitisation

Immediate hypersensitivity reactions can occur following injection of preparations containing the compound. Delayed contact dermatitis occurs more frequently following topical administration. Patients who have reacted to the compound with contact dermatitis can apply it to another unaffected site and not suffer a reaction; this is termed the paraben paradox (8).

Predicted to be non-sensitising in the murine local lymph node assay and in guinea pig tests (Buchler test and guinea pig maximisation test) (9).

Genotoxicity

Salmonella typhimurium TA98, TA100 negative (metabolic activation not specified) (10).
Salmonella typhimurium negative (strains and metabolic activation not specified) (11).

Other comments

Electron attachment rate constant k_e of 2.0 indicates the compound is non-carcinogenic (12).
Experimental toxicology and human health effects reviewed (13).

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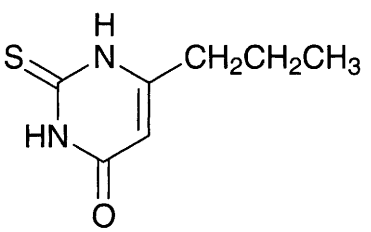
P337 6-propyl-2-thiouracil



$C_7H_{10}N_2OS$ **Mol. Wt.** 170.24 **CAS Registry No.** 51-52-5

Synonyms 2,3-dihydro-6-propyl-2-thioxo-4(1*H*)-pyrimidinone; Propacil; PTU; Thyreostat II

EINECS No. 200-103-2 **RTECS No.** YR 1400000

Uses Antithyroid agent.

Physical properties

M. Pt. 219-221°C

Solubility Water: 1 in 900 at 20°C and 1 in 60 in boiling water. Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1980 mg kg^{-1} (1).

LD_{Lo} intraperitoneal rat 400 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (3).

Produced thyroid tumours in mice, rats, hamsters and guinea pigs following oral administration; pituitary adenomas were also observed in mice (4).

Oral dog (6.5-8 months) 21-33 mg kg^{-1} day^{-1}, only hyperplasia of the thyroid gland was observed (4).

Teratogenicity and reproductive effects

A case of goitre in a newborn infant resulting from the mother's ingestion of 6-propyl-2-thiouracil has been reported (5).

Metabolism and toxicokinetics

$t_{1/2}$ in human plasma 2.5 hr and in rat plasma 4.8 hr. In rats, 75-90% of the ^{14}C-labelled compound administered orally, intravenously or intraperitoneally was excreted in the urine within 24 hr with 14% excreted in the bile as a glucuronide. Placental transfer has been demonstrated in guinea pigs (4).

Crosses the placenta and is excreted in breast milk. The compound is absorbed from the gastro-intestinal tract with peak plasma concentrations occurring 1-2 hr after oral administration. It is concentrated in the thyroid gland and is 75-80% bound to plasma proteins. Metabolisation occurs mainly in the liver and >50% is excreted in urine as the glucuronic acid conjugate and <2% as the unchanged drug (6).

Other effects

Other adverse effects (human)

A case of acute myeloblastic leukaemia has been reported following treatment with the compound (7).

The most common side-effect due to the compound is a mild leucopenia, which occurs in up to 26% of patients; other minor side-effects include nausea, vomiting and skin rashes. The most serious adverse effect is agranulocytosis with an incidence of 0.1-1.0%. The compound has also been implicated in hepatitis and hepatic necrosis with some fatalities. Other side-effects sometimes observed include fever, arthralgia, a lupus-like syndrome, vasculitis and nephritis, taste disturbances and abnormal hair loss (6).

Other comments

Not reported to occur in nature (4).

Cases treated with the compound have been reviewed, with discussion on the adverse effects of the treatment (8).

Hazards related to the compound have been reviewed (9).

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P338 propyne

$$CH_3C{\equiv}CH$$

C_3H_4 **Mol. Wt.** 40.06 **CAS Registry No.** 74-99-7

Synonyms allylene; methylacetylene; propine

EINECS No. 200-828-4 **RTECS No.** UK 4250000

Uses Organic synthesis. Welding torch fuel.

Physical properties

M. Pt. −104°C **B. Pt.** −23.3°C **Flash point** −51°C **Specific gravity** 1.787 at 0°C
Volatility v.p. 3876 mmHg at 20°C ; v.den. 1.38
Solubility Water: 3640 mg l^{-1} at 20°C. Organic solvents: benzene, chloroform, ethanol

Occupational exposure

DE-MAK 1000 ppm (1700 mg m^{-3})
FR-VME 1000 ppm (1650 mg m^{-3})
US-TWA 1000 ppm (1640 mg m^{-3})

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Inhalation rat (6 month) 29,000 ppm 6 hr day^{-1} 5 days wk^{-1}. 8/20 rats died. Signs of toxicity included excitement, ataxia, salivation, mydriasis and tremors (1).

Other comments

Occurs in exhaust gases of diesel engines and in cigarette smoke (2,3).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

References

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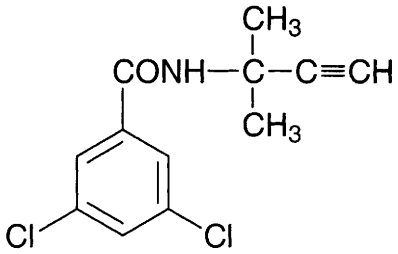
P339 propyzamide



$C_{12}H_{11}Cl_2NO$ **Mol. Wt.** 256.13 **CAS Registry No.** 23950-58-5

Synonyms 3,5-dichloro-*N*-(1,1-dimethyl-2-propynyl)-benzamide; kerb; pronamide; RH 315

EINECS No. 245-951-4 **RTECS No.** CV 3460000

Uses Selective systemic herbicide.

Physical properties

M. Pt. 155-156°C **Partition coefficient** log P_{ow} 3.05-3.27 (1) **Volatility** v.p. 85×10^{-5} mmHg at 25°C
Solubility Water: 15 ppm at 25°C. Organic solvents: aliphatic and aromatic solvents

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, guppy, goldfish 72-350 mg l^{-1} (2).

Invertebrate toxicity
Not dangerous to bees; LD_{50} >100 μg bee^{-1} (3).

Environmental fate

Degradation studies
Soil $t_{1/2}$ ~30 days at 25°C. Principal degradation product is 2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methyleneoxazoline (2).
Following application of 1-4 kg ha^{-1} duration of residual activity in soil is 2-6 months (2).
Biodegradation in plants and soil has been studied (4).
In soil the compound is cyclised to 2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-2-oxazoline, which is subsequently hydrolysed to *N*-(1,1-dimethylacetonyl)-3,5-dichlorobenzamide; several other metabolites are also formed. When the compound is applied to alfalfa the rate of metabolism is slow, but most of the metabolites identified in soil could be found in the plant (5).
13% of the compound applied to non-sterilised soil for 33 days at 25°C was metabolised to CO_2; no CO_2 was formed in sterilised soil (6).
Soil $t_{1/2}$ 10-120 days in aerobic soil. Degradation does not depend on soil texture but is enhanced by increasing soil temperature, soil moisture and pH. Soil sterilisation greatly reduced the degradation rate (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral duck >14 g kg^{-1} (2).
LD_{50} oral dog >10 g kg^{-1} (2).
LD_{50} oral ♀, ♂ rat 5620, 8350 mg kg^{-1}, respectively (2).
LC_{50} inhalation rat >5 mg l^{-1} (no duration given) (2).
LD_{50} percutaneous rabbit >3160 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Rats survived feeding at 4050 mg kg^{-1} diet for 3 months (2).

Carcinogenicity and chronic effects

♂, ♀ mice were fed 0, 1000 or 2000 ppm for 78 wk. Mice ingesting 1000 ppm gained slightly less weight than controls while mice ingesting 2000 ppm gained significantly less weight. Liver weights were increased in all treated mice. 33/99 ♂ mice receiving 2000 ppm and 21/100 mice receiving 1000 ppm developed neoplasms of the liver; 7/100 control ♂ mice also had hepatic neoplasms. Liver carcinomas were seen in 24/99 ♂ mice administered the high concentration, 18/100 ♂ mice administered the lower dose and 7/100 control mice. Treated ♀ mice did not develop an increased incidence of hepatic neoplasms. Hepatic lesions including adenomatous hyperplasia, degeneration, hyperplasia, intrahepatic cholestatis and necrosis were seen in ♂ mice without liver carcinomas; these lesions were not observed in ♀ mice. Most of the tumours found outside the liver were lymphomas. 22/99 ♂ mice given the high dose, 19/100 mice given the low dose and 8/100 control ♂ mice developed malignant neoplasms at all sites (7).

♂, ♀ rats were fed 0, 30, 100 or 300 ppm for 2 years. Treated ♀ gained less weight than controls and an increase in white blood cell counts and polymorphonuclear leukocytes was seen in some treated animals. 5/21 ♀ rats receiving 300 ppm, 3/22 ♀ rats receiving 100 ppm and 1/12 control ♀ rats developed benign and malignant neoplasms at all sites. Both control and treated ♀ rats developed neoplasms of the mammary gland and pituitary. Control animals suffered from chronic renal disease making it difficult for the authors to draw conclusions about the carcinogenicity of the compound (7).

Long-term exposure of rats to propyzamide 48.8 mg kg^{-1} day^{-1} in carcinogenicity studies resulted in ovarian histopathology in addition to thyroid and liver histopathology. Testis, thyroid and liver tumours were seen at ≥8.46 mg kg^{-1} day^{-1} (8).

Dogs were fed 0, 30, 100 or 300 ppm for 2 years. 2 ♂ dogs given the compound had chronic thyroiditis and 1 given the highest dose had chronic liver disease. Abnormal blood glucose and a decrease in the weight of the spleen were also seen in treated dogs which could not be explained (7).

Teratogenicity and reproductive effects

Oral rabbit (days 7-19 gestation) 0, 5, 20 or 80 mg kg^{-1} day^{-1}. At 80 mg kg^{-1} day^{-1} an increased incidence of gross and microscopic liver lesions, one maternal death, five abortions and a significant decrease in maternal body weight were observed. Anorexia, slight decrease in body weight and vacuolation of hepatocytes were seen at 20 mg kg^{-1}. There were no compound-related effects on the incidence of resorptions, foetal death or foetal body weight at any dose tested (1).

Gavage ♀ rat (6-16 day gestation) 0, 7.5 or 15 mg kg^{-1} day^{-1}. No adverse effects were reported for the mean number of implantation sites, the number of live or dead foetuses or the mean foetal body weight (1).

Metabolism and toxicokinetics

Following oral administration to rats and cows, 50% was recovered metabolised in rat faeces and 1% in rat urine; none of the compound was found in cow urine. Several metabolites were identified (9).

Irritancy

Slightly irritating to eyes and skin (no species given) (2).

Dermal rabbit (24 hr) 500 mg caused no irritation. In a similar study erythema was observed which subsided after 72 hr (1).

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 (3).

ADI 0.08 mg kg^{-1} (3).

Other comments

Has been found in groundwater (1).
Considered an endocrine disruptor in the female (13).
Metabolic pathways reviewed (14).

References

1. *Drinking Water Health Advisory – Pesticides* 1989, Lewis Publishers, Chelsea, MI, USA.
2. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
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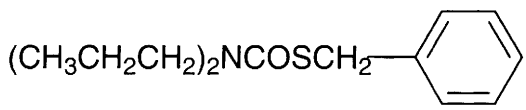
P340 prosulfocarb



$C_{14}H_{21}NOS$ **Mol. Wt.** 251.39 **CAS Registry No.** 52888-80-9

Synonyms *S*-benzyl dipropylthiocarbamate; *S*-(phenylmethyl) dipropyldicarbamothioate
Uses Herbicide.

Physical properties

M. Pt. –10°C **B. Pt.** 129°C at 33 Pa **Specific gravity** 1.042 **Partition coefficient** log P_{ow} 4.65 at 25°C
Volatility v.p. 0.069 mPa at 25°C
Solubility Water: 13.2 mg l^{-1} at 20°C. Organic solvents: acetone, chlorobenzene, ethanol, ethyl acetate, kerosene, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout 4.2, 1.7 mg l^{-1}, respectively (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* >120 mg^{-1} (1).
LD_{50} (48 hr) oral and contact bees >100 μg bee^{-1} (1).
LC_{50} (14 day) earthworms >1000 mg kg^{-1} (1).

Environmental fate

Degradation studies

Repeated treatments, each of 4 kg prosulfocarb ha^{-1}, made during the year preceding the sowing of barley increased the rate of soil biodegradation of prosulfocarb made just before sowing compared with the rate in field plots that had not been treated with prosulfocarb in the past (2).

Abiotic removal

Undergoes hydrolytic decomposition in soil, DT_{50} 10-35 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂ rats 1820, ♀ rats 1958 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation >4.7 mg l^{-1} (1).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral mallard ducks, bobwhite quail no-observed-effect level (5 day) 3160, 1780 mg kg^{-1}, respectively (1).
Oral rats and dogs no-observed-effect level for sub-chronic toxicity (duration unspecified) 1-10 mg kg^{-1} daily (1).

Carcinogenicity and chronic effects

Oral rats (2 yr) no-observed-effect level 0.5 mg kg^{-1} daily (1).
Oral mice (18 months) no-observed-effect level > 65 mg kg^{-1} daily (1).

Teratogenicity and reproductive effects

Non-teratogenic in rats and rabbits (1).

Irritancy

Slight to mild irritation to skin and eyes of rabbit (1).

Sensitisation

Not a skin sensitiser in guinea pigs (1).

Genotoxicity

Non-mutagenic in the Ames test (1).

Legislation

WHO Toxicity Class II (3).
Limited under EC Directive on Drinking Water Quality 80/788/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedules 5 and 6 (Release into Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

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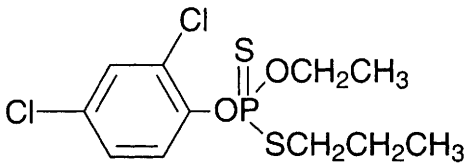
P341 prothiofos



$C_{11}H_{15}Cl_2O_2PS_2$ **Mol. Wt.** 345.25 **CAS Registry No.** 34643-46-4

Synonyms phosphorodithioic acid, *O*-(2,4-dichlorophenyl) *O*-ethyl *S*-propyl ester; dichlorpropaphos; prothiophos; Tokuthion; Toyodan; Bideron

EINECS No. 252-125-7 **RTECS No.** TD 5680000

Uses Non-systemic insecticide with contact and stomach action.

Physical properties

B. Pt. 125-128°C at 0.1 mmHg **Specific gravity** 1.3 at 20°C **Partition coefficient** log P_{ow} 5.67 at 20°C
Solubility Water: 0.07 mg l^{-1} at 20°C. Organic solvents: cyclohexanone, dichloromethane, isopropanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) golden orfe, goldfish, rainbow trout 4-8, 6-20, 0.5-1 mg l^{-1}, respectively (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia* 0.014 mg l^{-} (2).
EC_{50} (growth rate) *Scenedesmus subscpicatus* 2.3 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 940 mg kg^{-1} (3).
LD_{50} oral ♂ rat 1500 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >2.7 mg l^{-1} air (1).
LD_{50} dermal ♂ rat >5000 mg kg^{-1} (1).
LD_{50} dermal mouse, rat 1600, 3900 mg kg^{-1}, respectively (4).

Sub-acute and sub-chronic data

In 90-day feeding trials, no-effect level for rats was 8 mg kg^{-1} diet (1).

Other effects

Any other adverse effects

Cytochrome P_{450} and cytochrome b levels in rats decreased by 44.7 and 33.6%, respectively, following exposure to 12.2 mg m^{-3} for 4 months. However, levels of cytochrome P_{450} increased by 30% after exposure to 5.9 mg m^{-3} for 4 months. Levels of glucose 6-phosphatase were low after exposure to 5.9 and 12.2 mg m^{-3} and NADPH-cytochrome C reductase was lowered by the higher concentration. The enzyme levels returned to normal after 1 month, suggesting only mild cumulative effects (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).

Log P_{ow} exceeds the European Community recommended limit of 3.0 (8).
WHO Toxicity Class II (9).
EPA Toxicity Class III (2).

Other comments

Not dangerous to bees if used as recommended (1).

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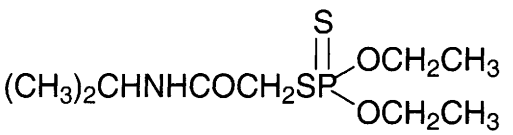
P342 prothoate



$C_9H_{20}NO_3PS_2$ **Mol. Wt.** 285.37 **CAS Registry No.** 2275-18-5

Synonyms phosphorodithioic acid, *O,O*-diethyl *S*-[2-[(1-methylethyl)amino]-2-oxoethyl] ester; phosphorodithioic acid, *O,O*-diethyl ester, *S*-ester with *N*-isopropyl-2-mercaptoacetamide; *O,O*-diethyl *S*-isopropylcarbamoylmethyl phosphorodithioate; Fostion

EINECS No. 218-893-2 **RTECS No.** TD 8225000

Uses Superseded acaricide and insecticide.

Physical properties

M. Pt. 28.5°C **Flash point** 160°C **Specific gravity** 1.151 at 32°C **Volatility** v.p. 97.76×10^{-6} mmHg at 40°C
Solubility Water: 2.5 g l^{-1} at 20°C. Organic solvents: miscible with most organic solvents

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)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) goldfish, trout 33, 20 mg l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail 22.5 mg kg^{-1} (1).
LD_{50} oral pheasant, mallard duck 12-19 mg kg^{-1} (2).
LD_{50} oral ♂, ♀ rat 8, 8.9 mg kg^{-1}, respectively (1).
LD_{50} oral mouse 19.8-20.3 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat 2.9 μg l^{-1} air (1).
LD_{50} percutaneous rat 655 mg kg^{-1} (1).
LD_{50} percutaneous rabbit 100-200 mg kg^{-1} (1).

Sub-acute and sub-chronic data

In 90-day feeding trials no-effect level for rats was 0.5 mg kg^{-1} day^{-1} and for mice 1 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} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).
EPA Toxicity Class I (1).

Other comments

Dangerous to bees (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, 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

P343 proxan-sodium

$$(CH_3)_2CHOC(S)SNa$$

$C_4H_7NaOS_2$ **Mol. Wt.** 158.22 **CAS Registry No.** 140-93-2

Synonyms sodium isopropylxanthate; isopropylxanthic acid, sodium salt

EINECS No. 205-443-5 **RTECS No.** FG 1581500

Uses Control of annual weeds in bean and pea crops.

Physical properties

M. Pt. 124°C
Solubility Water: 46% at 24°C. Organic solvents: acetone

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to the skin (R22, R38)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs (S2, S13)

Mammalian & avian toxicity

Acute data
LD_{Lo} parenteral mouse 600 mg kg^{-1} (1).

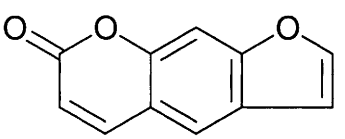
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (2).

References

1. *Summary Tables of Biological Tests* 1955, **7**, 696, Natl. Res. Council Chem.-Biol. Coord. Center.
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

P344 psoralen



$C_{11}H_6O_3$ **Mol. Wt.** 186.17 **CAS Registry No.** 66-97-7

Synonyms 7*H*-furo[3,2-*g*][1]benzopyran-7-one; 6,7-furanocoumarin; furo[2′,3′:7,6]coumarin; furo[4′,5′:6,7]coumarin

EINECS No. 200-639-7 **RTECS No.** LV 0944000

Uses As photochemical probe in biological systems. Photosensitising drug.

Physical properties

M. Pt. 158-161°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects
A CASE study predicted marginal carcinogenic properties (probability 57%) (1).

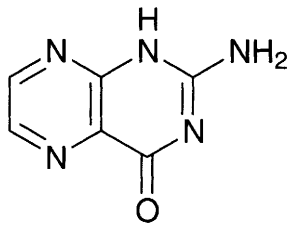
Genotoxicity

Escherichia coli lac$^-$ positive in the absence of light (2).

References

1. Rosenkranz, H. S. et al *Carcinogenesis (London)* 1990, **11**(2), 349-353.
2. Ashwood-Smith, M. J. et al *Mutat. Res.* 1978, **58**, 23-27

P345 pterin



$C_6H_5N_5O$ **Mol. Wt.** 163.14 **CAS Registry No.** 2236-60-4

Synonyms 2-amino-4(1*H*)-pteridinone; 2-amino-4(3*H*)-pteridinone; enol-pterin; 4-oxopterin; pteridoxamine

EINECS No. 218-799-1 **RTECS No.** UO 3505000

Mammalian & avian toxicity

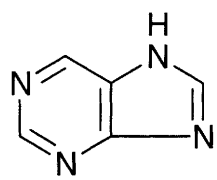
Metabolism and toxicokinetics

Metabolites were determined in human blood and lymphoid cells (erythrocytes, platelets, thymocytes, etc.). High concentrations of pteridines were found in bone marrow cell fractions indicating intensive pterin metabolism in these cells. Lymphocytes had the highest neopterin levels of the white blood cells investigated. Biopterin levels were constant in all white blood cells, except for thymocytes and lymphocytes from tonsils where levels were increased (1).

References

1. Andondonskaja-Renz, B. et al *Biochem. Clin. Aspects Pteridines* 1987, **5** (Cancer, Immunol., Metab. Dis. 83-95)

P346 purine



$C_5H_4N_4$ **Mol. Wt.** 120.11 **CAS Registry No.** 120-73-0

Synonyms 1*H*-purine; β-purine; isopurine; 7*H*-purine; 9*H*-purine; 3,5,7-triazaindole; 1*H*-imidazo[4,5-*d*]pyrimidine

EINECS No. 204-421-2 **RTECS No.** UO 7450000

Physical properties

M. Pt. 216-217°C

Solubility Water: freely soluble. Organic solvents: acetone, hot ethanol, hot ethyl acetate

Mammalian & avian toxicity

Acute data

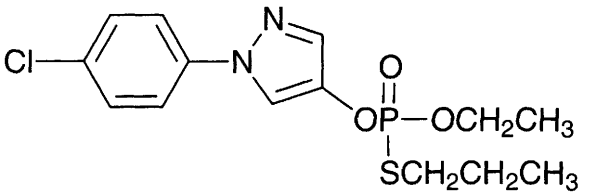
LD_{Lo} intraperitoneal rat 800 mg kg^{-1} (1).

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

References

1. *Clinical Proceedings of the Children's Hospital of the District of Columbia* 1962, **18**, 307.
2. *J. Med. Chem.* 1963, **6**, 480

P347 pyraclofos



$C_{14}H_{18}ClN_2O_3PS$ **Mol. Wt.** 360.80 **CAS Registry No.** 77458-01-6

Synonyms (*RS*)-[*O*-1-(4-chlorophenyl)pyrazol-4-yl *O*-ethyl *S*-propyl phosphorothioate]; (±)-*O*-[1-(4-chlorophenyl)-1*H*-pyrazol-4-yl] *O*-ethyl *S*-propyl phosphorothioate

Uses Insecticide used in the control of Lepidoptera, Coleoptera, Acarina, and nematodes in fruit, vegetables, field crops, ornamentals and in forestry. Also used in public health.

Physical properties

B. Pt. 164°C at 0.01 mmHg **Specific gravity** 1.271 at 28°C **Partition coefficient** log P_{ow} 3.77 at 20°C

Volatility v.p. 1.2×10^{-8} mmHg

Solubility Water: 33 mg l^{-1} (20°C). Organic solvents: miscible with most organic solvents

Ecotoxicity

Fish toxicity

LC_{50} (72 hr) carp, Japanese killifish 0.028, 1.9 mg l^{-1}, respectively (1).

Invertebrate toxicity

LD_{50} (contact) honeybees 0.953 μg bee^{-1} (1).

Environmental fate

Degradation studies

Half-life in soil at room temperature, under aerobic and anaerobic conditions, 50 days (1).

Mammalian & avian toxicity

Acute data

LC_{50} oral bobwhite quail, mallard ducks 164 and 348 mg kg^{-1} in diet, respectively (1).

LD_{50} rats, ♂ mice, and ♀ mice 237, 575, and 420 mg kg^{-1}, respectively (1).

LC_{50} inhalation rats, ♂ 1.69, ♀ 1.46 mg l^{-1} (duration unspecified) (1).

LD_{50} dermal rat >2000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
No-observed-effect level (2 years) rats, mice 0.101 and 1.03 mg kg^{-1} daily, respectively (1).

Metabolism and toxicokinetics
Following oral administration in rats, >90% of the dose is eliminated within 24 hr, principally in the urine (1).

Irritancy
Non-irritating to the skin and eyes of rabbits (1).

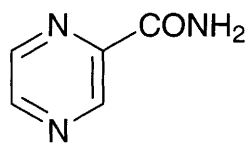
Legislation

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).

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

P348 pyrazinamide



$C_5H_5N_3O$ **Mol. Wt.** 123.11 **CAS Registry No.** 98-96-4

Synonyms 2-carbamoylpyrazine; pyrazinecarboxamide; pyrazinoic acid amide; Aldinamide; D-50; Eprazin; Pezetamid; Pyrafat; Tebrazid; Zinamide

EINECS No. 202-717-6 **RTECS No.** UQ 2275000

Uses Antibacterial agent used in treatment of tuberculosis.

Physical properties

M. Pt. 189-191°C
Solubility Water: 15 g l^{-1}. Organic solvents: chloroform, diethyl ether, ethanol, isooctane, isopropanol, methanol

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat, mouse 3000 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 2800 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 1700 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Gavage rat 50, 1500 or 2500 mg kg^{-1} day^{-1} for 14 days induced biliary and metabolic disorders in bile and metabolism in a dose-dependent manner. The high dose also increased the activities of alanine and aspartate aminotransferases in the blood and initiated lipid peroxidation (4).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice for carcinogenicity via feed. Negative results were reported in ♂ and ♀ rats and in ♂ mice. The study of carcinogenic activity in ♀ mice was considered inadequate (5).

Metabolism and toxicokinetics

Metabolites identified in human plasma included pyrazinoic acid, 5-hydroxypyrazinoic acid, and unchanged pyrazinamide following an oral dose of 500 mg (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).
In vitro human peripheral lymphocytes, chromosome aberrations positive (8).

Other effects

Other adverse effects (human)

Hepatotoxicity is the most serious side-effect of pyrazinamide therapy. Its frequency appears to be dose related (9).

Hyperuricaemia has been reported. This may be due to inhibition of uric acid excretion by the metabolite pyrazinoic acid (9).

Pellagra has also been reported (10).

References

1. *Am. Rev. Tuberculosis* 1954, **70**, 423.
2. *Drugs in Japan: Ethical Drugs* 6th ed., 1982, 641, Jakugyo Jiho Co., Tokyo, Japan.
3. *Chemotherapia* 1962, **5**, 39.
4. Slivka, Y. I. *Probl. Tuberk.* 1988, (10), 47-50 (Russ.) (*Chem. Abstr.* **110**, 128131a).
5. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-048, NIEHS, Research Triangle Park, NC, USA.
6. Gaitorde, C. D. et al *Indian Drugs* 1990, **27**(8), 436-437.
7. Zeiger, E. et al *Environ. Mol. Mutagen.* 1987, **9** (Suppl. 9), 1-109.
8. Roman, I. C. et al *Mutat. Res.* 1977, **48**(2), 215-224.
9. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
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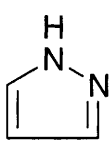
P349 pyrazole



$C_3H_4N_2$ **Mol. Wt.** 68.08 **CAS Registry No.** 288-13-1

Synonyms 1,2-diazole; 1*H*-pyrazole

EINECS No. 206-017-1 **RTECS No.** UQ 4900000

Uses Organic synthesis; inhibitor of alcohol dehydrogenase activity.

Physical properties

M. Pt. 67-70°C **B. Pt.** 186-188°C **Partition coefficient** log P_{ow} 0.02 (1)
Solubility Water: miscible. Organic solvents: benzene, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (48 hr) *Tetrahymena pyriformis* 130 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >100 mg kg^{-1} (2).
LD_{50} oral rat, mouse 1000, 1500 mg kg^{-1}, respectively (3,4).
LD_{50} intraperitoneal mouse 540 mg kg^{-1} (5).

Teratogenicity and reproductive effects
Intraperitoneal mouse, lowest toxic dose 24 mg kg^{-1} day^{-1} on days 8-14 of gestation (foetotoxicity) (6).
Oral rat, lowest toxic dose 100 mg kg^{-1}, on day 9 of gestation (foetotoxicity and teratogenic effects) (7).

Metabolism and toxicokinetics
Oxidised by rat liver microsomes to 4-hydroxypyrazole, to which several physiological actions of pyrazole have been ascribed (8).

Irritancy
Irritating to the skin, eyes, mucous membranes and upper respiratory tract (species unspecified) (9).

Genotoxicity

Salmonella typhimurium BA9, BA13 L-arabinose resistance test with and without metabolic activation negative (10).
Drosophila melanogaster sex-linked recessive lethal assay positive (11).

Other effects

Any other adverse effects
Inhibits liver alcohol dehydrogenase (12).
Increases hepatic microsomal coumarin 7-hydroxylase through an increase of microsomal $P_{450}C_{oh}$ (13).
Reported to induce thyroid necrosis (14).

References

1. Ebert, C. et al *Quant. Struct. – Act. Relat.* 1991, **10**(2), 101-106.
2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
3. Magnussen, G. et al *Experientia* 1972, **28**, 1198.
4. *J. Am. Pharm. Soc.* 1958, **47**, 70.
5. *J. Pharmacol. Exp. Ther.* 197, **178**, 199.
6. *Teratology* 1982, **25**(2), 43A.
7. *Res. Commun. Chem. Pathol. Pharmacol.* 1979, **26**, 65.
8. Clejan, L. A. et al *Drug Metab. Dispos.* 1990, **18**(4), 393-397.
9. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2987, Sigma-Aldrich, Milwaukee, WI, USA.
10. Alejandre-Duran, E. et al *Environ. Mutagen.* 1986, **8**(4), 611-619.
11. Mikheev, V. S. et al *Genetika (Moscow)* 1989, **25**(3), 561-564 (Russ.) (*Chem. Abstr.* **110**, 226954r).
12. Lelbach, W. *Experientia* 1969, **25**, 816.
13. Kojo, A. et al *Biochem. Pharmacol.* 1991, **42**(9), 1751-1759.
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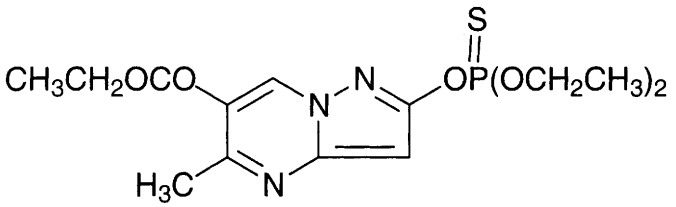
P350 pyrazophos



$C_{14}H_{20}N_3O_5PS$ **Mol. Wt.** 373.37 **CAS Registry No.** 13457-18-6

Synonyms *O*-6-(ethoxycarbonyl)-5-methylpyrazolo[1,5-*a*]pyrimidin-2-yl *O*,*O*-diethyl phosphorothioate; ethyl 2-diethyloxythiophosphoryloxy-5-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate; ethyl 2-[(diethoxyphosphinothioyl)oxy]-5-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxylate; *O*,*O*-diethyl *O*-(5-methyl-6-ethoxycarbonylpyrazolo[1,5-*a*]pyrimid-2-yl)-thionophosphate; Missile; Liafos; Afugan

EINECS No. 236-656-1 **RTECS No.** TF 2035000

Uses Fungicide. Insecticide.

Physical properties

M. Pt. 50-51°C **B. Pt.** 160°C (decomposition begins) **Specific gravity** 1.348 at 25°C
Partition coefficient log P_{ow} 3.8 **Volatility** v.p. 1.65×10^{-6} mmHg at 50°C
Solubility Water: 4.2 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, carbon tetrachloride, dichloromethane, ethanol, ethyl acetate, *n*-hexane, toluene, trichloroethylene, 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, carp 0.5, 6.1 mg l^{-1}, respectively (1).

Invertebrate toxicity
LD_{50} (24 hr) contact 0.25 μg bee^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, quail 120, 780 mg kg^{-1}, respectively (1-3).
LD_{50} dermal rat >2000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 5 mg kg^{-1} diet (1).
Oral rat, four-generations, 50 mg kg^{-1} diet caused no adverse effects (1).

Other effects

Any other adverse effects
Inhibits cholinesterase activity (species unspecified) (1).

Legislation

EEC maximum residue limits: pome fruit 0.3 ppm; cucurbits, stone fruit 0.1 ppm (1).
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 Community recommended limit of 3.0 (6).
WHO Toxicity Class II (7).
EPA Toxicity Class II (formulation) (2).
ADI 0.004 mg kg^{-1} body weight (2).

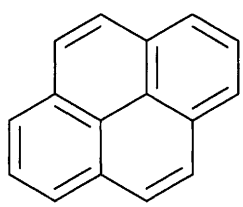
Other comments

In plants undergoes hydrolysis of the phosphate bond followed by formation of a β-glucoside pyrazolopyrimidine (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. Smit, F. M. *Meded. Rijksfac. Landbouwwet. Gent.* 1969, **34**, 763.
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. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

P351 pyrene



$C_{16}H_{10}$ **Mol. Wt.** 202.26 **CAS Registry No.** 129-00-0

Synonyms benzo[*def*]phenanthrene; β-pyrene

EINECS No. 204-927-3 **RTECS No.** UR 2450000

Occurrence In fossil fuels. Occurs ubiquitously in products of incomplete combustion, including tobacco smoke and fossil fuel emissions.

Physical properties

M. Pt. 149-151°C **B. Pt.** 404°C **Specific gravity** 1.271 at 23°C **Partition coefficient** log P_{ow} 5.00
Solubility Water: 150 μg l^{-1}. Organic solvents: acetone, benzene, carbon disulfide, diethyl ether, ethanol, toluene

Ecotoxicity

Fish toxicity

Saturated solution was not toxic to fathead minnow in 24 hr (1).

Fatal to brown trout at 5 ppm after 24 hr. Toxic effects were observed in bluegill sunfish, yellow perch and goldfish under the same conditions (2).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 1.8 mg l^{-1} (3).

Pyrene was not toxic at saturation to *Tetrahymena pyriformis* (16 hr) in the dark, but illumination with UVB radiation caused 100% mortality in 56 minutes (4).

The phototoxicity (as measured by LC_{50}s and EC_{50}s) of pyrene 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 27.6, >51,900 and >5620, respectively (5).

Bioaccumulation

Reported bioconcentration factors for rainbow trout, goldfish and fathead minnow are 72, 457 and 600-970 respectively (6-8).

Environmental fate

Anaerobic effects

Not inhibitory to anaerobic digestion at 1 mg l^{-1} (9).

Degradation studies

Utilised as sole carbon source by *Rhodococcus* and *Mycobacterium* species isolated from soil and sediments (10,11).

Mycobacterium sp., strain KR2 isolated from PAH-contaminated soil, utilised pyrene as sole carbon source. 60% of a 0.5 mg ml^{-1} dose was metabolised within 8 days at 20°C (12).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 800, 2700 mg kg^{-1}, respectively (13).

LC_{50} inhalation rat 170 mg m^{-3} (exposure not specified) (9).

LD_{50} intraperitoneal mouse 510-680 mg kg^{-1} (14).

Sub-acute and sub-chronic data

Oral rat, 2000 mg kg^{-1} diet for 100 days caused a reduction in growth rate. Livers were enlarged and of fatty appearance (15).

Tracheal implant in rat (dose and duration not specified) caused goblet-cell hyperplasia and cases of transitional hyperplasia (16).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (17).

Dermal mouse, 12 or 40 μg $animal^{-1}$ 3 × wk^{-1}. After 368 and 440 days of treatment, respectively, no change was observed at the site of application (18).

Dermal mouse 60 μl of 5% solution in decalin 2 × wk for 82 wk. Papillomas developed in 3/13 mice at 52 wk. In mice given the same dose in a decalin-*n*-dodecane vehicle 2 papillomas and 2 carcinomas developed in 13 mice after 82 wk, compared with 2/13 papillomas among controls (19).

Dermal mouse (study of initiating activity) 10 × 25 mg animal 3 × wk^{-1} starting 25 days after the last treatment, the animals received 18 wkly applications of 0.3 ml of 0.17% croton oil. At the end of the treatment with croton oil 6/20 animals developed papillomas, compared with 4/19 among the croton oil control group (20).

Subcutaneous mouse (18 months) 10 mg $animal^{-1}$ repeated 4 months later. 23/30 mice survived 1 yr and 9/30 survived 18 months. No subcutaneous tumour occurred. The average number of pulmonary tumours in the mice at 18 months was reported to be only 1.6 (21).

Intraperitoneal hamster (90 wk) 0.1 mg animal^{-1} wk^{-1} for 30 wk. 24/48 animals survived 50 wk and 7/48 survived 90 wk. One tumour of the trachea and 2 malignant lymphomas were observed among all the treated hamsters. No respiratory tract tumours occurred in 82 controls, while a high incidence was reported among positive controls treated with dibenzo[*a,i*]pyrene (22).
Transplacental exposure in mice, subcutaneous injection of 6 mg day^{-1} on days 18 and 19 of gestation did not induce an increase in tumour incidence in studies in which benzo[*a*]pyrene did have that effect (23).

Teratogenicity and reproductive effects
Intramuscular mouse, 4 mg day^{-1} during final wk of gestation increased survival, and hyperplastic changes were seen in explants of embryonic mouse kidney *in vitro*. These effects were similar but less marked than those produced by benzo[*a*]pyrene (24).

Metabolism and toxicokinetics
The 1-hydroxy-, 1,6- and 1,8-dihydroxy-, and the 4,5-dihydrodiol-, metabolites of pyrene have been identified in rats and rabbits (25).
Conversion of pyrene into 1-hydroxypyrene by rat liver post-mitochondrial fractions, Vmax 0.0577 ± 0.0108 μmol min^{-1} g^{-1} liver, Km 27.73 ± 13.54 μM. Intrinsic clearance in the rat 0.041-0.111 l min^{-1} kg^{-1} (26).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation (27).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (28).
Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (29).
Escherichia coli WP20 (λ), microscreen assay negative (30).
Drosophila melanogaster sex-linked recessive lethal assay negative (31).
In vitro mouse lymphoma L5178Y cells tk$^+$/tk$^-$ forward mutation assay positive (metabolic activation unspecified) (32).
In vitro Chinese hamster V79 lung cells, sister chromatid exchanges and chromosome aberrations positive (metabolic activation unspecified) (33).
In vivo rat and mouse hepatocytes DNA damage negative (34).
In vitro primary rat hepatocytes, chromosomal aberrations and sister chromatid exchanges negative (35).
In vivo mouse bone marrow cells sister chromatid exchanges negative (36).
In vivo mouse bone marrow cells, micronucleous assay negative (14).

Legislation

The log P_{ow} value exceeds the European Community recommended level of 3.0 (Directive on Classification, Packaging and Labelling of Dangerous Substances, 6th and 7th Amendments) (37).

Other comments

Residues have been identified in natural and drinking waters, sediments and fish (38,39).
Physical properties, occurrence, carcinogenicity, mammalian toxicity metabolism and mutagenicity reviewed (38,40).

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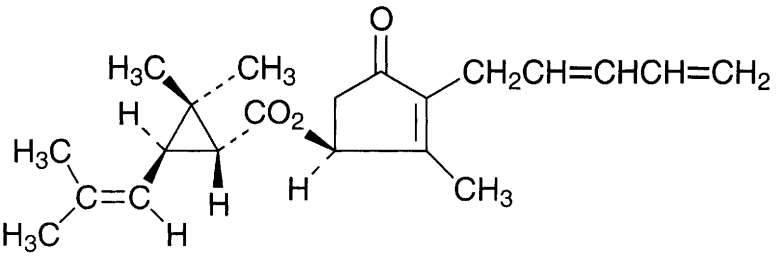
P352 pyrethrin I



$C_{21}H_{28}O_3$ **Mol. Wt.** 328.45 **CAS Registry No.** 121-21-1

Synonyms chrysanthemummonocarboxylic acid, pyrethrolone ester; (*Z*)-(*S*)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (1*R*)-*trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate

EINECS No. 204-455-8 **RTECS No.** GZ 1725000

Uses Insecticide. Acaricide.

Occurrence In chrysanthemum plant.

Physical properties

B. Pt. 170°C at 0.1 mmHg (decomp.)

Solubility Organic solvents: dichloromethane, ethanol, kerosene, nitromethane

Occupational exposure

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) – Keep away from food, drink and animal feeding stuffs (S2, S13)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 260 mg kg^{-1} (1).

LD_{Lo} intravenous rat 5 mg kg^{-1} (2).

Sub-acute and sub-chronic data

LC_{50} (5 days) oral Japanese quail, pheasant, mallard duck >5000 mg kg^{-1} diet (3).

Metabolism and toxicokinetics

Metabolised by NADPH-dependent oxidases of mouse liver microsomes, undergoing oxidation at the methyl and ethylene substituents to form alcohols, aldehydes, carboxylic acids and epoxides (4).

Rapidly hydrolysed at the ester bond in the stomach of mammals (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).

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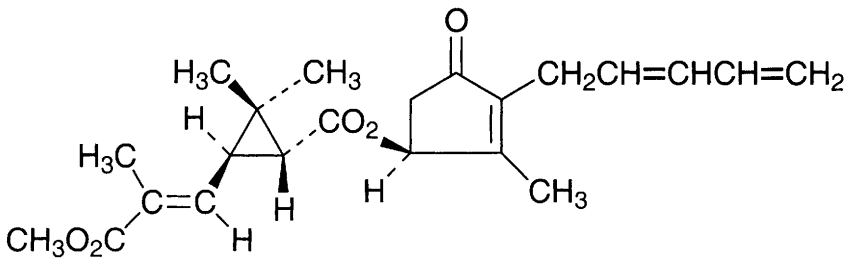
P353 pyrethrin II



$C_{22}H_{28}O_5$ **Mol. Wt.** 372.46 **CAS Registry No.** 121-29-9

Synonyms ENT 7543; (+)-pyrethronyl (+)-pyrethrate; (*Z*)-(*S*)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (*E*)-(1*R*)-*trans*-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate

EINECS No. 204-462-6 **RTECS No.** GZ 0700000

Uses Insecticide. Acaricide.

Occurrence In chrysanthemum plant.

Physical properties

B. Pt. 200°C at 0.1 mmHg (decomp.)

Solubility Organic solvents: dichloromethane, ethanol, kerosene, nitromethane

Occupational exposure

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) – Keep away from food, drink and animal feeding stuffs (S2, S13)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) coho salmon, brown trout, channel catfish, bluegill sunfish, yellow perch, scud, 11-130 μg l^{-1} (1,2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 130, 200 mg kg^{-1}, respectively (3,4).

LD_{50} intravenous rat 1 mg kg^{-1} (5).

Sub-acute and sub-chronic data

LC_{50} (5 days) oral Japanese quail, pheasant, mallard duck >5000 mg kg^{-1} diet (6).

Metabolism and toxicokinetics
Metabolised by mouse liver microsomes undergoing hydrolysis of the methoxycarbonyl group and oxidation of the ethene groups (7).
Rapidly hydrolysed at the ester bond in the stomach of mammals (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).

Other comments

Use, mammalian and environmental toxicity reviewed (2).
Toxicity reviewed (10).

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P354 pyrethrum

CAS Registry No. 8003-34-7

Synonyms Alfadex; Buhach; *Chyrsanthemum cineraeaefolium* chrysanthemates; Kicker; Pyrenone; pyrethrins; Frieste flowers

EINECS No. 232-319-8 **RTECS No.** UR 4200000

Uses Insecticide. Acaricide.
Occurrence In chrysanthemum plant. Pyrethrum or pyrethrins constitute the 6 insecticidal constituents, pyrethrin I and II, cinerin I and II, and jasmolin I and II.

Physical properties

Flash point 76°C
Solubility Organic solvents: ethanol, carbon tetrachloride, dichloromethane, nitromethane, kerosene

Occupational exposure

DE-MAK 5 mg m^{-3} (inhalable fraction or aerosol)
FR-VME 5 mg m^{-3}
UK-LTEL 5 mg m^{-3} **UK-STEL** 10 mg m^{-3}
US-TWA 5 mg m^{-3}

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) brown trout, bluegill sunfish, coho salmon, channel catfish 25-110 mg l^{-1} (static bioassay) (1-3).

Invertebrate toxicity
LC_{50} (96 hr) *Gammarus lacustris, Gammarus fasciatus* 11-12 μg l^{-1} (4).
LC_{50} (48 hr) *Daphnia pulex* 25 μg l^{-1} (5).
LD_{50} bee, oral 22 ng, contact 130-290 ng bee^{-1} (1).

Environmental fate

Abiotic removal
Readily oxidised to become inactive on exposure to air (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 200, 900 mg kg^{-1}, respectively (7-9).
LD_{50} dermal rabbit 5000 mg kg^{-1} (7).
LD_{50} intraperitoneal rat 200 mg kg^{-1} (10).
LD_{Lo} intravenous rat 5 mg kg^{-1} (11).

Teratogenicity and reproductive effects
Oral rat, lowest toxic dose 500 mg kg^{-1} day^{-1} on days 6-15 of gestation (foetal death) (12).

Metabolism and toxicokinetics
Rapidly hydrolysed at the ester bond in the stomach of mammals (13).

Irritancy
Slightly irritating to eyes, mucosa and skin in humans (7,14).

Sensitisation
Dermatitis had been reported in sensitised persons (7,14).

Legislation

EEC maximum residue limits: cereals 3 ppm; fruit and vegetables 1 ppm (7).
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).
WHO Toxicity Class II (17).
EPA Toxicity Class III (formulation) (1).
ADI 0.04 mg kg^{-1} body weight (1).

Other comments

Use, mammalian and environmental toxicity reviewed (18).
Used in synergistic formulations, principally piperonyl butoxide, which are more stable than pyrethrum alone. Toxicity reviewed (19).

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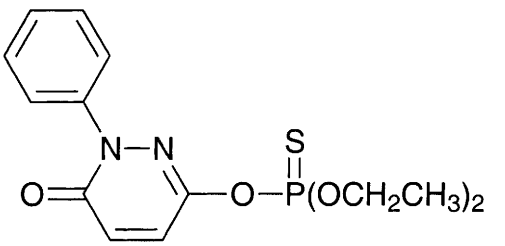
P355 pyridaphenthion



$C_{14}H_{17}N_2O_4PS$ **Mol. Wt.** 340.34 **CAS Registry No.** 119-12-0

Synonyms *O*-(1,6-dihydro-6-oxo-1-phenylpyridazin-3-yl) *O,O*-diethyl phosphorothioate; *O*-(1,6-dihydro-6-oxo-1-phenyl-3-pyridazinyl) *O,O*-diethyl phosphorothioate

EINECS No. 204-298-5

Uses Insecticide, acaricide.

Physical properties

M. Pt. 54.5-56.0°C **Specific gravity** 1.325 at 20°C **Partition coefficient** log P_{ow} 3.2
Volatility v.p. 0.00147 mPa at 20°C
Solubility Water: 100 ppm at 20°C. Organic solvents: acetone, methanol

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) goldfish, loach 11.5, 11 mg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} (3 hr) *Daphnia magna* 0.02 mg l^{-1} (1).

LD_{50} bee 0.08 μg bee^{-1} (1).

Eggs of the predacious mite *Amblyseins gossipi* were placed on leaf discs and sprayed for 40 sec with pyridaphenthion. The eggs were then dried and transferred to new leaf discs. The eggs were highly susceptible to 400 ppm; no development beyond the larval stage occurred (2).

Environmental fate

Degradation studies

In soil DT_{50} 11-24 days (1).

Mammalian & avian toxicity

Acute data

LC_{50} oral Japanese quail 68 mg kg^{-1} (1).

LD_{50} oral ♂ rat, ♀ rat 769, 850 mg kg^{-1}, respectively (3).

LD_{50} oral mouse 459 mg kg^{-1} (3).

LD_{50} dermal rat 2100 mg kg^{-1} (1).

LC^{-1} (4 hr) inhalation ♀ rats 1.1 mg l^{-1} air (1).

LD_{50} intraperitoneal mouse 64 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Oral ♂ rats, ♀ rats (2 yr) no-observed-effect level 0.17, 0.22 mg kg^{-1} diet (1).

Teratogenicity and reproductive effects

No adverse effects observed in teratogenicity studies with rats (1).

Metabolism and toxicokinetics

O-ethyl-*O*-(3-oxo-2-phenyl-2*H*-pyridazine-6-yl) phosphorothioate and the corresponding phosphate are found in mice and rats, along with the parent compound (1).

Genotoxicity

No mutagenic effects observed in studies with rats (1).

Legislation

WHO Toxicity Class III (5).

Limited under EC Directive on Drinking Water Quality 80/788/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).

Included in Schedules 5 and 6 (Release into Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

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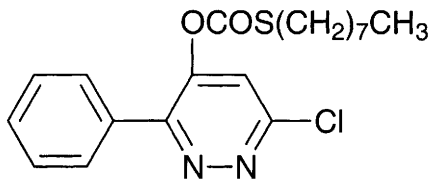
P356 pyridate



$C_{19}H_{23}ClN_2O_2S$ **Mol. Wt.** 378.92 **CAS Registry No.** 55512-33-9

Synonyms 6-chloro-3-phenylpyridazin-4-yl *S*-octyl thiocarbonate; *O*-(6-chloro-3-phenyl-4-pyridazinyl) *S*-octyl thiocarbonate; Lentagran; Tough

EINECS No. 259-686-7 **RTECS No.** FG 3880000

Uses Herbicide.

Physical properties

M. Pt. 27°C **B. Pt.** 220°C at 0.1 mmHg **Flash point** 200°C (open cup) **Specific gravity** 1.16 at 20°C
Partition coefficient log P_{ow} >3.0 **Volatility** v.p. 1×10^{-6} mmHg at 20°C
Solubility Water: 1.5 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) catfish, rainbow trout 48, 80 mg l^{-1}, respectively (1-3).
LC_{50} (96 hr) bluegill sunfish, carp >100 mg l^{-1} (1-3).

Invertebrate toxicity
LD_{50} oral bee >100 μg bee^{-1} (3).
LD_{50} contact bee >160 μg bee^{-1} (3).

Environmental fate

Degradation studies
Undergoes hydrolysis yielding 3-phenyl-4-hydroxy-6-chloropyridazine (1).
Hydrolysis $t_{1/2}$ <1 wk in soil (1).
In biologically active water, rapidly transformed into the same metabolite as in soil, $t_{1/2}$ 16 days (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail, rat, mouse, pheasant 1500, 2000, 10,1000 >10,000 mg kg^{-1}, respectively (1-3).
LC_{50}(4 hr) inhalation rat >4300 mg m^{-3} (1).
LD_{50} dermal rabbit >3400 mg kg^{-1} (1,3).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral Japanese quail >1000 mg kg^{-1} diet (1).
Oral dog (12 month) no-adverse-effect level 8 mg kg^{-1} day^{-1} (1).

Carcinogenicity and chronic effects
Oral rat (28 month) no-adverse-effect level 18 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics
Following oral administration to rats pyridate is rapidly and completely hydrolysed to its principal metabolite 3-phenyl-4-hydroxy-6-chloropyridazine, which is detoxified by formation of *O*- and *N*-glucuronides. The principal metabolite and its conjugates are rapidly and completely excreted (1).

Irritancy
Moderately irritating to skin, non-irritating to rabbit eyes (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).
Log P_{ow} exceeds the European Union recommended limit of 3.0 (6).
WHO Toxicity Class III (7).
EPA Toxicity Class III (formulation) (3).

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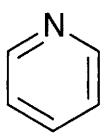
7. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

P357 pyridine



C_5H_5N **Mol. Wt.** 79.10 **CAS Registry No.** 110-86-1
Synonyms azabenzene; azine
EINECS No. 203-809-9 **RTECS No.** UR 8400000

Uses Solvent. Organic synthesis. Fungicide.
Occurrence Aroma component of plants and cooked meat, fish and vegetables. Residues have been identified in drinking and natural waters, soil and air samples (1).

Physical properties

M. Pt. –42°C **B. Pt.** 115°C **Flash point** 20°C (closed cup) **Specific gravity** 0.9780 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.65 **Volatility** v.p. 10 mmHg at 13.2°C ; v.den. 2.73
Solubility Water: miscible. Organic solvents: benzene, diethyl ether, ethanol, petroleum ether

Occupational exposure

DE-MAK 5 ppm (16 mg m^{-3})
FR-VME 5 ppm (15 mg m^{-3})
FR-VLE 10 ppm (30 mg m^{-3})
SE-LEVL 2 ppm (7 mg m^{-3})
SE-STEL 3 ppm (10 mg m^{-3})
UK-LTEL 5 ppm (16 mg m^{-3})
UK-STEL 10 ppm (33 mg m^{-3})
US-TWA 5 ppm (16 mg m^{-3})

UN No. 1282 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid
Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful by inhalation, in contact with skin and if swallowed (R11, R20/21/22)
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)

Ecotoxicity

Fish toxicity
LD_{50} intraperitoneal rainbow trout 650 mg kg^{-1} (2).
LC_{50} (24 hr) mosquito fish 1350 mg l^{-1} (3).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 210-740 ppm, Microtox test (4).
EC_{50} (24 hr) *Tetrahymena pyriformis* 520 mg l^{-1} (5).
EC_{50} (48 hr) *Daphnia magna* 940 mg l^{-1} (6).

Environmental fate

Nitrification inhibition
75% inhibition of ammonia oxidation in activated sludge at 50 mg l^{-1}, 38% inhibition at 10 mg l^{-1} (7).

Degradation studies
Under anaerobic conditions, degraded after a lag period of 2 months (8).
Degraded aerobically within 9 days in mineral medium inoculated with 10% sewage sludge (8).
ThOD 3.13 mg O_2 l^{-1}; BOD_{50} 0.06 mg O_2 l^{-1} at 10 mg l^{-1} in unadapted sewage; COD 0.05 mg O_2 l^{-1} (9,10).
Degraded by *Micrococcus luteus* isolated from soil (11).

Abiotic removal
Estimated volatilisation $t_{1/2}$ 90 hr for model river water (12).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 16-32 days (13).

Adsorption and retention
Freundlich adsorption coefficient of 5.78 suggests a cationic adsorption mechanism (14).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, redwing blackbird >1000 mg kg^{-1} (15).
LD_{50} oral rat 890 mg kg^{-1} (16).
LC_{50} (4 hr) inhalation rat 4000 ppm (17).
LD_{50} dermal rabbit 1100 mg kg^{-1} (16).
LD_{50} subcutaneous rat 1000 mg kg^{-1} (18).
LD_{50} intraperitoneal mouse, rat 110, 860 mg kg^{-1}, respectively (19,20).
LD_{50} intravenous mouse 540 mg kg^{-1} (19).

Sub-acute and sub-chronic data

Oral rat 0.1% diet caused weight loss and death within 14 days (21).

Inhalation rat 10 or 50 ppm 7 hr day^{-1} 5 days wk^{-1} for 6 months increased the liver:body weight ratio (21).

Teratogenicity and reproductive effects

Chicken egg, 20 ml egg^{-1} at 96 hr of incubation caused hypoplasia of the legs (22).

Metabolism and toxicokinetics

Absorbed through mammalian skin, lungs and gastro-intestinal tract (21).

Intraperitoneal administration to rats, guinea pigs, rabbits and ferrets led to urinary excretion of pyridine *N*-oxide (23).

Undergoes *N*-methylation in rabbit, hamster, guinea pig, cat and gerbil. Principal urinary metabolite is *N*-methylpyridinium hydroxide (24,25).

Irritancy

Dermal rabbit (24 hr) 10 mg caused mild irritation. 2 mg instilled into rabbit eye caused severe irritation (exposure not specified) (17).

Sensitisation

Skin sensitisation and photosensitisation have been reported in humans (26).

Genotoxicity

Salmonella typhimurium TA98, with metabolic activation marginally positive (27).

Saccharomyces cerevisiae D61.M induction of mitotic aneuploidy positive (metabolic activation unspecified) (28).

In vitro Chinese hamster fibroblasts, with and without metabolic activation chromosome aberrations negative (29).

In vitro mouse lymphoma L5178Y cells, tk^+/tk^- forward mutation assay with and without metabolic activation negative (30).

Allium cepa clastogenic acitivity was demonstrated by a significant increase in the frequency of chromosome breaks and exchanges (31).

Other effects

Other adverse effects (human)

May cause central nervous depression. Large doses produce gastro-intestinal disturbances, and kidney and liver damage (32).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (33).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (34).

Other comments

Environmental fate reviewed (1).

Metabolism of pyridine reviewed (35).

Physical properties, use, safety precautions and mammalian toxicity reviewed (26,36-39).

Autoignition temperature, 482°C.

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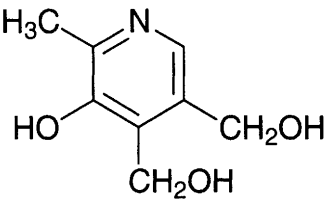
P358 pyridoxine



$C_8H_{11}NO_3$ **Mol. Wt.** 169.18 **CAS Registry No.** 65-23-6

Synonyms 5-hydroxy-6-methyl-3,4-pyridinedimethanol; adermin; bezatin; pirivatol; pyridoxol; vitamin B_6

EINECS No. 200-603-0 **RTECS No.** UV 1300000

Uses Food supplement. In treatment of premenstrual syndrome.

Occurrence Present in many foodstuffs; especially good sources are yeast, liver and cereals.

Physical properties

M. Pt. 159-162°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4000 mg kg^{-1} (1).

LD_{50} subcutaneous rat 3100 mg kg^{-1} (1).

LD_{50} intravenous rat, mouse 660, 1200 mg kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal rat, mouse 970, 1500 mg kg^{-1}, respectively (2,3).

Teratogenicity and reproductive effects

Intraperitoneal ♂ rat 125, 250, 500 or 1000 mg kg^{-1} day^{-1} for 2 or 6 wk. A delay in spermination, degeneration of elongated spermatids and Sertoli cell alterations were observed in the 500 and 1000 mg groups treated for 2 wk. In the 6 wk group delayed spermination was also observed in the 250 mg group. In the 500 and 1000 mg groups germ cells were generally degenerated and markedly reduced in number and Sertoli cells showed more severe alterations (4).

Oral rat, 200-800 mg kg^{-1} day^{-1} on days 6-15 of gestation did not induce any teratogenic effect (5).

Metabolism and toxicokinetics

Rapidly converted into pyridoxamine phosphate by mouse and human erythrocytes. Rat, hamster and rabbit erythrocytes have significantly lower pyridoxamine phosphate oxidase activity. In rats pyridoxine phosphate oxidase activity was high in the liver, moderate in the brain and kidney, and not measurable in skeletal muscle and heart (6).

Following oral administration of tritiated pyridoxine to mice, 50% of the radioactivity was absorbed for the intestine in 7 min. Pyridoxine and pyridoxal were detected in the intestine and liver. Pyridoxal and pyridoxal phosphate, but not unmetabolised pyridoxine, were detected in the peripheral blood (7).

Other effects

Other adverse effects (human)

Doses of ≥500 mg day^{-1} for prolonged periods may result in sensory nervous damage (8).

Other comments

Deficiency syndromes and toxicity reviewed (8,9).
Deficiency, though rare because of widespread distribution in foods, leads to the development of peripheral neuritis in adults and affects the central nervous system in children (10).

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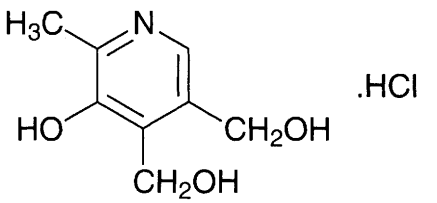
P359 pyridoxine hydrochloride



$C_8H_{12}ClNO_3$ **Mol. Wt.** 205.64 **CAS Registry No.** 58-56-0

Synonyms 5-hydroxy-6-methyl-3,4-pyridinedimethanol hydrochloride; pyridoxal hydrochrloride; 2-methyl-3-hydroxy-4,5-bis(hydroxymethyl)pyridine hydrochloride; vitamin B_6 hydrochloride; Aderoxin; Benadon; Campoviton 6; Beesix; Gravidox; Hexa-Betalin

EINECS No. 200-386-2 **RTECS No.** UV 1350000

Uses Food supplement. In cosmetics.
Occurrence Present in significant concentrations in many foodstuffs, particularly liver, peanuts, cereals and yeast.

Physical properties

M. Pt. 204-206°C (decomp.)
Solubility Water: 22%. Organic solvents: acetone, ethanol, propylene glycol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 4000, 5500 mg kg^{-1}, respectively (1).
LD_{50} subcutaneous rat, mouse 2500-3000 mg kg^{-1} (1).
LD_{50} intravenous rat, mouse, rabbit, pigeon 150-660 mg kg^{-1} (1).
LD_{50} intramuscular cat 500 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral rat, 6000, 18,000 or 30,000 mg kg^{-1} diet. Ataxia developed in the high-dose group by the 2nd wk, in the mid-dose group by the 9th wk and the low-dose group by the 15th wk. Food consumption and body weight gain were reduced in a similar dose-dependent manner. Water intake and urinary excretion increased in a dose-dependent manner (2).

Oral dog, 150 mg kg^{-1} day^{-1} for ~100 days caused ataxia and spastic, dysmetric leg movements, degeneration and loss of axons in the dorsal funiculus of the spinal chord, loss of axons and myelins, and secondary changes of myelin sheaths (3).

Teratogenicity and reproductive effects

Intraperitoneal ♂ rat 125, 250, 500 or 1000 mg kg^{-1} day^{-1} for 6 wk. Weights of testes and epididymis were dramatically decreased in the 500 and 1000 mg groups and weight of epididymis in the 125 and 250 mg groups were also decreased significantly. Mature spermatid counts and sperm counts in the epididymis were reduced in the 250, 500 and 1000 mg groups (4).

Oral rat 20-80 mg kg^{-1} day^{-1} on days 6-15 of gestation did not cause any maternal toxicity, foetotoxicity or teratogenicity (5).

Metabolism and toxicokinetics

Following oral administration to rats metabolised to pyridoxal, pyridoxamine and pyridoxic acid, which were excreted in the urine (2).

Genotoxicity

Salmonella typhimurium TA97a, TA102 with metabolic activation weakly positive (6).

In vitro human lymphocytes, sister chromatid exchanges positive (7).

Other effects

Other adverse effects (human)

No toxic effects were reported following oral doses of 300 mg day^{-1} or intravenous doses of 200 mg day^{-1} (8).

Any other adverse effects

Intraperitoneal rat, single doses of 50 mg $animal^{-1}$ prevented normal secretion of prolactin, which may have been due to a direct effect on the pituitary (9).

Other comments

Average adult minimum requirement ~1.25 mg day^{-1} in individuals ingesting 100 g protein day^{-1}. Requirement increases with amount of protein in the diet. A level of 2.0 mg day^{-1} is recommended for adults (10).

Involved as a co-enzyme in a large number of metabolic reactions, including metabolism of amino acids, fats and carbohydrates and for the synthesis of physiological regulators such as noradrenaline, serotonin and histamine (11).

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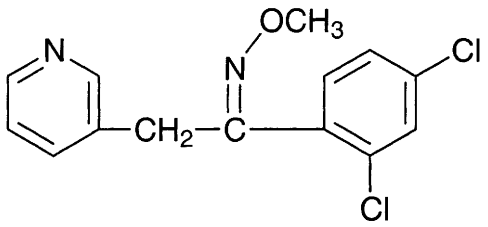
P360 pyrifenox



$C_{14}H_{12}Cl_2N_2O$ **Mol. Wt.** 295.17 **CAS Registry No.** 88283-41-4

Synonyms 2',4'-dichloro-2-(3-pyridyl)acetophenone *O*-methyloxime; 1-(2,4-dichlorophenyl)-2-(3-pyridinyl)ethanone *O*-methyloxime; Dorado; Corona; Felin; Podigrol

RTECS No. KM 5772000

Uses Fungicide.

Physical properties

B. Pt. >150°C at 0.1 mmHg **Specific gravity** 1.28 at 20°C **Partition coefficient** log P_{ow} 3.4 at pH 5.0, 3.7 at pH 7.0, 3.7 at pH 9.0, all at 25°C (2) **Volatility** v.p. 1.4×10^{-5} mmHg at 25°C
Solubility Water: 300 mg l^{-} at pH 5.0, 150 at pH 7.0, 130 at pH 9.0. Organic solvents: acetone, chloroform, diethyl ether, dimethylformamide, ethyl acetate, *n*-hexane, isopropanol, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout, mirror carp, 6.6, 7.1, 12.2 mg l^{-1}, respectively (1,2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* 3.6 mg l^{-1} (1).
LD_{50} (48 hr) oral bee 59 μg bee^{-1}; contact bee 70 μg bee^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail, mallard duck >2000 mg kg^{-1} (1).
LD_{50} oral rat, mouse 1700, 2900 mg kg^{-1}, respectively (1-3).
LC_{50} inhalation rat >2000 mg m^{-3} (highest feasible concentration) (exposure not specified) (1,2).
LD_{50} dermal rat >5000 mg kg^{-1} (1,4).
LD_{50} intraperitoneal rat 950 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral rat and dog (90 day) no-adverse-effect level 80 mg kg^{-1} diet for rat, 40 mg kg^{-1} diet for dogs (1).

Metabolism and toxicokinetics
Following oral administration to rats rapidly absorbed, metabolised and excreted in the urine and faeces. There are no indications of bioretention in tissue or organs (1).

Irritancy
Slight irritant to guinea pig skin and to rabbit eyes (dose and exposure unspecified) (1,2).

Sensitisation
Reported to be non-allergenic (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).
Log P_{ow} exceeds European Union recommended limit of 3.0 (7).
WHO Toxicity Class III (8).
ADI 0.1 mg kg^{-1} (2).

Other comments

Stable to UV light and to hydrolysis in water at 50°C at pH 3-9 (1).

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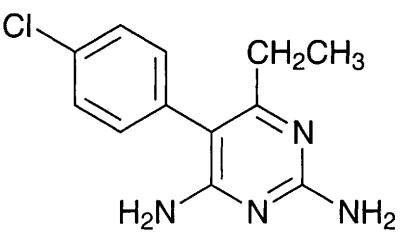
P361 pyrimethamine



CAS Registry No. 58-14-0

Synonyms 5-(4-chlorophenyl)-6-ethyl-2,4-pyrimidinediamine; 2,4-diamino-5-(*p*-chlorophenyl)-6-ethylpyrimidine; Daraprim

EINECS No. 200-364-2 **RTECS No.** UV 8140000

Uses Antimalarial. Also used in combination with a sulfonamide in the treatment of toxoplasmosis.
Occurrence Not known to occur in nature.

Physical properties

M. Pt. 233-234°C (capillary);240-242°C (copper block)
Solubility Water: practically insoluble. Organic solvents: slightly soluble in ethanol and soluble in boiling ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 92 mg kg^{-1} (1).
LD_{Lo} oral hamster 250 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 74 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 70 mg kg^{-1}(4).
LD_{Lo} subcutaneous mouse 160 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Oral rat 190 mg kg^{-1} day^{-1} in diet, lethal within 142 days (6).
Oral rhesus monkeys (daily) in diet almost uniformly fatal within 9-18 days. 25% of animals died within 36 days after daily doses of 2.5 mg kg^{-1} body weight (6).
Bone-marrow and renal toxicity were observed in rats and rhesus monkeys treated as above (6).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (7).
National Toxicology Program tested rats and mice via dosed-feed. Negative evidence of carcinogenicity in ♂ and ♀ rats and ♀ mice. Inadequate study of carcinogenicity in ♂ mice (8).

Teratogenicity and reproductive effects

Doses of 25-50 mg kg^{-1} administered to rats on the 9-13th day of pregnancy induced malformations in the embryo skeletons (9,10).
Injection of 0.1-1.5 mg into the yolk sac before or up to 4 days after commencing incubation induced a high incidence of malformations in chick embryos (11).
Goettingen minature pigs were given pyrimethamine mixed with mashed feed during gestational days 11-35. Major malformations such as cleft palate, club-foot and micrognathia were observed in 11/16 newborns from three pregnant sows which received 3.6 mg kg^{-1} day^{-1}. Two sows of a high-dose group (2.2 mg kg^{-1}) showed severe anaemia and low appetite during the experiment and did not give birth. No malformation was found in 22 newborns of low-dose groups (0.9 and 1.8 mg kg^{-1}) of 130 offspring which died before weaning. Major teratoses such as cleft palate were found in eight newborns (12).
Pyrimethamine injected into the rat on days 12, 13, and 14 of gestation induced several types of malformations, including limb and facial deformaties. The appearance of vascular pathology, followed by malformation in the same regions indicated a vascular cause for pyrimethamine-induced foetal defects (13).

Metabolism and toxicokinetics

Following administration of single oral doses of 100 mg to human subjects, the average concentration in the serum fell slowly, reaching 0.12 mg l^{-1} nine days after dosing. Urinary excretion, which accounted for 20-30% of the drug administered, continued for at least 30 days (14).
Pyrimethamine is almost completely absorbed from the gastro-intestinal tract and peak plasma concentrations of 200 ng ml^{-1} are obtained 2-6 hours after oral administration of 25 mg by mouth. It is mainly concentrated in the kidneys, lungs, liver and spleen and about 80-90% is bound to plasma proteins (15).
Pyrimethamine crosses the placental barrier and is also excreted into the mother's milk (16,17).
In rhesus monkeys, ^{14}C-labelled pyrimethamine administered orally, intravenously or intramuscularly, was completely but slowly absorbed from the gastro-intestinal tract and underwent metabolism; 82-84% of the radioactivity was found in the urine and 3.5-5.2% in the faeces (16,18).

Genotoxicity

Concentrations of 0.15 mg ml^{-1} in the feed caused a 3-4 fold increase in the number of X-linked recessive lethals in *Drosophila melanogaster* (19).
Following *in vivo* treatment with pyrimethamine, chromosome abnormalities have been observed in mouse bone-marrow cells and in blastomeres from pregnant rats (20).
Chromosomal abnormalities were observed in metaphases of bone-marrow cells examined in 3/5 patients receiving total doses of 200-300 mg pyrimethamine (21).

Human peripheral lymphocytes cultured with 0.02 mg ml^{-1} pyrimethamine for 48 and 72 hr showed significantly increased numbers of cells with chromosomal aberrations compared with controls (22).
Mitotic malsegregation of *Saccharomyces cerevisiae* D.61M chromosome VII was not induced by pyrimethamine (23).
A suspected aneugen, pyrimethamine was analysed in a variety of *in vitro* mammalian cell cultures using different end-points which included: micronuclei, kinetochore-positive micronuclei in binucleated cells and changes in the number of chromosomes or aberrations of mitosis and division. Human lymphocytes, human diploid fibroblasts and Chinese hamster transformed cells were used as target cells. The compound came out as negative, except in one study with primary Chinese hamster fibroblasts for induction of numerical chromosomal aberrations (24).

Other effects

Other adverse effects (human)

Prolonged administration to man may cause depression of haematopoiesis due to interference with folic acid metabolism. Skin rashes and hypersensitivity reactions can also occur (15).
Acute overdosage can cause gastro-intestinal effects and CNS stimulation with vomiting, excitability, and convulsions. Tachycardia, respiratory depression, circulatory collapse, and death may follow (15).
Overdosage in infants has been documented (25,26).

Other comments

A review on pyrimethamine appears in the IARC Monograph volume 13 (27).
When heated to decomposition it emits very toxic fumes of Cl^{-1} and NO_x.

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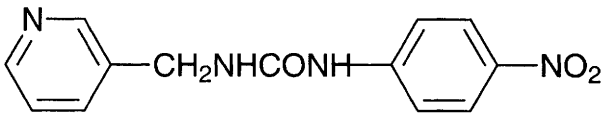
P362 pyrinuron



$C_{13}H_{12}N_4O_3$ **Mol. Wt.** 272.26 **CAS Registry No.** 53558-25-1

Synonyms pyriminil; RH 787; *N*-(4-nitrophenyl)-*N'*-(3-pyridinylmethyl)urea; *N*-(3-pyridylmethyl)-*N'*-(*p*-nitrophenyl)urea; Vacor

EINECS No. 258-626-7 **RTECS No.** YT 9690000

Uses Superseded rodenticide.

Physical properties

M. Pt. 223-225°C (decomp.)

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken, pigeon, monkey, pig 760-2000 mg kg^{-1} (1-3).

LD_{50} oral rat 6.7-98 mg kg^{-1} (3,4).

Metabolism and toxicokinetics

Metabolites identified in the urine of rats, dogs and humans include: pyriminil glucuronide, aminopyriminil, acetamidopyriminil, *p*-aminophenylurea, *p*-acetamidophenylurea, *p*-nitroaniline, *p*-phenylenediamine, *p*-acetamidoaniline, nicotinic acid, nicotinuric acid and nicotinamide (2).

Other effects

Other adverse effects (human)

A dose of 780 mg was fatal within 150 days. A dose of 2340 mg was fatal within 1 day although 1 patient survived 40 days after ingesting 7000 mg (2).

Lowest toxic dose, oral man 5.6 mg kg^{-1} central nervous effects (5).

Produces central nervous effects and peripheral nervous disorders. Destroys the B-cells of the pancreas and hence can cause diabetic state (6).

Any other adverse effects

Oral rat, single dose of 100 mg kg^{-1} caused local haemorrhage and oedematous changes in the periventricular area of the brain, scattered haemorrhage in the posterior and anterior horns, spongy degeneration and demyelinisation in the fasciculus gracilis and cuneatus of the white matter, and degenerative changes in the sciatic nerve. Necrosis of the axon, myelin sheaths and glia cells in the spinal chord were also observed (7).

In a sub-acute study in chickens, reduction in food consumption, body weight, egg production and egg weight were reported. Histopathological changes in the lungs, liver, kidney, ovarian loose connective tissue and endocardium were reported (dose and duration unspecified) (1).

Suppressed insulin release from rat pancreatic islet cells *in vitro*. Pyriminil induces diabetes mellitus, but suppression of insulin release may not be related to cAMP and C-kinase (2).

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).

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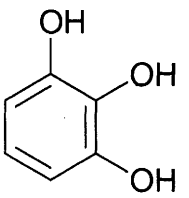
P363 pyrogallol



$C_6H_6O_3$ **Mol. Wt.** 126.11 **CAS Registry No.** 87-66-1

Synonyms 1,2,3-benzenetriol; C.I. 76515; C.I. oxidation base 32; 2,3-dihydroxyphenol; Fourrine 85; pyrogallic acid; Fouramine brown AP; 1,2,3-trihydroxybenzene

EINECS No. 201-762-9 **RTECS No.** UX 2800000

Uses Metal complexing agent. Antioxidant. Colorant. In hair dyes. In photographic developers. Manufacture of polymers. Reducing agent. Formerly used in treatment of psoriasis and parasitic skin diseases.

Physical properties

M. Pt. 131-133°C **B. Pt.** 309°C **Specific gravity** 1.453 at 4°C with respect to water at 4°C
Volatility v.p. 10 mmHg at 167.7°C
Solubility Water: 625 g l^{-1} at 25°C. Organic solvents: acetone, benzene, carbon disulfide, chloroform, diethyl ether, ethanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful by inhalation, in contact with skin and if swallowed – Possible risk of irreversible effects – Harmful to aquatic organisms, may cause long-term effects in the aquatic environment (R20/21/22, R40, R52/53)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S36/37, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) goldfish ~18 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (24 hr) *Daphnia magna* 54 mg l^{-1} (2).

Environmental fate

Degradation studies

Degraded anaerobically by *Pelobacter massiliersis* isolated from marine mud sediments (3).

Degraded by fungi *Chaetomium cupreum, Drechslera* and *Fusarium oxysporum vasinfectum* which utilises it as sole carbon source (4).

ThOD 1.52 mg $O_2 l^{-1}$; BOD_5 1% of ThOD; COD 95% of ThOD (5).

Abiotic removal

Degraded in water by treatment with hydroxyl radicals produced by irradiation with UV light (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, mouse, rabbit, 75, 300, 1600 mg kg^{-1}, respectively (7-9).

LD_{50} subcutaneous mouse 570 mg kg^{-1} (10).

LD_{50} intraperitoneal mouse 400 mg kg^{-1} (11).

Teratogenicity and reproductive effects

Oral rat, lowest toxic dose 3000 mg kg^{-1} day^{-1} on days 6-15 of gestation (foetotoxicity) (12).

Metabolism and toxicokinetics

Readily absorbed from gastro-intestinal tract. Little is absorbed through the intact skin. Readily conjugated with hexuronic acid, sulfuric acid and other acids, and excreted in the urine within 24 hr. A fraction is excreted unchanged (species unspecified) (13).

Metabolites in rats include 3-methoxycatechol and 2-methoxyresorcinol (14).

Irritancy

Dermal rabbit (24 hr) 500 mg caused severe irritation. 20 mg instilled into rabbit eye for 24 hr caused moderate irritation (15).

Sensitisation

Has been reported to cause dermatitis, photosensitivity and stomatitis in humans (16).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation negative (17,18).

Saccharomyces cerevisiae D7 mitotic gene conversion positive at alkaline pH (metabolic activation unspecified) (19).

In vitro mouse lymphoma L5178Y cells tk^+/tk^- forward mutation with and without metabolic activation positive (20).

In vitro Chinese hamster V79 lung cells, sister chromatid exchanges and induction of micronucleated cells positive (metabolic activation unspecified) (18).

In vitro human lymphocytes, chromosomal aberrations with and without metabolic activation positive (21).

Other effects

Other adverse effects (human)

Therapeutic use caused systemic effects similar to phenol poisoning. Methaemoglobinaemia, haemolysis and kidney damage were also reported (22).

Legislation

In the UK maximum concentration in hair dyes 5% (22).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (23).

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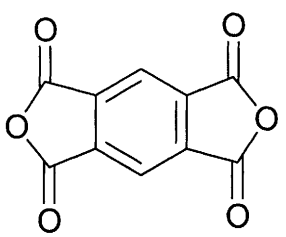
P364 pyromellitic dianhydride



$C_{10}H_2O_6$ **Mol. Wt.** 218.12 **CAS Registry No.** 89-32-7

Synonyms PMDA; 1,2,4,5-benzenetetracarboxylic 1,2:4,5-dianhydride; 1*H*,3*H*-benzo(1,2-c4,5-c')difuran-1,3,5,7-tetrone

EINECS No. 201-898-9 **RTECS No.** DB 9300000

Uses Principal commercial use is as a raw material for polyimide resins. Also used as an intermediate in the production of film, enamels and varnishes.

Physical properties

M. Pt. 285-287°C **B. Pt.** 397-400°C **Specific gravity** 1.68 at 25°C with respect to water at 4°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 breath dust – Avoid contact with the skin – In case of conntact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves and eye/face protection (S2, S22, S24, S26, S37/39)

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig, rat, mouse 1595-2595 mg kg^{-1} (1,2).

Sub-acute and sub-chronic data
Oral rat (6 month) no-adverse-effect level was determined to be 0.07 mg kg^{-1} day^{-1}. Doses >4.4 mg kg^{-1} affected the kidney, liver and reproductive tract (2).

Teratogenicity and reproductive effects
Oral rat reported to be non-embryotoxic at 230 mg kg^{-1} (≤0.1 LD_{50}) (2).

Sensitisation
Unspecified route rat (6 month) >4.4 mg kg^{-1} weak allergen (2).

Other effects

Other adverse effects (human)
In humans, mucosal and skin irritant and allergen. Clinical symptoms include asthma, a flu-like syndrome and pulmonary haemorrhage (3).

Other comments

Reviews on human health effects and experimental toxicology listed (4).

References

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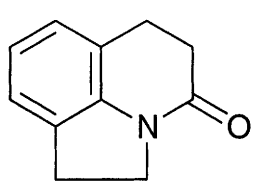
P365 pyroquilon



$C_{11}H_{11}NO$ **Mol. Wt.** 173.21 **CAS Registry No.** 57369-32-1
Synonyms 1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one; Coratop; Forgoren
RTECS No. UY 9480000
Uses Insecticide. Fungicide.

Physical properties

M. Pt. 112°C **Specific gravity** 1.29 at 20°C **Partition coefficient** log P_{ow} 1.57
Volatility v.p. 1.2×10^{-6} mmHg at 20°C
Solubility Water: 4 g l^{-1} at 20°C. Organic solvents: acetone, benzene, dichloromethane, isopropanol, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) catfish, perch, rainbow trout 13-21 mg l^{-1} (1,2).

Invertebrate toxicity
Practically non-toxic to honeybees; LD_{50} (oral) >20, (contact) >1000 μg bee^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 320 mg kg^{-1} (1,2).
LD_{50} dermal rat >3100 mg kg^{-1} (1,2).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 600 mg kg^{-1} diet (1,2).

Irritancy
Mild skin irritant, minimal eye irritant in rabbits (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).
WHO Toxicity Class II (5).
ADI 0.015 mg kg^{-1} body weight (2).

Other comments

Stable to hydrolysis and to temperature up to 320°C (1).

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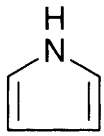
P366 pyrrole



C_4H_5N **Mol. Wt.** 67.09 **CAS Registry No.** 109-97-7

Synonyms 1*H*-pyrrole; 1-aza-2,4-cyclopentadiene; azole; divinylenimine; imidole; monopyrrole

EINECS No. 203-724-7 **RTECS No.** UX 9275000

Uses Organic synthesis. Corrosion inhibitor. Manufacture of polymers. Electrolyte. Solvent.

Occurrence Aroma component of plant, cooked meat and fish. In fossil fuels and bone oil.

Physical properties

M. Pt. –23°C **B. Pt.** 131°C **Flash point** 33°C (closed cup) **Specific gravity** 0.968 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.75 **Volatility** v.den. 2.31

Solubility Water: sparingly soluble. Organic solvents: benzene, diethyl ether, ethanol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 2100 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 410 ppm, Microtox test (2).

EC_{50} (duration unspecified) *Tetrahymena pyriformis* 525 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >100 mg kg^{-1} (4).

LD_{Lo} oral rabbit 150 mg kg^{-1} (5).

LD_{Lo} intraperitoneal rabbit 250 mg kg^{-1} (5).

LD_{50} subcutaneous mouse 61 mg kg^{-1} (6).

Irritancy

Vapour or mist irritated the eyes, mucous membranes and upper respiratory tract (species unspecified) (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA102 with and without metabolic activation negative (8).

Bacillus subtilis H17 (Rec+), M45(Rec–) without metabolic activation positive (9).

Other effects

Other adverse effects (human)

Repeated exposure can cause damage to the liver, kidneys and heart (7).

Has a depressant action on the central nervous system (10).

Any other adverse effects

Intramuscular rabbit 0.05, 0.1 or 0.2 ml $animal^{-1}$. The higher doses significantly reduced serum cholesterol 24 hr later. 0.2 ml injection caused some fatalities (11).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

Other comments

Mammalian toxicity reviewed (11).

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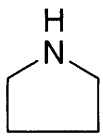
P367 pyrrolidine



C_4H_9N **Mol. Wt.** 71.12 **CAS Registry No.** 123-75-1

Synonyms azacyclopentane; tetrahydropyrrole; tetramethylenimine

EINECS No. 204-648-7 **RTECS No.** UX 9650000

Uses Strong base. Organic synthesis. Curing agent for epoxy resins. Tobacco flavour.
Occurrence Aroma component of plants, and in cooked meats.

Physical properties

M. Pt. –63°C **B. Pt.** 87-88°C **Flash point** 2°C **Specific gravity** 0.8618 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.46 **Volatility** v.p. 128 mmHg at 39°C ; v.den. 2.45
Solubility Water: miscible. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 1922 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive

Ecotoxicity

Fish toxicity
Not toxic to brown trout, bluegill sunfish, yellow perch and goldfish at 5 ppm for 24 hr. Test condition: 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).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >100 mg kg^{-1} (2).
LD_{50} oral rat 300 mg kg^{-1} (3).
LC_{50} (2 hr) inhalation mouse 1300 mg m^{-3} (3).
LD_{50} intravenous mouse 56 mg kg^{-1} (4).

Metabolism and toxicokinetics

Undergoes α-hydroxylation in rat liver microsomes in the presence of NADPH and oxygen *in vitro* (5).

Genotoxicity

Saccharomyces cerevisiae induction of aneuploidy negative (6).

Other effects

Other adverse effects (human)

Extremely destructive to tissue of the mucous membranes and upper respiratory tract, eyes and skin (7). Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and oedema (7).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

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P368 pyruvic acid

$$CH_3C(O)CO_2H$$

$C_3H_4O_3$ **Mol. Wt.** 88.06 **CAS Registry No.** 127-17-3

Synonyms acetylformic acid; α-ketopropionic acid; 2-oxopropanoic acid; pyroracemic acid

EINECS No. 204-824-3 **RTECS No.** UZ 0829800

Occurrence Intermediate in carbohydrate metabolism in animals and in alcoholic fermentation.

Physical properties

M. Pt. 11.8°C **B. Pt.** 165°C (decomp.) **Flash point** 83°C
Specific gravity 1.267 at 15°C with respect to water at 4°C
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity

Not toxic to brown trout, bluegill sunfish, yellow perch or goldfish at 5 ppm for 24 hr. Test condition: 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).

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous mouse 3500 mg kg^{-1} (2).

Metabolism and toxicokinetics

In muscle, pyruvic acid (derived from glycogen) is reduced to lactic acid during exertion. Converted into alanine in the liver (3).

Other effects

Other adverse effects (human)

Extremely destructive to tissue of the mucous membranes, upper respiratory tract, skin and eyes (4). Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and oedema (4).

References

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Q1 quartz

SiO_2

O_2Si **Mol. Wt.** 60.08 **CAS Registry No.** 14808-60-7

Synonyms D&D; Min-U-Lil; chert; agate; amethyst; onyx; flint; α-quartz; β-quartz; sand; silica, crystalline; silicic anhydride; Snowit

EINECS No. 238-878-4 **RTECS No.** VV 7330000

Uses Used in jewellery, fibre optics and electronics. In oscillator circuits to control electromagnetic wave frequencies.

Occurrence In sedimentary strata containing sandstone and quartzite rocks and in igneous rocks and minerals. The largest reserves of high purity quartz occur in Brazil. In total, quartz constitutes ~12% of continental land masses (1).

Physical properties

M. Pt. 1710°C **B. Pt.** 2230°C **Specific gravity** 2.65

Occupational exposure

DE-MAK 0.15 mg m^{-3} (respirable fraction of aerosol)
FR-VME 0.1 mg m^{-3} (respirable dust)

SE-LEVL 0.1 mg m^{-3} (respirable dust)
UK-LTEL MEL 0.3 mg m^{-3} (respirable crystalline dust)
US-TWA 0.1 mg m^{-3} (respirable dust)

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal rat 200 mg kg^{-1} (form unspecified) (2).
LD_{50} intravenous rat 500 mg kg^{-1} (form unspecified) (3).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (4).
Intrapleural cavity injection rat, single dose of 20 mg $animal^{-1}$ induced malignant histiocytic lymphomas in 6/35 rats, malignant schwannomas in 2/35 rats, but no mesotheliomas (5).
Intratracheal instillation in rats (22 month) single dose of 20 mg^{-1} animal induced lung tumours in 30/67 animals compared with 1/75 controls (6).
Intrapulmonary rabbit (6 month) unquantified amount in 0.5 ml saline (particle size ~2 μm). 4/5 animals developed malignant lung tumours: 3 adenocarcinomas involving both lungs and 1 sarcoma involving the pleura. No silicotic lesion was found, but fibrous capsules were formed around the quartz deposits. Epithelial hyperplasia and metaplasia were observed in the principal airways (7).
Inhalation rat (2 yr) 0 or 52 mg m^{-3} (particle size 1.7-2.5 μm) 6 hr day^{-1} 5 day wk^{-1} for 4, 8, 12, 16 or 24 months. The incidence of epidermoid carcinomas of the lungs in treated rats still alive at 494 days, when the first tumour appeared, was 10/53 among ♀ and 1/47 among ♂ rats. 0/89 controls developed lung tumours. Additional lesions in treated rats included pulmonary adenomatosis, cuboidal metaplasia of the alveolar epithelium, in addition to alveolar proteinosis, lymphoreticular hyperplasia and nodular fibrosis (8).
Intraperitoneal rat (18 month) single injection of 20 mg quartz. Mean survival time was 462 days for treated and 332 days for controls. Malignant lymphomas, developed in 9/64 treated rats and 1/12 controls (9).

Metabolism and toxicokinetics

Quartz is slightly soluble in body fluids forming silicic acid, which is excreted in the urine (10).

Genotoxicity

In vitro Chinese hamster V79 *HPRT*$^{+/-}$ cells inhibition of junctional intercellular communication negative (11).
In vitro Syrian hamster embryo cells, induction of micronuclei positive (12).
In vitro Chinese hamster V79 cells, sister chromatid exchanges negative (13).
In vivo mouse bone marrow polychromatophilic erythrocytes, induction of mircronuclei negative (14).

Other effects

Other adverse effects (human)

Occupational exposure to crystalline silica may lead to silicosis, which is a nodular pulmonary fibrosis. Although rapidly progressive, silicosis has been reported following massive exposure, the typical course is 1 yr to decades later. A clear exposure-response relationship has been demonstrated between cumulative exposure and development of silicosis. Some cohort studies have shown an association between silicosis and lung or stomach cancer (1,15-17).

Any other adverse effects

Proliferation of thymus-derived T-lymphocytes in the spleen has ben reported following dust exposure of rodents (18).
No pathological change was observed in rats or dogs following oral administration (19).

Other comments

Uses, occurrence, carcinogenicity, toxicity and mutagenicity reviewed (1,17,20).
β-Quartz interchanges to α-Quartz at 575°C, α-quartz interchanges to α-tridymite at 870°C.

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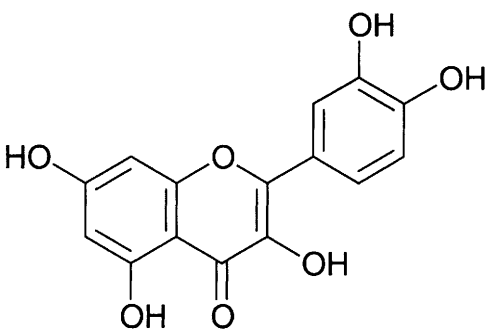
Q2 quercetin



$C_{15}H_{10}O_7$ **Mol. Wt.** 302.24 **CAS Registry No.** 117-39-5

Synonyms 3,3′,4′,5,7-pentahydroxyflavone; 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4*H*-benzopyran-4-one; C.I. Natural Red 1; C.I. Natural Yellow 10 & 13; C.I. 75670; xanthaurine

EINECS No. 204-187-1

Uses Natural colouring agent.

Occurrence Occurs very widely in the plant kingdom as condensation products with sugars.

Physical properties

M. Pt. 314°C (decomp.)

Solubility Water: practically insoluble in water, soluble in aqueous alkaline solutions. Organic solvents: ethanol (3.4 g l^{-1}), boiling ethanol (43.5 g l^{-1}), acetic acid

Environmental fate

Degradation studies

Catabolised by *Rhizobium loti* and *Bradyrhizobium* strains in an arabinose-based medium via a novel C-ring cleavage to give phloroglucinol and protocatechuic acid (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 159, 161 mg kg^{-1}, respectively (2).
LD_{50} subcutaneous mouse 97 mg kg^{-1} (2).
LD_{50} intravenous mouse 18 mg kg^{-1} (3).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (4).
No differences in the incidence and multiplicity of lung adenomas were seen in strain A mice fed a diet of quercetin and mice fed a basal diet (5).
Oral rats were fed a diet containing 1 or 5% quercetin for 540 days or 10% for 850 days. Controls were fed a normal basal diet. No significant difference was found between the incidence of tumours in the experimental and control groups (6,7).
Oral non-inbred weaning rats (58 wk) 0.1% quercetin in feed. Controls were fed a basic grain diet. Intestinal and bladder tumours were observed in 0/9 ♂ and 0/10 ♀ controls and 6/7 ♂s and 14/18 ♀s in quercetin-treated rats. These tumours included 4 adenomas, 7 fibroadenomas and 9 adenocarcinomas (3 with mesenteric metastases) (8).
The effect of dietary quercetin on pancreatic carcinogenesis was evaluated in rats pre-treated with nitrosomethylurea. Pancreatic nodules and focal acinar cell hyperplasia were observed in 100% of treated rats. Dysplastic foci were found in 73% of animals. Mitosis was increased and apoptosis diminished in focal acinar cell hyperplasias (9).

Teratogenicity and reproductive effects

Oral pregnant rats 2-2000 mg kg^{-1} on day 9 of pregnancy or daily from day 6 to 15. A decrease in the mean weight of day 20 foetuses compared with controls was observed, but no dose-related teratogenic effects (10).
♂ Mice 16, 32, 80, or 160 mg kg^{-1} administered fractionally over 5 successive days by intraperitoneal injection. Five wk after the final injection the maximum number of sperm with abnormal heads or tails (14.8%) were observed with mice receiving a total dose of 80 mg kg^{-1}. The control value was 0.98%. Concomitant with this was a 32.1% reduction in testicular weight and a 28% reduction in sperm count (11).

Genotoxicity

Salmonella typhimurium base-pair substitution and frameshift assays positive with and without metabolic activation (12).
Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (13).
Drosophila melanogaster recessive sex-linked lethal test positive (14).
Micronuclei induction assay *in vivo* in bone marrow polychromatic erythrocytes in mice negative. Micronuclei induction assays *in vitro* with or without metabolic activation positive in V79 cells and human lymphocytes. It appears to act as a clastogenic agent in human lymphocytes, with or without metabolic activation, inducing a significant majority of kinetochore-negative micronuclei (15).

Other effects

Any other adverse effects

Growth inhibition IC_{50}s (48 hr) CHO cells 0.8×10^{-4} M, mouse fibroblast (3T3) cells 1.2×10^{-4} M, normal rat kidney (NRK) cells 0.7×10^{-4} M (16).

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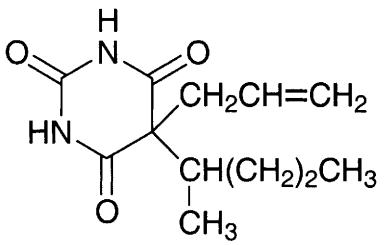
Q3 quinalbarbitone



$C_{12}H_{18}N_2O_3$ **Mol. Wt.** 238.29 **CAS Registry No.** 76-73-3

Synonyms barbosec; Evronal; Hypatrol; innesonal; meballymal; 5-allyl-5-(1-methylbutyl)barbituric acid; 5-(1-methylbutyl)-5-(2-propenyl)-2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione; secobarbital; seconal

EINECS No. 200-982-2 **RTECS No.** CP 9450000

Uses Sedative.

Physical properties

M. Pt. 100°C

Solubility Water: slightly soluble. Organic solvents: chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 270 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 120 mg kg^{-1} (2).

LD_{50} intravenous rat 80 mg kg^{-1} (3).

Metabolism and toxicokinetics

May be absorbed through human skin (4).

Crosses the placenta, appearing in the foetus within 30 sec of administration (5).

Following oral administration ~90% was absorbed from the gastro-intestinal tract within 2 hr (6).
~30-45% of the drug is bound to plasma proteins (6).
Inactive metabolites include 5-allyl-5-(3'-hydroxy-1'-methylbutyl)barbituric acid (hydroxysecobarbital) and 5-(2',3'-dihydroxypropyl-5-(1'-methylbutyl)barbituric acid (secodiol), which are excreted in the urine as free acids or glucuronides (6).
Distributed into the milk of lactating women (6).

Other effects

Other adverse effects (human)
Produces hypnotic effects within 15 min of oral administration (6).
Induced an increase in aggressive response tests in volunteers (7).
Lowest toxic dose, oral woman 32 mg kg^{-1} (central nervous system effects) (8).

Any other adverse effects
In rats, metabolites have been shown to cause the destruction of cytochrome P_{450} (9).

Legislation

Limited under EC Directive on Drinking Water 80/778/EEC. Substances extractable in chloroform guide level 0.1 mg l^{-1} dry residue (10).

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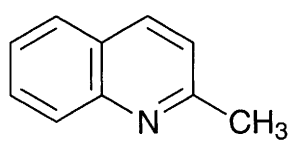
Q4 quinaldine



$C_{10}H_9N$ **Mol. Wt.** 143.19 **CAS Registry No.** 91-63-4

Synonyms 2-methylquinoline; Khinaldin

EINECS No. 202-085-1 **RTECS No.** UZ 9625000

Uses Anaesthetic in transport and handling of fish.
Occurrence Occurs in coal tar.

Physical properties

M. Pt. –2°C **B. Pt.** 246-247°C **Flash point** 110°C **Specific gravity** 1.058
Partition coefficient log P_{ow} 2.23 (calculated) (1)
Solubility Organic solvents: chloroform, diethyl ether

Ecotoxicity

Fish toxicity
No toxic effect in fertilisation of rainbow trout at 0.05% (2).

Invertebrate toxicity
LC_{10} (24 hr) *Tetrahymena pyriformis* 0.40 g l^{-1} (3).
LC_{50} (96 hr) *Xenopus laevis* embryo 26.4 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1230 mg kg^{-1} (5).
LD_{50} dermal rabbit 1870 mg kg^{-1} (5).

Irritancy
Dermal rabbit (24 hr) 10 mg caused mild irritation and 750 μg instilled into rabbit eye (72 hr) caused severe irritation (5).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation negative (6).

Other comments

Metabolite of tryptophan in rat intestine (7).

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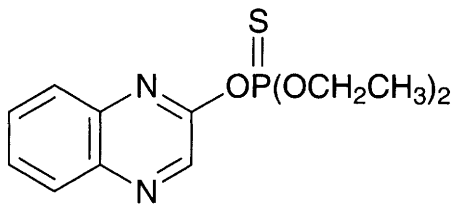
Q4 qui

Q5 quinalphos



$C_{12}H_{15}N_2O_3PS$ **Mol. Wt.** 298.30 **CAS Registry No.** 13593-03-8

Synonyms diethquinalphion; *O,O*-diethyl *O*-(2-quinoxalinyl) ester of phosphorothioic acid; *O,O*-diethyl *O*-quinoxalin-2-yl phosphorothioate

EINECS No. 237-031-6 **RTECS No.** TF 6125000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 31-32°C **B. Pt.** 142°C at 0.0003 mmHg **Specific gravity** 1.235 at 20°C
Partition coefficient log P_{ow} 4.438 (1) **Volatility** v.p. 2.6×10^{-6} mmHg at 20°C
Solubility Water: 22 mg l^{-1} at 24°C, 17.8 mg l^{-1} at 20°C. Organic solvents: acetone, acetonitrile, diethyl ether, ethanol, *n*-hexane, ethyl acetate, toluene, xylene

Occupational exposure

UN No. 2783
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) – 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) carp, goldfish 1, 10 mg l^{-1}, respectively (1).
Walking catfish (15 day) 0.025 mg l^{-1} caused a decrease in testis weight, seminiferous tubule diameter, and 3-β- and 17-β-hydroxy-steroid dehydrogenases activities in the testes and an increase in testicular cholesterol concentrations (2).
LC_{50} (96 hr) *Saccobranchus fossilis* 1.6 mg l^{-1}, static bioassay (3).

Invertebrate toxicity
Very toxic to bees; LD_{50} oral 0.07, topical 0.17μg bee^{-1} (4).

Environmental fate

Degradation studies
5-50 ppm in soil degraded within 5 days by 5 species of algae isolated from soil, and the filamentous cyanobacteria *Phormidium tenue* and *Nostoc linckia* (5).
Primary $t_{1/2}$ in soil 2 wk. Not susceptible to enhanced biodegradation with repeated soil applications (6).
Hydrolysed to 2-hyroxyquinoxaline in soil (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 26-71 mg kg^{-1} (1,7).
LC_{50} (4 hr) inhalation rat 0.45 g m^{-3} (4).
LD_{50} dermal rat 300-1750 mg kg^{-1} (1,8).
LD_{50} intraperitoneal rat, mouse 34-39 mg kg^{-1} (9).
LD_{50} subcutaneous rat, mouse 55-56 mg kg^{-1} (9).

Sub-acute and sub-chronic data

LC_{50} (8 day) oral quail, mallard duck 150-220 mg kg^{-1} diet (1).
Oral chicken (20 day) 5 mg day^{-1} caused a significant reduction in total red blood cell and thrombocyte counts. Serum alkaline phosphatase activity was significantly increased, whereas serum total protein was markedly reduced. Liver changes similar to those of second-grade cirrhosis were observed. The lungs were severely congested and oedematous changes in the heart were revealed (10).
Oral rat (up to 21 or 45 days postnatal and 21 days with sacrifice at 45 days postnatal for withdrawal) 0.5 mg kg^{-1}. Acetylcholinesterase activity in the brain decreased after exposure but recovered with withdrawal. Superoxide radical generation in the brain increased by 43%, 59% and 39%, respectively. Superoxide dismutase and catalase activities increased by 30 and 50%, respectively, with partial recovery after withdrawal (11).
Oral rat (60 days) 0.52 and 1.04 mg kg^{-1}. Significant decreases in body, brain and liver weights were observed. Hepatic cytochrome P450 content and its dependent monooxygenases were induced 1.8-2.5 fold, while neuronal aryl hydrocarbon hydroxylase was induced to 1.8 fold. The hepatic antioxidant defence system (catalase, glutathione reductase, superoxide dismutase and glutathione peroxidase) was significantly stimulated (12).

Carcinogenicity and chronic effects

Oral rat (2 yr) no-adverse effect level 3 mg kg^{-1} diet (1).

Teratogenicity and reproductive effects

Intraperitoneal ♂ rat lowest dose 6.5 mg kg^{-1} day for 26 days (changes in endocrine system and fertility) (13).
Oral rat, lowest toxic dose 23 mg kg^{-1} day^{-1} on days 6-20 of gestation (foetotoxicity) (14).

Metabolism and toxicokinetics

In plants, following aerial application, 33% is absorbed by the leaf surface and penetrates into the plant while two-thirds is removed by evaporation within 14 days. Following oral administration to rats, quinalphos is rapidly absorbed. Metabolites are excreted in the urine within a short time. The major plant and mammalian metabolite is the hydrolysis product 2-hydroxyquinoxaline and its conjugates (1).

Irritancy

Non-irritating to skin and eyes of rabbits (1).

Genotoxicity

Salmonella typhimurium TA98, TA1535, TA1537 with metabolic activation positive (15).
In vitro human lymphocytes, chromosomal aberrations and sister chromatid exchanges positive (metabolic activation unspecified) (16).
In vivo mouse bone marrow micronucleus assay and germ cell chromosome assay positive (17).
In vitro Allium cepa and barley meristems, chromosomal aberrations positive (18).

Other effects

Any other adverse effects

Inhibits cholinesterase activities (1).

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).

The log P_{ow} value exceeds the European Community recommended level of 3.0 (Directive on Classification, Packaging and Labelling of Dangerous Substances, 6th and 7th amendments) (21).
WHO Toxicity Class II (22).
EPA Toxicity Class II (formulation).

Other comments

Toxic to honeybees following spray application on plants at a concentration of 0.05% (23).

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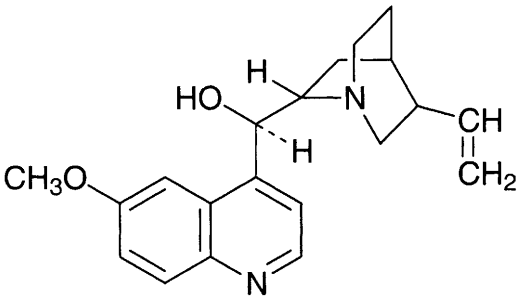
Q5 qui

Q6 quinine



$C_{20}H_{24}N_2O_2$ **Mol. Wt.** 324.42 **CAS Registry No.** 130-95-0

Synonyms (8α,6*R*)-6′-methoxycinchonine; chinine

EINECS No. 205-003-2 **RTECS No.** VA 6020000

Uses Antimalarial.

Occurrence The bark of *Cinchona officinalis* and Rubiaceae.

Physical properties

M. Pt. 174°C

Solubility Water: 1 g 1900 ml^{-1}. Organic solvents: benzene, chloroform, dry diethyl ether, ethanol, glycerol

Environmental fate

Abiotic removal

Quinine in aqueous 2-hydroxy-2-methylpropanoic acid was irradiated, the reaction products were: deoxyquinine, 7-(2-hydroxyprop-2-yl)-7′,8′-dihydroquinine, 7′,8′-dihydrodeoxyquinine, and the cyclic product 4′-(2-hydroxyprop-2-yl)-1′,4′-dihydroquinine (1).

Mammalian & avian toxicity

Acute data

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

LD_{Lo} oral rabbit, rat, guinea pig 500, 800, 1800 mg kg^{-1}, respectively (3-5).

LD_{Lo} subcutaneous cat, dog, mouse, rat, rabbit 100-231 mg kg^{-1} (3,6,7).

LD_{Lo} intramuscular rat 300 mg kg^{-1} (8).

LD_{Lo} intraperitoneal mouse 115 mg kg^{-1} (9).

LD_{Lo} intravenous cat, rabbit 70, 100 mg kg^{-1}, respectively (3,6).

Teratogenicity and reproductive effects

Human reproductive effects include abortion (oxytocic effect), stillbirth, retinal ganglion degeneration and limb and visceral anomalies (10).

Rat (3 month) ≤200 mg kg^{-1} (quinine hydrochloride) caused no teratogenic effects (11).

Congenital malformations, particularly of the optic and auditory nerves, have occurred following administration to pregnant women (12).

Metabolism and toxicokinetics

Apparent volume of distribution, clearance and other pharmacokinetic parameters are altered by malaria infection. Following oral administration peak concentrations in the circulation occur at ~1 to 3 hr. Absorption from the gastro-intestinal tract is rapid and almost complete. Plasma protein binding is ~70% in healthy subjects rising to ≥90% in malaria sufferers. Distribution is throughout the body. Extensive metabolism occurs in the liver

and excretion is mainly via the urine. Unchanged quinine excreted ranges from <5 to 20%. Elimination $t_{1/2}$ is ~11 hr in healthy subjects. Can cross the placenta and is excreted in breast milk (13-15).
Vmax for 3-hydroxyquinine formation in the liver of the common brush-tailed possum (*Trichosurus vulpecula*) was 1512 ± 510 pmol mg^{-1} protein min^{-1} (♂s) and 1680 ± 690 pmol mg^{-1} protein min^{-1} (♀s), approximately threefold higher than found in human livers. Mean apparent Michaelis constant (Km) for 3-hydroxyquinine formation by possium liver 31.9 ± 16 μM (♂s) and 16.1 ±5 (♀s) (16).

Irritancy
Oedema and erythema may occur in patients (17).

Sensitisation
Thrombocytopenic purpura, urticaria and flushing of the skin with intense pruritus may occur in patients with hypersensitivity (12).
Drinks containing quinine at levels as low as 20 μg l^{-1} have triggered thrombocytopenic purpura in previously sensitised people (18).
Topical application may cause contact and photocontact allergy. Photosensitivity can also be induced by systemic administration (19,20).
Eczematous dermatitis reported (19).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (quinine hydrochloride) (21).
Escherichia coli PQ37 SOS chromotest with and without metabolic activation negative (quinine hydrochloride) (21).
Escherichia coli induced base-pair substitution type mutation (strains, metabolic activation unspecified) (22).

Other effects

Other adverse effects (human)
May cause a series of adverse effects, collectively called cinchonism: impaired hearing, headache, tinnitus, nausea, vomiting, diarrhoea, vertigo and abdominal pain. Other effects include hypoprothrombinaemia and agranulocytosis. Large doses can be fatal and cause gastro-intestinal effects, oculotoxicity, cardiotoxicity and central nervous system disturbances (12).

Any other adverse effects
Can cause reversible hearing loss, in isolated cochlea preparations it alters the micro mechanism tuning of the organ of Corti (23).

Other comments

Usually administered as the sulfate, hydrochloride or dihydrochloride (12).

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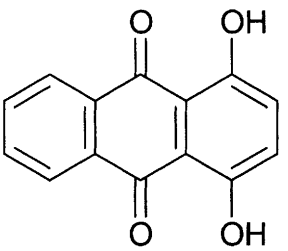
Q7 quinizarin



$C_{14}H_8O_4$ **Mol. Wt.** 240.22 **CAS Registry No.** 81-64-1

Synonyms 1,4-dihydroxy-9,10-anthracenedione; Chinizarin; C.I. 58050; Smoke Orange R; 1,4-dihydroxyanthraquinone

EINECS No. 201-368-7 **RTECS No.** CB 6600000

Uses Fungicide. In the synthesis of antitumour agents. Antioxidant in synthesis of lubricants.

Physical properties

M. Pt. 198-199°C **B. Pt.** 450°C **Volatility** v.p. 1.0 mmHg at 196.7°C ; v.den. 8.3
Solubility Organic solvents: benzene, ethanol, diethyl ether

Environmental fate

Degradation studies

Degradation by microflora in water at pH 6.5-8.5 for anthraquinone derivatives including quinizarin were BOD_5 0.03-0.11 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >316 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 2100 mg kg^{-1} (3).
LD_{50} intravenous mouse 320 mg kg^{-1} (4).

Irritancy

500 mg instilled into rabbit eye for 24 hr produced mild effects. Irritating to skin, mucous membranes and upper respiratory tract (species unspecified) (5).

Genotoxicity

Salmonella typhimurium TA102, TA1537 with and without metabolic activation positive (6).
In vitro primary rat hepatocytes unscheduled DNA synthesis negative (6,7).
In vitro human lymphocytes without metabolic activation induced weak dose-independent toxic effects in a sister chromatid exchange test, with metabolic activation caused an enhancement of these effects (8).

Other effects

Any other adverse effects

Observed to restrict rat colonic absorption of sodium, but not water, and caused an apparent release of potassium into the lumen (9).
In vitro studies indicated inhibition of mitochondrial adenine nucleotide translocation and oxidative phosphorylation (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

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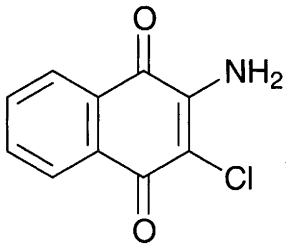
Q7 qui

Q8 quinoclamine



$C_{10}H_6ClNO_2$ **Mol. Wt.** 207.62 **CAS Registry No.** 2797-51-5

Synonyms 2-amino-3-chloro-1,4-naphthoquinone; 2-amino-3-chloro-1,4-naphtholenedione; mageton; ACNQ

EINECS No. 220-529-2 **RTECS No.** QL 7350000

Uses Herbicide and algicide used on paddy rice crops.

Physical properties

M. Pt. 198-200°C **Specific gravity** 1.66 **Partition coefficient** log P_{ow} 1.5 **Volatility** v.p. 0.06 mPa at 25°C
Solubility Organic solvents: acetic acid, acetone, chlorobenzene, nitrobenzene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 0.7 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (3 hr) *Daphnia* >10 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂, ♀ rat 1360, 1600 mg kg^{-1}, respectively (1).
LD_{50} oral ♂, ♀ mouse 1350, 1260 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation rat >0.79 mg l^{-1} (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) 5.7 mg kg^{-1} day^{-1} in diet showed no observable adverse effect (1).

Genotoxicity

Salmonella typhimurium TA100, TA98, TA1535, TA1537, TA1538 with and without metabolic activation negative (2).
Escherichia coli WP2 *hcr* with and without metabolic activation negative (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/877/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class III (5).

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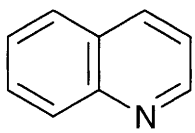
Q9 quinoline



C_9H_7N **Mol. Wt.** 129.16 **CAS Registry No.** 91-22-5

Synonyms 1-azanaphthalene; 1-benzazine; benzopyridine; leucoline; chinoleine; Leukol; Quinolin; B500

EINECS No. 202-051-6 **RTECS No.** VA 9275000

Uses Dye manufacture. Anatomical specimen preservative. Solvent for resins and terpenes. Antimalarial. Solvent.

Physical properties

M. Pt. –14.5°C **B. Pt.** 237.7°C **Flash point** 101°C **Specific gravity** 1.0900 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.03 **Volatility** v.p. 1 mmHg at 59.7°C ; v.den. 4.45
Solubility Water: 60 g l^{-1}. Organic solvents: acetone, benzene, carbon disulfide, diethyl ether, ethanol

Occupational exposure

UN No. 2656 **HAZCHEM Code** 3Z **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 0.44 mg l^{-1} (1).
LC_{50} (27 day) rainbow trout 11.5 mg l^{-1} (1).
Trout, bluegill sunfish, yellow perch and goldfish showed no ill-effects when placed in 5 ppm for 24 hr. Water characteristics: pH 7.0; dissolved oxygen, 7.5 pm; total hardness (soap method) 300 ppm; methyl orange alkalinity, 310 ppm; free carbon dioxide, 5 ppm; and temperature, 12.8°C (2).

Invertebrate toxicity

EC_{50} *Daphnia magna* (24 hr) 76 mg l^{-1} (3).
NOEC *Daphnia magna* (21 day) 0.80 mg l^{-1}, reproductive effects (3).
LC_{50} (48 hr) *Daphnia magna* 35 mg l^{-1} (1).

Toxicity to other species

LD_{Lo} subcutaneous frog 150 mg kg^{-1} (4).

Bioaccumulation
[^{14}C]-quinoline in pelleted food was fed to rainbow trout. After 2 hr, 67% was estimated to be un-ionised and available for absorption across the gastric epithelium. Rates of gallbladder emptying appeared to exceed rates of hepatic bile secretion until ~8 hr after a single feeding (5).
Confirmed to be non-accumulative or low accumulative (6).

Environmental fate

Nitrification inhibition
Inhibition of ammonia oxidation by activated sludge percentage inhibition: 6, 52, 85% by 5, 10, 100 mg l^{-1}, respectively (7).

Degradation studies
Was anaerobically degraded by microorganisms from aquifer sediments to carbon dioxide and methane (8).
Degraded by *Pseudomonas diminuta* 31/1 Fal and *Bacillus circulans* 31/2 Al, the 1st metabolite was 2-oxo-1,2-dihydroquinoline and 6-hydroxy-2-oxo-1,2-dihydroquinoline was an intermediate (9).
BOD_5, 69% of ThOD; COD 65% of ThOD (0.05 N $K_2Cr_2O_7$); $KMnO_4$, 31% of ThOD (0.01 N $KMnO_4$); ThOD 2.5 mg O_2 l^{-1} (10).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 331-460 mg kg^{-1} (11,12).
LD_{50} dermal rabbit 540 mg kg^{-1} (13).
LD_{Lo} subcutaneous rabbit 200 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Oral ♂ Sprague-Dawley rats were given 0.05, 0.10 or 0.25% in diet for 16-40 wk. Mortality and liver weights were high and body weight gain was low. Rats given the high dose died or became moribund within 40 wk due to rupture of vascular tumours of the liver or general toxic effects (12).

Carcinogenicity and chronic effects
Intraperitoneal CD-1 mice (1 yr) 32, 65 and 129 μg kg^{-1} on days 1, 8 and 15 of life, respectively. >78% incidence of liver tumours was observed in ♀ mice, there was not a significant increase in tumours in ♂ mice compared with the controls (14).
Suprascapular injection Sprague-Dawley rats (78 wk) 25.8 mg kg^{-1} in dimethyl sulfoxide on first day of life, 12.9 mg kg^{-1} wkly at wk 2-7 and 25.8 mg kg^{-1} at wk 8. The rats were killed at 78 wk. There was no significant tumorigenic activity (14).

Irritancy
Dermal rabbit (24 hr) 10 mg caused mild irritation and 250 μg instilled into rabbit eye (duration unspecified) caused severe irritation (13).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (15).
In vivo rat liver unscheduled DNA synthesis equivocal (16).
In vivo mouse bone marrow chromosomal aberrations, sister chromatid exchanges negative (17).

Other effects

Any other adverse effects
Potent inducer of mutagenic response in rat liver 48 hr after oral dosing with 200-500 mg kg^{-1} (16).
Inhalation rat (6 hr) 17 ppm no mortality in a group of 3 animals; all animals died at 4000 ppm for 5.5 hr (12).
Animals (unspecified) show respiratory distress, lethargy and prostration leading to coma in oral and dermal studies (12).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (19). Autoignition temperature 480°C.

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Q10 Quinoline Yellow

CAS Registry No. 8004-92-0

Synonyms C.I. Acid Yellow 3; C.I. Food Yellow; Dye Quinoline Yellow; Japan Yellow; Quinoline Yellow KT; C.I. 47005; Canary Yellow; D & C Yellow No. 10

RTECS No. GC 5796000

Uses Textile dye for silk, wool, nylon. Paper dye. Colouring agent in medicines, cosmetics (except near eye) and food.

Physical properties

Solubility Water: soluble. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >2 g kg^{-1} (1).

Irritancy
Severe urticarial reaction reported in one patient (2).

Sensitisation
Purified compound is not a contact allergen in guinea pigs. Contact allergy ellicited by commercial grade is caused by contaminating quinophthalone (3).

Legislation

Estimated acceptable daily intake, 10 mg kg^{-1} body weight (4).

Other comments

Toxicity reviewed (5).

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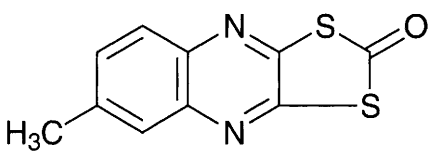
Q11 quinomethionate



$C_{10}H_6N_2OS_2$ **Mol. Wt.** 234.30 **CAS Registry No.** 2439-01-2

Synonyms 6-methyl-1,3-dithiolo[4,5-*b*]quinoxalin-2-one; carbonic acid, dithio-, cyclic *S*,*S*-(6-methyl-2,3-quinoxalinediyl)ester; oxythioquinox; chinomethionat; Frostan; Erade

EINECS No. 219-455-3 **RTECS No.** FG 1400000

Uses Acaricide, fungicide, insecticide.

Physical properties

M. Pt. 172°C **Partition coefficient** log P_{ow} 3.78 at 20°C (1) **Volatility** v.p. 2×10^{-7} mmHg at 20°C
Solubility Water: 1 mg l^{-1} at 20°C. Organic solvents: hot benzene, dimethylformamide, 1,4-dioxane, toluene

Occupational exposure

Supply classification irritant
Risk phrases Irritating to the eyes – May cause sensitisation by skin contact (R36, 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) bluegill sunfish, rainbow trout 0.12, 0.22 mg l^{-1}, respectively (1).

Invertebrate toxicity
LD_{50} >100μg bee^{-1} (2).

Toxicity to other species
At 10 mg l^{-} agar media, it severly inhibited the growth of *Pleurotus ostreatus* (3).

Bioaccumulation
Saccharomyces cerevisiae adsorbed quinomethionate when added during fermentation (4).

Environmental fate

Degradation studies
It was degraded when added to fermenting *Saccharomyces cerevisiae* cultures (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, starling >100, >500 mg kg^{-1}, respectively (5).
LD_{50} oral rat, guinea pig 1100-1500 mg kg^{-1} (6,7).
LD_{Lo} oral mouse 1070 mg kg^{-1} (8).
LC_{50} (1 hr) inhalation rat >20 mg l^{-1} air (1).
LD_{50} dermal rat 500->5000 mg kg^{-1} (1,9).
LD_{50} intraperitoneal mouse 473 mg kg^{-1} (10).
LD_{Lo} intraperitoneal rat 95 mg kg^{-1} (11).

Carcinogenicity and chronic effects
In a 2-yr feeding trial rats receiving 60 mg kg^{-1} showed no ill-effects (1).

Metabolism and toxicokinetics
Rapidly metabolised (metabolites unspecified), following oral administration, by rats with ~75% eliminated within 3 days (1).

Irritancy
Irritating to mammalian (unspecified) 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} (12).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (14).
WHO Toxicity Class Table 5 (15).
EPA Toxicity Class III (2).
ADI 0.006 mg kg^{-1} body weight (2).

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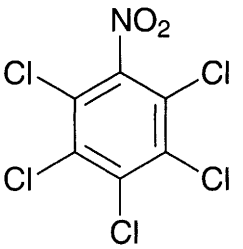
Q12 quintozene



$C_6Cl_5NO_2$ **Mol. Wt.** 295.34 **CAS Registry No.** 82-68-8

Synonyms pentachloronitrobenzene; nitropentachlorobenzene; Brassicol; Terrachlor; Avicol; PCNB

EINECS No. 201-435-0 **RTECS No.** DA 6650000

Uses Fungicide

Physical properties

M. Pt. 143-144°C **B. Pt.** 328°C (decomp.) **Specific gravity** 1.718 at 25°C
Partition coefficient log P_{ow} 4.77 (1) **Volatility** v.p. 5.0×10^{-5} mmHg at 20°C ; v.den. 10.2
Solubility Water: 0.1 mg l^{-1} at 20°C. Organic solvents: aromatic solvents, carbon disulfide, chlorinated hydrocarbons, ketones

Occupational exposure

US-TWA 0.5 mg m^{-3}
Supply classification irritant
Risk phrases May cause sensitisation by skin contact (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
There were no fatalities amongst golden orfe and rainbow trout over 96 hr at 1.2 mg l^{-1} water (2).

Invertebrate toxicity
LOEC *Colpidium campylum* ≤10 mg l^{-1} (3).
EC_{50} (30 min) *Photobacterium phosphoreum* 3.8 ppm Microtox test (4).
An unspecified application rate to garden soil reduced density of actinomycetes from 360,000 to 360 g^{-1}, and completely eliminated all fungal and protozoan propagules from the soil (5).
LD_{50} contact >100 μg bee^{-1} (6).

Bioaccumulation
Bioconcentration factor trout 161±31 (12 day exposure) (1).

Environmental fate

Nitrification inhibition
Very slight inhibition of nitrification in soil for 30 days at 1000 ppm (7).

Degradation studies
In soil $t_{1/2}$ 4-10 months (2).
Biodegradation occurs mainly to pentachloroaniline and (methylthio)pentachlorobenzene (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >12,000 mg kg^{-1} in aqueous suspension and 1650-1710 mg kg^{-1} in maize oil (2).
LC_{50} (duration unspecified) inhalation rat 1400 mg m^{-3} (8).
LC_{50} (duration unspecified) inhalation mouse 2 g m^{-3} (8).
LD_{50} dermal rat 4 g kg^{-1} (9).
LD_{50} intraperitoneal rat 5000 mg kg^{-1} (2).

Carcinogenicity and chronic effects
No adequate evidence of carcinogenicity to humans, limited evidence of carcinogenicity to animals, IARC classification group 3 (10).
In 2-yr feeding trials no-effect level for rats was 25 mg kg^{-1} diet and for dogs 30 mg kg^{-1} diet. At higher dosages, there was liver hypertrophy with some histopathological changes and, in dogs, liver damage including fibrosis (2).
National Toxicology Program tested ♂, ♀ mice via food. No evidence of carcinogenicity was found for either sex (11).
Oral mice 464 mg kg^{-1} for 3 wk then 1206 ppm for 75 wk. 2/18 ♂ and 4/18 ♀ mice developed hepatomas compared with 8/79 and 0/87 controls. 10/17 ♂ and 1/17 ♀ mice of a different strain also developed hepatomas compared with 5/90 and 1/82 controls (12).
♂ and ♀ albino mice were painted 2 × wk^{-1} with 0.3% quintozene in acetone for 12 wk and then with 0.5% croton oil in acetone for 20 wk; controls were painted with acetone. 50 skin tumours were seen in 13 treated survivors compared with 12 in the surviving controls. One tumour in a treated mouse had progressed to a squamous-cell carcinoma; a squamous-cell carcinoma was also seen in a control mouse killed 31 wk after the start of croton oil treatment (12).

Metabolism and toxicokinetics
Following oral administration of 2 g to rabbits, 62% was excreted unchanged in the faeces, 12% was excreted as pentachloroaniline and 14% as *N*-acetyl-*S*-pentachlorophenylcysteine (12).
Pentachloroaniline and methylpentachlorophenyl sulfide were found in biological tissues of rats and beagle dogs fed quintozene over an extended period of time; none of the parent compound was detected (12).
Pentachloroaniline and pentachlorophenyl sulfide were found in fatty tissue of pregnant mice fed 500 mg kg^{-1} 4 × day^{-1}. The metabolites were also found in foetuses, indicating transplacental movement (12).

Irritancy
Prolonged skin contact may result in sensitisation (species unspecified) (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (13).
In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchange negative, without metabolic activation chromosomal aberrations positive, with metabolic activation some evidence for an increase in chromosomal aberrations (14).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (16).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (17).
EEC MRL salads, French chicory 0.5 ppm (2).
WHO Toxicity Class Table 5 (18).
EPA Toxicity Class III (formulation) (6).
ADI 0.01 mg kg^{-1} body weight (6).

Other comments

Not dangerous to bees when used as recommended (2).
Properties, metabolism, toxicity and carcinogenicity reviewed (19).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (20).

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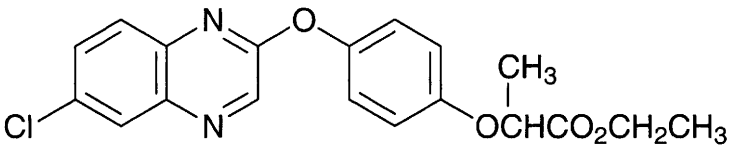
Q13 quizalofop-ethyl



$C_{19}H_{17}ClN_2O_4$ **Mol. Wt.** 372.81 **CAS Registry No.** 100760-10-9

Synonyms 2-[4-[(6-chloro-2-quinoxalinyl)oxy]phenoxy]propanoic acid, ethyl ester; DDX 6202

RTECS No. UA 2458255

Uses Herbicide.

Physical properties

M. Pt. 91.7-92.1°C **B. Pt.** 220°C at 0.2 mmHg **Specific gravity** 1.35 at 20°C
Partition coefficient log P_{ow} 4.28 at 23°C **Volatility** v.p. 6.49×10^{-9} mmHg (20°C)
Solubility Water: 300 μg l^{-1} at 20°C. Organic solvents: acetone, benzene, ethanol, hexane, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 10.7, 0.46-2.8 mg l^{-1}, respectively (1,2).

Environmental fate

Degradation studies
The main breakdown product is 4-(6-chloro-2-quinoxalinyloxy)phenol. Persistence in soil, ~3 wk (2).
Persistence in a range of arable soils was less than 3 months in field trials (3).

Adsorption and retention
In field trials was found not to leach below 5 cm in a range of arable soils (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck 2000 mg kg^{-1} (2).
LD_{50} oral ♂, ♀ rat and mouse 1480-2360 mg kg^{-1} (1).
LD_{50} dermal rat, mouse >10,000 mg kg^{-1} (2).
LC_{50} (4 hr) inhalation rat 5.8 mg l^{-1} (4).

Sub-acute and sub-chronic data
Rats given 40 mg kg^{-1} diet showed no ill-effects in 90-day feeding trial (2).
Oral rat (104 wk) no-observed-effect level 0.9 mg kg^{-1} day^{-1} (4).

Irritancy
Non-irritant to rabbit skin (2).

Sensitisation
Non-sensitising to guinea pig skin (2).

Genotoxicity

Salmonella typhimurium negative (details unspecified) (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).
Log P_{ow} exceeds the European Union limit of 3.0 (7).
WHO Toxicity Class III (8).
EPA Toxicity Class III (formulation) (4).

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R1 radon

Rn **Mol. Wt.** 222.02 **CAS Registry No.** 10043-92-2

RTECS No. VE 3750000

Uses As a radiation source, antineoplastic. Label in the study of surface reactions. To initiate chemical reactions. Determination of radium or thorium.
Occurrence In earth's crust 4×10^{-17} wt%.
Ubiquitous throughout the geosphere, biosphere and atmosphere, as a result of the radioactive decay of radium-226. High concentrations exist in areas with uranium-rich alum shales, granites, pegmatites, uranium mineralisation or eskers and porous soils (1).

Physical properties

M. Pt. –71°C **B. Pt.** –62°C **Specific gravity** 9.73 g l^{-1} at 0°C and 760mmHg
Solubility Water: 230 ml l^{-1} at 20°C. Organic solvents: soluble

Occupational exposure

SE-LEVL 2.5 Mbq m^{-3} annual dose (underground work)

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1. Cohort and case-control studies of underground miners exposed to radon and its decay products have reported an increase in lung cancer rates, particularly among uranium miners (1).
Inhalation experiments in ♂ rats and ♂ and ♀ dogs found an increased incidence of respiratory tract tumours. Experiments with rats showed a dose-response relationship. Most studies do not report tumours in sites other than the lung, but one study mentions tumours of the upper lip and urinary tract in rats. The incidence of respiratory-tract tumours in rats exposed to radon and its decay products was increased by inhalation of cigarette smoke or cerium hydroxide and by repeated intraperitoneal injections of benzo-5,6-flavone (1).

Teratogenicity and reproductive effects

Three-month old ♂ BALB/c mice were exposed to 0.45-0.63 Gy at a site of high natural radiation and a high atmospheric radon concentration. Control mice were exposed to 0.0013 Gy at a less radioactive site. After exposure, the mice were mated to non-irradiated three-month old ♀ mice over 6 months. In the control group 13/50 (26%) pairs of mice were sterile, compared with 9/51 (17%) in the low-exposure group (0.45 Gy) and 18/38 (47%) in the high-exposure group (0.63 Gy) (2).

Metabolism and toxicokinetics

Following inhalation exposure of experimental animals to radon and its decay products, the highest concentrations of short-lived decay products occur in the tracheobronchial and pulmonary region and in the kidney (1).

Genotoxicity

Drosophila melanogaster sex-linked recessive mutation assay positive (3).
In vitro human peripheral blood lymphocytes chromosomal aberrations positive (4).
In vivo rabbit lymphocytes chromosomal aberrations negative (5).
In vivo rat, Chinese hamster and Syrian hamster deep-lung fibroblasts, micronuclei positive (6).
Some studies of groups of people occupationally or residentially exposed to high levels of radon and its decay products found an increased incidence of chromosomal aberrations (1).

Other comments

Human health effects, experimental toxicology, environmental effects and exposure levels reviewed (1).
Radiation and disease in underground miners reviewed (7).
Review of radon as an occupational or domestic carcinogen (8,9).
Radon and lung cancers reviewed (10).
Radon dosimetry and risks reviewed (11).
Properties, health effects, epidemiological studies, dosimetry and risk estimation of indoor air radon reviewed (12).
Review of possible carcinogens in indoor air (13).

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R2 RDX

$C_3H_6N_6O_6$ **Mol. Wt.** 222.12 **CAS Registry No.** 121-82-4

Synonyms hexahydro-1,3,5-trinitro-1,3,5-triazine; cyclonite; hexogen; cyclotrimethylenenitramine

EINECS No. 204-500-1 **RTECS No.** XY 9450000

Uses High explosive. Rat poison.

Physical properties

M. Pt. 202°C

Occupational exposure

FR-VME 1.5 mg m^{-3}
UK-LTEL 1.5 mg m^{-3} **UK-STEL** 3 mg m^{-3}
US-TWA 0.5 mg m^{-3}

Ecotoxicity

Invertebrate toxicity

Ceriodaphnia dubia (7 day) no significant effect on survival but reduced reproductive success (1).
NOEC *Ceriodaphnia dubia* 3.64 mg l^{-1}; LOEC *Ceriodaphnia dubia* 6.01 mg l^{-1}, chronic value *Ceriodaphnia dubia* 4.68 mg l^{-1} (1).

Environmental fate

Degradation studies

Phanerochaete chrysosporium cultures degraded 66% of [^{14}C] compound to $^{14}CO_2$ in 30 days. In soil 75% of [^{14}C] compound was degraded to $^{14}CO_2$ in 30 days (2).
Corynebacterium sp. 22-1 can degrade the compound at an optimal pH and temperature of pH 9 and 30°C, respectively (3).

Abiotic removal

Undergoes UV photolysis into NO_2 and NO_3 in <10 min (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 59, 100 mg kg^{-1}, respectively (5,6).
LD_{Lo} oral cat, rabbit 100, 500 mg kg^{-1}, respectively (7).
LD_{50} intravenous mouse, guinea pig 19, 25 mg kg^{-1}, respectively (8).
LD_{Lo} intraperitoneal rat 10 mg kg^{-1} (8).

Sub-acute and sub-chronic data

Oral (13 wk) 10 ♂ and 10 ♀ rat 30, 100 or 300 mg kg^{-1} day^{-1}, toxic effects in rats were hypotriglyceridaemia, behavioural changes and mortality (9).

Metabolism and toxicokinetics

In humans it is slowly absorbed from the gastro-intestinal tract after ingestion and also from the lungs after inhalation (10-13).

In laboratory animals it is metabolised primarily in the liver by microsomal enzymes, producing several kinds of one-carbon fragments: CO_2, bicarbonate ion and formic acid (11,14,15).

Other effects

Other adverse effects (human)

Symptomatic effects following acute exposure include hyperirritability, nausea, vomiting, generalised epileptiform seizures, and prolonged postictal confusions and amnaesia (16).

Two cases of acute symptoms occurred five months apart, in which employees were engaged in manual sieving of large amounts of powdered compound. After 4 and 6 hr work, respectively, both men felt unwell, with nausea, vertigo and convulsions. Both were treated with diazepam and later clonazepam. Both men recovered without problems. Little is known about the toxicology of the compounds, but its effects are known to be exacerbated by alcohol consumption (17).

Any other adverse effects

Pathological changes are generally nonspecific and consist of congestion in various organs, swelling and degeneration of renal tubular epithelium, fatty degeneration of the liver, and areas of hyaline degeneration of heart muscle (species unspecified) (18).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (19).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (20).

Included in the UK List of Classified and Authorised Explosives 1994. UK Class and Division 3.2. Competent Authority Reference GB 32046 (21).

Other comments

An ambient water quality criterion for the protection of human health and sensitive populations has been calculated as 103 $\mu g\ l^{-1}$ (16).

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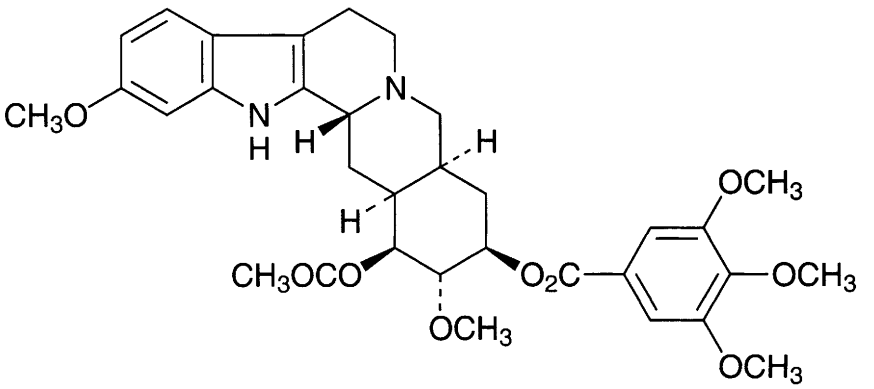
R3 reserpine



$C_{33}H_{40}N_2O_9$ **Mol. Wt.** 608.69 **CAS Registry No.** 50-55-5

Synonyms yohimban-16-carboxylic acid, 11,17-dimethoxy-18-[(3,4,5-trimethoxybenzoyl)oxy]-, methyl ester, (3β,16β,17α,18β,20α)-; Anquil; Loweserp; Quiescin; Rausedyl; Serpine; Triserpin

EINECS No. 200-047-9 **RTECS No.** ZG 0350000

Uses Antihypertensive. In veterinary practice as a tranquiliser and sedative for cattle, cats, dogs and horses.
Occurrence In the roots of *Rauwolfia* sp.

Physical properties

M. Pt. 264-265°C (decomp.) **Partition coefficient** log P_{ow} 4.1446 (1)
Solubility Water: very sparingly soluble. Organic solvents: glacial acetic acid, benzene, chloroform, ethyl acetate, methylene chloride

Ecotoxicity

Fish toxicity
0.3 ml administered to ♂, ♀ cichlid on alternative days for 15 days. In ♂ it reduced body and gonadal weights, in ♀ it reduced the gonadal weight but increased body weight. DNA and RNA levels in the gonads of both sexes were reduced (2).

Bioaccumulation
Estimated bioconcentration factor 344 (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >100 mg kg^{-1} (4).
LD_{50} oral rat 420 mg kg^{-1} (5).
LD_{50} oral mouse 200-500 mg kg^{-1} (5,6).

Oral human 50 mg kg^{-1} caused death (7).
LD_{50} intravenous dog, rabbit, mouse 0.5, 15, 21 mg kg^{-1}, respectively (8-10).
LD_{50} intravenous rat 15-18 mg kg^{-1} (9,11).
LD_{50} intraperitoneal rabbit, rat 7, 44 mg kg^{-1}, respectively (12,13).
LD_{50} intraperitoneal mouse 5-70 mg kg^{-1} (6,14).
LD_{50} subcutaneous rat, mouse 25, 52 mg kg^{-1}, respectively (15,16).
Subcutaneous mouse 2.5 or 10 mg kg^{-1} caused gastric erosion and haemorrhage (17).
Mice given 0.25 mg kg^{-1} subcutaneously or 1 mg kg^{-1} intraperitoneally showed suppression of the immune response of lymph-node cells (18).

Carcinogenicity and chronic effects
Insufficient evidence of carcinogenicity to humans, limited evidence of carcinogenicity to animals, IARC classification group 3 (19).
Oral ♀ C3H mouse 0.24 μg day^{-1} in feed. 15/24 developed mammary carcinomas, the earliest was observed by 216 days and the latest by 15 months; 12/12 controls also developed mammary tumours, the earliest by 320 days and the latest by 17 months (20).
Oral $B6C3F_1$ mouse (104 wk) 5 or 10 mg kg^{-1} in diet. Of the ♀ 7/48 of the high dose and 7/49 of the low dose developed mammary tumours, no tumours were found in the controls. Of the ♂ 5/49 of the high dose and 1/50 of the low dose developed carcinomas of the seminal vesicles; no carcinomas were found in the controls (6).
Oral rat (18 month) 100 μg kg^{-1} in diet. Lymphosarcomas and hepatomas appeared in ♀ after 18 month and ♂ after 20 month. Overall 16% of test animals but no controls developed tumours (21).
Oral Fischer 344 rat (105 wk) 5 or 10 mg kg^{-1} in diet. In ♂ 24/48 (15 benign and 9 malignant) developed adrenal medullary pheochromocytomas and of the low dose the corresponding figure was 18/49 (14 benign and 4 malignant); in the controls only 3 benign and 1 malignant pheochromocytoma developed in 3/48 rats. In ♀ the high-dose group had a combined incidence of pheochromocytomas of 4/49 (3 benign and 1 malignant), the low-dose group had a corresponding incidence of 3/48 (all benign); in the controls only 1/49 developed a benign pheochromocytoma (6).
There are many studies into the relationship between reserpine and breast cancer in humans; the data obtained from these studies are variable with many positive findings not consistent with each other. Those studies with the most satisfactory methodology showed little or no increased risk of breast cancer (19).
A case control study found reserpine use was not associated with an overall risk of breast cancer (22).
The National Toxicology Program tested rats and mice orally, 5 or 10 ppm in diet for 103 wk followed by observation for 2 wk. There was no evidence of carcinogenicity in ♀ rats. ♂ rats and mice, and ♀ mice were positive for carcinogenicity as indicated by adrenal medullary pheochromocytomas, undifferentiated carcinomas of the seminal vesicles and increased incidences of mammary cancer, respectively (23,24).

Teratogenicity and reproductive effects
Rabbits given 0.04 mg kg^{-1} intramusculary early or late in gestation had an interruption of pregnancy (25).
Guinea pigs given reserpine on days 14-15 of gestation suffered death and resorption of their foetuses (26).
250 μg kg^{-1} given to rats subcutaneously on day 1, 3 or 6 of gestation led to an interruption of pregnancy (27).
The offspring of rats given 0.8-1.5 mg kg^{-1} on day 9 of gestation or 1.5-2 mg kg^{-1} on the 10th day of gestation had eye defects and spina bifida (28).
Hydronephrosis and deformities of the brain ventricles were found in the offspring of rats injected with 1 mg kg^{-1} day^{-1} for 3 days in the last third of gestation (29).
Intramuscular rabbit 0.16 mg kg^{-1} at mid-gestation suffered no foetotoxicity (25).
A reduction in maze learning ability was seen in rats administered prenatally with 0.1 mg kg^{-1}; however, other studies showed no decrease in thisability to learn mazes (30).
Studies of postnatal neuroendocrine function in rats that had been exposed prenatally showed a permanent increase in sympathoadrenal tone for those exposed early in gestation, and chemical changes in brain transmitters for those whose dams were treated subcutaneously with 1 mg kg^{-1} 6,5 or 4 days prior to delivery (31).
Chicks exposed *in ovo* developed various permanent alterations in postnatal function including behavioural changes and in biochemical maturation (32).
In pregnant rats injected intraperitoneally with 1 mg kg^{-1} on alternate days from 1-21 days of gestation there was

a reduction in maternal body weight, which may have been due to reduced water and food intake. There was a significant incidence of abortion and offspring had reduced body weights, but there was no increase in malformations in the offspring (33).

Metabolism and toxicokinetics

Humans given 0.25 mg [^{3}H]reserpine orally had peak blood levels of radioactivity within 1-2 hr, the radioactivity was bound tightly to red blood cells and the levels remained constant for a 96-hr period. Disappearance from the plasma was biphasic: the 1st component $t_{1/2}$ 4.5 hr and the 2nd $t_{1/2}$ 271 hr (34).

In humans 6% of an oral 0.25 mg [^{3}H]reserpine dose was detected in urine within 24 hr, mainly as the metabolite trimethoxybenzoic acid. Radiolabel was still detected in urine, faeces and plasma 11-12 days after administration (34).

Intravenous rat 400 μg [^{14}C]reserpine, peak radioactivity levels occurred in most tissues within 1 hr and were followed by a rapid decline for up to 6 hr (35).

Intravenous guinea pig 2 mg [^{3}H]reserpine, maximum levels in the brain were reached by 20-30 min after which they declined rapidly (36).

Virtually no unchanged reserpine was detected in the urine of rats, dogs, rhesus monkeys or mice; 35% was found excreted in mouse faeces (37,38).

After oral administration to rats it is rapidly hydrolysed to methyl reserpate. This reaction appears to occur in the intestinal mucosa (37).

After oral or intravenous administration to mice it is metabolised to trimethoxybenzoic acid, which is eliminated rapidly in the urine (38).

Absorbed from the human gastro-intestinal tract with bioavailability of 50%. Excreted slowly in the urine and faeces following extensive metabolism. ~8 and 60% excreted in the urine (as metabolites) and faeces (unchanged), respectively, in the first 4 days. Crosses the blood-brain barrier and placenta and occurs in breast milk (39).

Irritancy

100 mg or 0.1 ml instilled into rabbit eye caused moderate to severe irritation which persisted for >24 hr, eyes recovered from treatment by 21 days (40).

Pruritus and rashes reported in humans (39).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 TA1538, TA1950 with and without metabolic activation negative (41-44).

Aspergillus nidulans induction of non-disjunction and crossing over negative (metabolic activation unspeciifed) (45).

In vitro human peripheral leucocytes chromosomal aberrations negative (metabolic activation unspecified) (46).

In vitro mouse bone marrow cells mitosis stimulated and chromosomal aberrations induced (metabolic activation unspecified) (47).

In vitro rat primary hepatocytes unscheduled DNA syntheses negative (48).

In vitro Chinese hamster cells without metabolic activation sister chromatid exchanges and chromosomal aberrations negative (49,50).

In vitro mouse lymphoma cell L5178Y tk+/tk- with and without metabolic activation negative (51).

In vitro human (unspecified type) cell without metabolic activation sister chromatid exchanges and chromosomal aberrations negative (52).

In vivo mouse dominant lethal mutations negative (53).

Other effects

Other adverse effects (human)

Side-effects include nasal congestion, headache, drowsiness, depression, dizziness, lethargy, diarrhoea and increased gastric acid secretion. In infants of mothers treated prior to delivery, cyanosis, respiratory distress and anorexia have occurred. Higher doses can cause flushing, bradycardia, coma, severe (possibly suicidal) depression, hypotension, hypothermia, respiratory depression and convulsions. Other effects include impotence, decreased libido, breast engorgement and disturbed appetite (39).

Hypertensive patients receiving reserpine had increased prolactin levels in their serum, due to the blocking of prolactin-inhibiting factor (54,55).

Any other adverse effects

Fayoumi laying hens oral in feed exhibited a total increase in serum bilirubin at all doses tested. 1.5 and 6 mg 15 kg^{-1} feed increased serum alanine aminotransferase by 28 and 32%, respectively. 1.5 mg 15 kg^{-1} feed also increased serum alkaline phosphatase by 52%. There was no effect on total serum protein but serum albumin did decrease (56).

Administration to rats of 2.5 mg kg^{-1} inhibited thymidine incorporation into rat DNA by 50-70% (57).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (58).

Other comments

Physical Properties, use, toxicity, carcinogenicity and reproductive effects reviewed (30).

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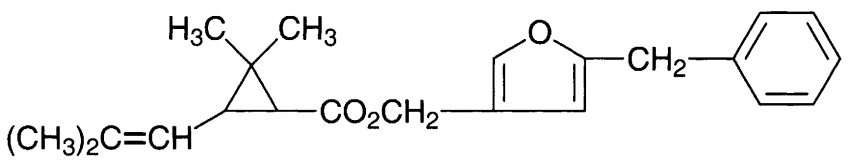
R4 resmethrin



$C_{22}H_{26}O_3$ **Mol. Wt.** 338.45 **CAS Registry No.** 10453-86-8

Synonyms cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propanyl)-, [5-(phenyl methyl)-3-furanyl]methyl ester; cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methylpropenyl)-, (5-benzyl-3-furyl)methyl ester; Chyaron; Penncapthrin; Pyresthrin; Penick

EINECS No. 233-940-7 **RTECS No.** GZ 1310000

Uses Insecticide.

Physical properties

M. Pt. 56.6°C (pure (1*RS*)-*trans*-isomer) **Specific gravity** 0.958-0.968 at 20°C
Partition coefficient log P_{ow} 5.43 at 25°C **Volatility** v.p. 1.128×10^{-8} mmHg at 30°C
Solubility Water: 37.9 μg l^{-1} at 25°C. Organic solvents: hexane, 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} (48 hr) rainbow trout, perch 0.27, 0.51 μg l^{-1}, respectively (1).

Invertebrate toxicity

LD_{50} (oral) 0.069, (contact) 0.015 μg bee^{-1} (2).

Environmental fate

Abiotic removal

Decomposed by light and air (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral bird (unspecified) 75 mg kg^{-1} (4).
LD_{50} oral rat >2500 mg kg^{-1}, respectively (2).
LD_{50} oral mouse 1390 mg kg^{-1} (5).
LC_{50} inhalation mouse 99 mg kg^{-1} (duration unspecified) (5).
LC_{50} (4 hr) inhalation rat >9.49 g m^{-3} air (2).
LD_{50} dermal rabbit, rat 2500, >3000 mg kg^{-1}, respectively (3,6).
LD_{Lo} intravenous rat 160 mg kg^{-1} (7).

Sub-acute and sub-chronic data

Rats given 3000 mg kg^{-1} diet showed no ill-effects in 90-day feeding trials (3).

Teratogenicity and reproductive effects

Rabbits and rat given 25 or 50 mg kg^{-1} day^{-1}, respectively, showed no teratogenic effects (details unspecified) (3).

Metabolism and toxicokinetics

Ester hydrolysis and oxidation, followed by conjugation, was the main metabolic pathway in laying hens (8).

Irritancy

Non-irritating to mammalian (unspecified) skin and eyes (3).

Sensitisation

Non-sensitising to guinea pig skin (details unspecified) (3).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA104, TA1535, TA1537,TA1538 with and without metabolic activation negative (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 III (12).
EPA Toxicity Class III (formulation) (2).
ADI 0.125 mg kg^{-1} (2).

Other comments

Consists of 20-30% (1*RS*)-*cis*- and 80-70% (1*RS*)-*trans*-isomers (3).
Environmental health effects reviewed (13).

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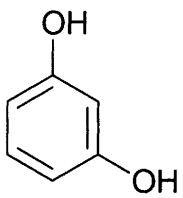
R5 resorcinol



$C_6H_6O_2$ **Mol. Wt.** 110.11 **CAS Registry No.** 108-46-3

Synonyms 1,3-benzenediol; 1,3-dihydroxybenzene; *m*-hydroquinone; *m*-hydroxyphenol; 3-hydroxyphenol; resorcin

EINECS No. 203-585-2 **RTECS No.** VG 9625000

Uses In tanning. Manufacture of pharmaceuticals, adhesives, synthetic resins and dyestuffs. Used in antiseptic preparations.

Occurrence Found in wood smoke (1).

Physical properties

M. Pt. 109-111°C **B. Pt.** 276-280°C **Flash point** 171°C **Specific gravity** 1.28 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.77-0.80 **Volatility** v.p. 53 mmHg at 190°C ; v.den. 3.79 **Solubility** Water: 1 g in 0.9 ml. Organic solvents: acetic acid, acetone, benzene, diethyl ether, ethanol, tetrachloromethane

Occupational exposure

FR-VME 10 ppm (45 mg m^{-3})
SE-LEVL 10 ppm (45 mg m^{-3})
UK-LTEL 10 ppm (46 mg m^{-3}) **UK-STEL** 20 ppm (92 mg m^{-3})
US-TWA 10 ppm (45 mg m^{-3}) **US-STEL** 20 ppm (90 mg m^{-3})

UN No. 2876 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification harmful, dangerous for the environment
Risk phrases Harmful if swallowed – Irritating to eyes and skin – Very toxic to aquatic organisms (R22, R36/38, R50)

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} (48,96 hr) fathead minnow 72.6, 53.4 mg l^{-1}, respectively (2).
LC_{50} (48 hr) goldfish 57 mg l^{-1} (3).

Invertebrate toxicity

LC_0 (24 hr) *Daphnia magna* 0.8 mg l^{-1} (4).
LC_{50} (24-96 hr) grass shrimp 170-42 mg l^{-1} (4).
EC_{50} (48 hr) *Palaemonetes pugio* 78 mg l^{-1} (2).
Saccharomyces cerevisiae yeast test IC_{50} 287 mg l^{-1} (5).
EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 264 mg l^{-1} Microtox test (6).

Toxicity to other species

LD_{Lo} (48 hr) *Rana palustris* 270 mg kg^{-1} (7).

Environmental fate

Carbonaceous inhibition

Inhibition of glucose degradation in *Pseudomonas fluorescens* 200 mg l^{-1} (4).

Degradation studies

Adapted culture, 89% removal after 48 hr incubation (feed) 446 mg l^{-1} (4).
Decomposition by soil microflora in 8 days (4).
Adapted activated sludge, 90% COD, 57.5 mg COD g^{-1} dry inoculum hr^{-1} (4).
$t_{1/2}$ of 0.16-0.24 days in an aerobic screening test using activated sludge acclimated to cresols (8).
BOD_5 61% reduction of dissolved oxygen with a sewage inoculum (9).
COD_5 90% in an activated sludge system (10).
Biodegradable (11).

Abiotic removal

Autoxidation in aquatic environment at pH 9 $t_{1/2}$ 67 days at 25°C (4).
Does not significantly absorb ultraviolet light above 295 nm at low concentrations in methanol or acidic aqueous solution. However, in dilute alkaline solutions resorcinol does absorb ultraviolet light above 295 nm (12,13).
The pK_a value of 9.15 suggests it will increasingly dissociate with an increase of pH. Direct photolysis in environmental waters will not occur under acidic conditions, but may potentially occur in alkaline waters (14).
Reacts with photochemically produced hydroxyl radicals; atmospheric $t_{1/2}$ estimated as 1.9 hr (15).
Phenols are generally resistant to aqueous environmental hydrolysis, therefore resorcinol is not expected to hydrolyse significantly in water (16).

Adsorption and retention

Based on a water solubility of 1230 g l^{-1} and a log K_{ow} of 0.8, the soil adsorption coefficient is estimated at 2-65, indicating high to very high soil mobility (17).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig 301, 370 mg kg^{-1}, respectively (1,18).
LD_{Lo} oral human 29 mg kg^{-1} (19).
LD_{50} dermal rabbit 3360 mg kg^{-1} (20).
LD_{50} subcutaneous rat 450 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, insufficient evidence for carcinogenicity in experimental animals, IARC classification group 3 (21).

National Toxicology Program gavage rats and mice long-term study. No evidence of carcinogenicity (22).

Metabolism and toxicokinetics

Readily absorbed from gastro-intestinal tract and, in suitable solvent, is readily absorbed through human skin. Excreted in urine, free and conjugated with hexuronic, sulfuric or other acids (23).

Absorption and metabolic fate of 2% resorcinol applied topically in aqueous alcohol solution was determined in 3 human subjects. After 2 weeks of application (twice daily) of 800 mg to about 30% of body surface, an average of 1.64% of the dosage was excreted in 24 hr urine specimens as the glucuronide or as the sulfate conjugate (24).

Oral administration of 112 mg kg^{-1} to 3 ♂ and 3 ♀ Fischer 344 rats, sacrificed after one day, revealed no evidence of specific organ accumulation of the compound. More than 90% of the total administered dose was recovered from the excreta in 24 hr, primarily in urine with 1-2% eliminated in the faeces and <0.1% as carbon dioxide. Cannulation of the common bile duct followed by intravenous injection of 11.2 mg kg^{-1} resorcinol indicatedthat excretion in bile was rapid and proceeds via enterohepatic circulation to be excreted in urine. Less than 50% of the parent compound was excreted in urine. Major metabolites included glucuronide conjugates (10-20%), and diconjugate with glucuronide and sulfate (5-10%) and diglucuronide conjugate (<2%). Repeated daily exposure of 225 mg kg^{-1} for 5 days did not alter the rate or relative metabolite ratio of excretion (25).

Irritancy

100 mg instilled into rabbit eye caused severe irritation (18).

Sensitisation

Application of 3-25% solutions of resorcinol to skin has been shown to cause allergic contact dermatitis in man (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (26).

Human lymphocytes treated with resorcinol produced minor increases in the number of micronucleated cells (27).

Drosophila melanogaster sex-linked recessive lethal (SLRL) assay; by feed negative, by injection equivocal (28).

Other effects

Other adverse effects (human)

Prolonged exposure of rubber workers to ≤0.3 mg m^{-3} resorcinol in air caused no reported adverse effects (29).

Human pathology reports from poisoning include siderosis of the spleen and kidney tubule damage (30).

Ingestion of 8 g resorcinol by a child resulted in hypothermia, hypotension, decreased respiration, tremors, icterus and haemoglobinaemia (1).

Any other adverse effects

Absorption can cause methaemoglobinaemia, cyanosis, convulsions and death (31).

Legislation

Maximum permitted concentration (USA) in food products 2.5 g kg^{-1} (food) (32).

Other comments

Reviews on human health effects, experimental toxicology and exposure conditions listed (33).

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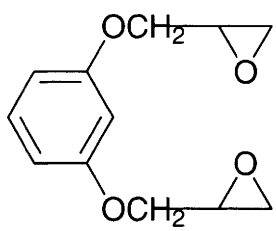
R6 resorcinol diglycidyl ether



$C_{12}H_{14}O_4$ **Mol. Wt.** 222.24 **CAS Registry No.** 101-90-6

Synonyms 1,3-bis(2,3-epoxypropoxy)benzene; Araldite ERE 1359; *m*-bis(2,3-epoxypropoxy)benzene; 1,3-diglycidyloxybenzene; 2,2′-[1,3-phenylenebis(oxymethylene)]bisoxirane

EINECS No. 202-987-5 **RTECS No.** VH 1050000

Uses Limited application in the aerospace industry. A liquid epoxy resin and diluent in manufacture of other epoxy resins.

Physical properties

B. Pt. 172°C at 0.88 mmHg **Flash point** 176°C (open cup) **Specific gravity** 1.21 at 25°C

Occupational exposure

Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Possible risk of irreversible effects – May cause sensitisation by skin contact (R23/24/25, R40, R43)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – Avoid contact with the skin – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S24, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rabbit, rat 980, 1240, 2570 mg kg^{-1}, respectively (1).
LD_{50} intraperitoneal rat, mouse 178, 243 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).
Gavage ♂ ♀ rat (103 wk) 81% (in corn oil) 5 hr wk^{-1} corresponding to 25-50 mg kg^{-1} or 50-100 mg kg^{-1}. High mortality observed in 50 mg kg^{-1} group. Hyperkeratosis and hyperplasia of forestomach, squamous cell papillomas, squamous cell carcinomas in forestomach of ♂ and ♀ mice and rats (3).
National Toxicology Program evaluation of resorcinol diglycidyl ether in rats and mice by gavage positive (4).

Irritancy
Dermal rabbit (25 hr) 500 mg hr caused moderate irritation (5).
In humans severe burns in contact with skin (6).

Genotoxicity

Induced chromosomal aberrations and sister chromatid exchanges in Chinese hamster cells with and without metabolic activation (7).
Mouse lymphoma cell L5178Y tk+/tk– forward mutation assay without metabolic activation positive (8).
Drosophila melanogaster sex-linked recessive lethal induction by feeding and reciprocal translocation induction (9).
Drosophila melanogaster sex chromosome loss, nondisjunction and translocation (10).
Did not induce micronuclei in bone marrow of mice *in vivo* (11).

Other comments

Reviews on human health effects and experimental toxicology listed (12).

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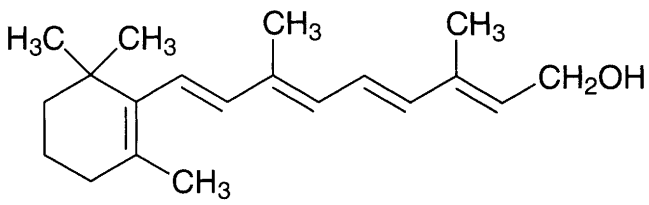
R7 retinol



$C_{20}H_{30}O$ **Mol. Wt.** 286.46 **CAS Registry No.** 68-26-8

Synonyms retinol (all-*trans*); Anatola; Biosterol; Hi-A-vita; Opthalamin; vitamin A (all-*trans*); Vogan

EINECS No. 200-683-7 **RTECS No.** VH 6750000

Uses Used therapeutically as a antixerophthalmic vitamin.

Occurrence In animals but not plants.

Physical properties

M. Pt. 62-64°C **B. Pt.** 120-125°C at 0.005 mmHg (distills)

Solubility Organic solvents: chloroform, diethyl ether, absolute ethanol, methanol, vegetable oils

Environmental fate

Abiotic removal

Rapidly degraded by ultraviolet light and daylight (1).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

LD_{50} (10 day) oral mouse 4100 mg kg^{-1} (2).

Teratogenicity and reproductive effects

Gavage pregnant ICR/SIM mice (doses unspecified but sufficient to cause overt signs of toxicity) on days 8-12 of gestation caused teratogenic effects (3).

In vitro hydra assay disturbed development of hydra embryos by interfering with differentiation at or near adult toxic treatment levels (4).

Microinjection of retinol intra-amniotically on day 10 of gestation to rat embryos which were then cultured until day 11.5. 2000 ng ml^{-1} caused no dysmorphogenesis but did cause an increase in all growth parameters compared with controls (5).

Prenatal exposure in humans of 40,000 IU day^{-1} throughout pregnancy caused facial anomalies, high arched palate without cleft and extremely small ear canals with false fibrous eardrum in front of 1 normal eardrum in the offspring; 60, 000 IU day^{-1} resulted in an infant without a right ear, cleft palate and cleft lip (6).

Large doses taken early in pregnancy may cause birth defects in humans (1,7,8).

Metabolism and toxicokinetics

Readily absorbed from the human gastro-intestinal tract. Stored in the liver and released bound to a α_1-globulin in the blood. The proportion not stored in the liver is excreted as metabolites in faeces and urine. Glucuronide conjugation and subsequent oxidation gives rise to the metabolites, retinal and retinoic acid. Found in human milk, but does not readily diffuse across the placenta (1).

Sensitisation

Perioral dermatitis reported in humans (9).

Other effects

Other adverse effects (human)

Over long periods excessive amounts can give rise to hypervitaminosis A characterised by irritability, anorexia, vomiting, weight loss, fatigue, fever, dry hair, headache, anaemia and pains in joints. Children may show increased intracranial pressure, tinnitus and visual disturbances. May cause arrested bone growth. Acute intoxication can cause erythema, dizziness, sedation and desquamation (1).

Normochromic macrocytic anaemia reported in a patient receiving 150,000 IU daily orally for several months (9).

High intake can lead to fibrosis in the liver causing portal hypertension and hepatocellular dysfunction (10).

Other comments

Reproductive, teratogenic effects extensively reviewed (6).

Human monocytes obtained from non-smoking healthy people were made tumoricidal by incubation *in vitro* for 24 hr with retinol (11).

It is essential for normal differentiation and integrity of respiratory epithelium, deficiency has been associated with increased susceptibility to lung injury (12).

Rats given a retinol-deficient diet (low, medium, adequate, 6, 40, 100 μg kg^{-1} day^{-1}, respectively). Deficiency caused adverse developmental effects to the heart (13).

Pretreatment of mice with retinol reduced by 70% the kidney DNA adduct formation caused by a single administration of the genotoxic mycotoxin ochratoxin (14).

Salmonella typhimurium retinol inhibited 29-48% of the mutagenic activity of solvent extracts of coal dust, diesel emission particles, airborne particles, fried beef and tobacco snuff (15).

Vitamin A levels are cumulative so effects on reproduction are greatly dependent of the duration of use (6).

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R8 rhenium

Re

Re **Mol. Wt.** 186.21 **CAS Registry No.** 7440-15-5

EINECS No. 231-124-5 **RTECS No.** VI 0780000

Uses Catalyst. In electrotubes and semiconductors. To improve the workability of tungsten and molybdenum alloys. Plating jewellery. Mirror backings.

Occurrence In gadolinite, molybdenite, columbite, rare earth minerals and some sulfide ores. Average concentration in Earth's crust is 1×10^{-9} (1 ppb).

Physical properties

M. Pt. 3180°C **B. Pt.** 5900°C **Specific gravity** 21.02

Ecotoxicity

Invertebrate toxicity

Chlamydomonas reinhardti growth rate was enhanced by 1-20 ppm (form unspecified) (1).

Tetrahymena pyriformis 0.04 ppm enhanced growth; >50 ppm inhibited growth (form unspecified) (2,3).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse >10 g kg^{-1} (form unspecified) (4).

Other comments

No toxic manifestations have been reported in experimental animals or humans (5).

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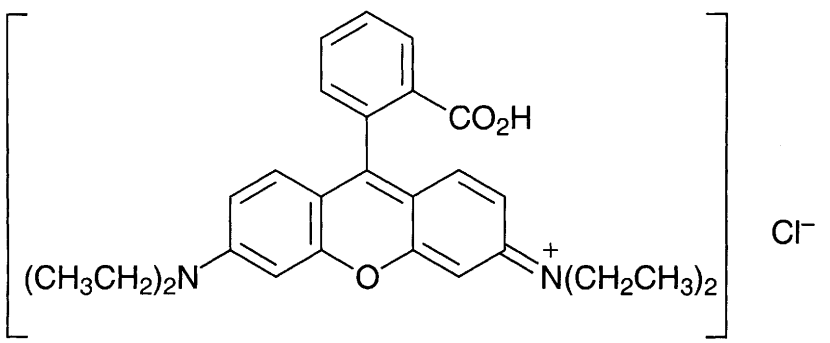
R9 rhodamine B



$C_{28}H_{31}ClN_2O_3$ **Mol. Wt.** 479.02 **CAS Registry No.** 81-88-9

Synonyms C.I. Food Red 15; tetraethylrhodamine; ammonium, [9-(*o*-carboxyphenyl)-6-(diethylamino)-3*H*-xanthen-3-ylidene]diethyl-, chloride; FD&C Red No. 19; Basic Violet 10; C.I. Basic Violet 10; C.I. 45170; Rhodamine B

EINECS No. 201-383-9 **RTECS No.** BP 3675000

Uses Colorimetric reagent for cadmium used as water tracer. Colouring in lipsticks, soap and pharmaceuticals, dyestuff for silk, cotton, wool, nylon, acetate fibres, paper and leather.

Physical properties

M. Pt. 210-211°C (decomp.)
Solubility Water: very soluble. Organic solvents: benzene, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) *Oryzias latipes* 12 mg l^{-1} (1).

Invertebrate toxicity
Not inhibitory to presumptive *Escherichia coli* in marine waters at concentrations ≤100 mg l^{-1} and exposure durations ≤16 hr (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 887 mg kg^{-1} (3).
LD_{50} intravenous rat 89 mg kg^{-1} (4).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (5).
Subcutaneous administration to rats over 68 wk (total dose 3600 mg kg^{-1}) equivocal tumorigenic effects (6).

Teratogenicity and reproductive effects
TD_{Lo} (7-10 days gestation) intraperitoneal mouse 60 mg kg^{-1} embryotoxic (7).

Metabolism and toxicokinetics
Metabolised similarly in rats, rabbits and dogs. Extensively absorbed from the gastro-intestinal tract. 3 to 5% of a 1% dose administered in diet was recovered unchanged in urine or faeces. Deethylated enzymatically to *N,N'*-diethyl-3,6-diaminofluoran and 3,6-diaminofluoran (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (9).
Escherichia coli WP2s (λ) microscreen assay without metabolic activation positive (10).
In vivo intravenous injection 1 mg kg^{-1} to rabbits. Polar metabolites and small amounts of unaltered dye present in urine. Urine tested in *Salmonella typhimurium* TA98, TA100 with or without metabolic activation negative. The commercial preparation (dyestuff) itself was weakly mutagenic in the Ames test (11).
In vitro Muntiacus muntjac fibroblasts chromosomal aberrations positive (12).
Chinese hamster ovary cell chromosomal aberration without metabolic activation positive (13).
Drosophila melanogaster somatic (wing primordia) and germ line cells positive (14).

Other comments

In cultured human lip fibroblasts, C.I. Food Red 15 inhibits production of glycosaminoglycan (15).
In the use of trace dyes in the environment, such as for studying groundwater flow, the concentration of dye is recommended not to exceed 1-2 mg l^{-1}, and not to persist for more than 24 hr in groundwater at the point of groundwater withdrawal or discharge (16).

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R10 rhodium

Rh

Rh **Mol. Wt.** 102.91 **CAS Registry No.** 7440-16-6

EINECS No. 231-125-0 **RTECS No.** VI 9069000

Uses With platinum as an alloy. Electroplating silverware. Spongy or black rhodium is used as a catalyst in oxidation and hydrogenating reactions.

Occurrence In all native platinum, also in the minerals rhodite, sperrylite, iridosmine and some nickel-copper ores. Constitutes ~1×10^{-7}% of the Earth's crust.

Physical properties

M. Pt. 1966°C **B. Pt.** 3727°C **Specific gravity** 12.41 at 20°C

Occupational exposure

FR-VME 1 mg m^{-3} (metal)
UK-LTEL 0.1 mg m^{-3} (metal fume and dust) **UK-STEL** 0.3 mg m^{-3} (metal fume and dust)
US-TWA 1 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat, rabbit 198, 215 mg kg^{-1}, respectively (as $RhCl_3$) (1).

Metabolism and toxicokinetics

Whole-body retention $t_{1/2}$ of 1750-3230 days have been extrapolated for ^{106}Ru-$^{106}RhO_2$ in dogs following a single dose. 82-85% of the total body burden still remained in the lung, with the rest translocated mainly to the lymph nodes, 3.25 hr after administration (2).

Other effects

Any other adverse effects

Following intravenous administration of a single dose in LD_{50} study, no histological lesions were seen in surviving rats and rabbits after 100 or 30 days, respectively (form unspecified) (1).

Other comments

Has antitumour and immunosuppressive properties (3,4).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).

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R11 rhodium trichloride

$RhCl_3$

Cl_3Rh **Mol. Wt.** 209.26 **CAS Registry No.** 10049-07-7

Synonyms rhodium chloride ($RhCl_3$); rhodium(III) chloride; trichlororhodium

EINECS No. 233-165-4 **RTECS No.** VI 9275000

Physical properties

M. Pt. 450-500°C (decomp.) **B. Pt.** 800°C (sublimes)
Solubility Water: insoluble

Occupational exposure

US-TWA 1 mg m^{-3} (as Rh)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1300 mg kg^{-1} (1).
LD_{50} intravenous rat, rabbit 198, 215 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal rat 280 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Charles River CD Swiss mice were given 5 ppm (as metal) in their drinking water for life. Body weight was suppressed at 6 of 16 intervals, compared with mean of controls. Malignant tumours, predominantly lymphomas-leukaemias and adenocarcinomas or papillary adenocarcinomas of the lung, were increased at a minimally significant level of confidence ($P>0.05$). All the tumours were malignant. Longevity was 708 ± 16.5 days compared with 696 ± 19.2 days for controls (4).

Teratogenicity and reproductive effects

Intratesticular injection to albino rats destroyed the interstitium and the testes were totally necrosed within 2 days. Testes weight declined. ~70% of the spermatozoa disintegrated by separation of the head and tail (5).

Other effects

Any other adverse effects

In vitro mouse 3T3-L1 fibroblast-like cells ID_{50} 43-94 mg l^{-1} (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides; guide level 25 mg l^{-1} (7).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

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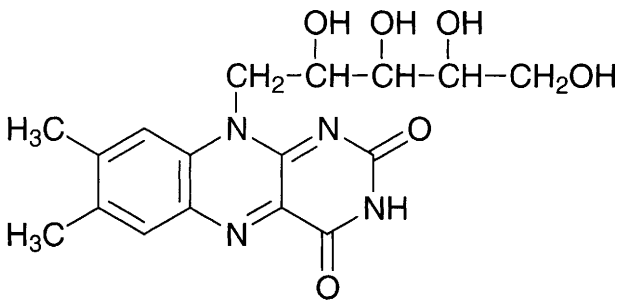
R12 riboflavin



$C_{17}H_{20}N_4O_6$ **Mol. Wt.** 376.37 **CAS Registry No.** 83-88-5

Synonyms Beflavin; Flavaxin; Lactobene; Riboderm; vitamin B_2; vitamin G; riboflavine; Ribipca; Lactoflavine

EINECS No. 201-507-1 **RTECS No.** VJ 1400000

Uses Enzyme co-factor vitamin; nutritional factor for all species.

Occurrence Found in eggs, meat and vegetables; richest natural source is yeast.

Physical properties

M. Pt. 278-282°C (decomp.)

Solubility Water: 1 g dissolves in 3-15 litres (variation due to differences in crystal structure)

Environmental fate

Abiotic removal

In solution degradation is accelerated by light (1).

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rat 5000 mg kg^{-1} (2).

LD_{50} intraperitoneal rat 560 mg kg^{-1} (2).

LD_{Lo} intravenous mouse 365 mg kg^{-1} (3).

Metabolism and toxicokinetics

In vitro transfer across the perfused human placenta indicated that the rate of uptake was in excess of diffusion (4).

In vitro uptake in everted sacs of rat intestine indicate that there was saturable uptake in the duodenum, jejunum and ileum. Uptake by the intestinal mucosa was via a nonsaturable energy-independent mechanism, consistent with simple passive diffusion (5).

Readily absorbed from the gastro-intestinal tract of humans and widely distributed in the body. Little is stored. Converted into the coenzyme flavine mononucleotide and then into another coenzyme, flavine adenine dinucleotide. ~60% of these coenzymes are bound to plasma proteins. Excretion, partly as metabolites, occurs via the urine; as the dose increases larger amounts are excreted unchanged. Occurs in breast milk and crosses the placenta (1).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation negative (6).

Other effects

Other adverse effects (human)

No adverse effects reported. Bright yellow urine follows large doses (1).

Other comments

There was an inhibition of riboflavin supplies in rats, dogs and human carcinoma patients following γ-irradiation (7).

Absorption within 12 hr in humans. Following oral administration of multivitamin preparations, absorption from tablet and or soft elastic gelatin capsule found to be equivalent (8).

Toxicity reviewed (9).

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R13 ricin

CAS Registry No. 9009-86-3

Synonyms Ricine; Ricins

RTECS No. VJ 2625000

Uses Experimentally in cancer research. Tool for cell-surface properties studies.

Occurrence Toxic lectin isolated from castor bean.

Mammalian & avian toxicity

Acute data

LD_{Lo} oral human 2 mg kg^{-1} (1).
LD_{Lo} oral rat 100 mg kg^{-1} (2).
LC_{50} inhalation mouse 9 mg m^{-3}, dog, rat 24-50 mg m^{-3}, monkey 100 mg m^{-3} (duration unspecified) (3).
LD_{50} intraperitoneal rat 1.5-2 μg kg^{-1} (4).
LD_{100} intraperitoneal mouse 25 μg kg^{-1} (5).
LD_{50} intratracheal dog, rat 5 μg kg^{-1} (3).
LD_{50} subcutaneous mouse 22.1 μg kg^{-1} (3).
LD_{50} intravenous mouse 2.2 μg kg^{-1} (3).

Teratogenicity and reproductive effects

In vitro mouse 2-cell embryo development was adversely affected by concentrations as low as 0.01 pg ml^{-1}. No blastocysts were obtained from 4-8-cell embryos treated with 10 pg ml^{-1}. Protein synthesis was affected. Intraperitoneal injection to pregnant mice had no significant effect on implantation frequency and number of liver foetuses at 1.35 μg kg^{-1}, but frequency of stillborn and abnormal foetuses was increased. The weight of foetuses, compared with controls, was influenced by the gestation day when administered (6).

Genotoxicity

In vitro rat hepatoma cells RNA synthesis inhibition (due to protein synthesis inhibition) (7).

Other effects

Other adverse effects (human)

Fatal to a child who ate 5 castor beans and an adult who ate 20 beans (8).

Any other adverse effects

Target organs for ricin toxicity are dependent on route of administration; following oral ingestion the gastro-intestinal tract is most severly affected; after parenteral administration it is preferentially distributed to the liver spleen and muscle (9,10).
Fatal dose by intravenous route in laboratory animals is as low as 300 ng kg^{-1} body weight (8).

Other comments

Mice given an LD_{100} dose had their survival time extended (lethality was not prevented) by difluoromethylornithine and dexamethasone (5).
Biochemical, cellular, tissue effects, mutagenesis and genetic toxicity currently under study by National Toxicity Program (11).
Potential as anticancer agent (8).

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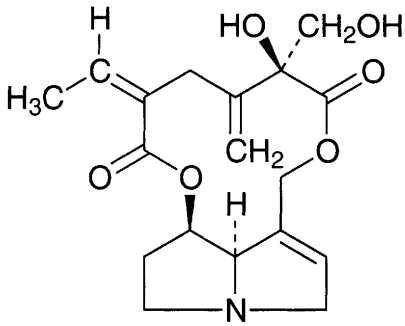
11. National Toxicology Program *Review of Current DHHS, DoE, and EPA Research Related to Toxicology* 1992, 169, Research Triangle Park, NC, USA

R14 ridelline



$C_{18}H_{23}NO_6$ **Mol. Wt.** 349.38 **CAS Registry No.** 23246-96-0

Synonyms 13,19-didehydro-12,18-dihydroxysenecionan-11,16-dione; *trans*-15-ethylidene-12β-hydroxy-12α-hydroxymethyl-13-methylenesenec-1-enine; senecionan-11,16-dione, 13,19-dihydro-12,18-dihydroxy-; riddelliin; riddelliine

RTECS No. VJ 3850000

Uses An experimental tumourigen.

Occurrence An alkaloid found in plants of the genera *Crotalaria*, *Amsinckia*, and *Senecio* in the United States.

Physical properties

M. Pt. 187°C

Solubility Water: <1 mg ml^{-1} at 25°C. Organic solvents: acetone, 95% ethanol, chloroform, DMSO

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 25 mg kg^{-1} (1). LD_{50} intravenous mouse 105 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Gavage ♂ and ♀ Fischer rats 0-10 mg kg^{-1} and ♂ and ♀ B6C3F1 mice 0-25 mg kg^{-1} 5 × wk^{-1}. Animals were necropsied after 13 wk of treatment or following a 7 or 14 wk recovery period. In both rats and mice body weight gains were inversely proportional to dose and the body weights of ♀ rats dosed with 1.0 and 3.3 mg kg^{-1} and mice dosed with 10.0 and 25.0 mg kg^{-1} remained depressed during the 14 wk recovery period. After 13 wk of treatment dose-related liver damage and intravascular macrophage accumulation in rats and enlarged liver cells in mice were seen. These lesions persisted during the 14 wk recovery period and hepatic foci of cellular alteration in ♀ rats and ♂ and ♀ mice increased in severity. Adenomas of the liver occurred in 2/10 ♀ rats receiving 10 mg kg^{-1} for 13 wk and 1/5 (same dose) after a 14 wk recovery period (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

In mating trials with gavage mice and rats, pup weights from treated dams at birth and during suckling were lower than controls. Riddelline may thus cross the placenta and/or be found in milk in rodents (4).

Genotoxicity

Induction of chromosome aberrations in CHO cells without metabolic activation negative, with metabolic activation positive with very high induction frequencies (5). Induction of sister chromatid exchanges in CHO cells with and without metabolic activation positive (5).

Gavage Fischer rats and B6C3F1 mice dosed with up to 25.0 mg kg^{-1} for 5 or 30 days showed an increase in unscheduled DNA and S-phase synthesis in primary hepatocytes (3).

Micronucleated polychromatic erythrocyte assay using bone marrow of mice after 5 days of dosing or of mice and rats after 30 days of dosing negative (6).

Unscheduled DNA synthesis in rat hepatocytes of mice after 5 or 30 days of dosing negative. Unscheduled DNA synthesis in ♂ mice after 5 or 30 days dosing equivocal and in ♀ mice after 30 days dosing positive (6).

S-Phase synthesis assay using hepatocytes of rats after 5 and 30 days dosing positive (even at low doses) and of ♂ and ♀ mice after 30 days dosing. Rats and mice of both sexes showed a depression of S-phase synthesis at high doses (6).

Other effects

Any other adverse effects

Chronic administration of riddelline caused lung oedema and liver damage in mice and rats but had no oestrogenic, antitumour or antibacterial activity (7).

Other comments

A pyrrolizidine alkaloid which has been found to contaminate human food sources (3).

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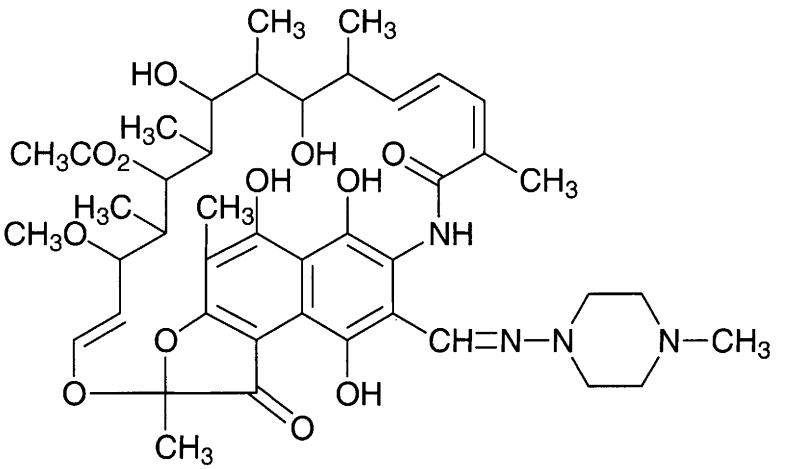
R15 rifampicin



$C_{43}H_{58}N_4O_{12}$ **Mol. Wt.** 822.95 **CAS Registry No.** 13292-46-1

Synonyms 3-[[(4-methyl-1-piperazinyl)imino]methyl]rifamyci; naphtho[2,1-*b*]furan-1,11(2*H*)-dione, 5,6,9,17,19,21-hexahydroxy-23-methoxy-2,4,12,16,18,20,22-heptamethyl-8-[*N*-(4-methyl-1-piperazinyl)formimidoyl]-2,7-(epoxypentadeca[1,11,13]trienimino)-, 21-acetate; rifadin; rifampin; riforal; rifa; Sinerdol; Tubocin

EINECS No. 236-312-0 **RTECS No.** VJ 7000000

Uses Antibiotic with activity against Gram-positive and Gram-negative bacteria. Used in the treatment of leprosy and tuberculosis, in association with other antimycobacterial drugs.

Physical properties

M. Pt. 183-188°C

Solubility Water: slightyl soluble (pH 6). Organic solvents: chloroform, dimethylsulfoxide

Ecotoxicity

Invertebrate toxicity

Sewage filter effluent microorganisms, 5 µl ml^{-1} completely suppresses microbial growth (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 500, 1570 mg kg^{-1}, respectively (2,3).

LD_{50} subcutaneous rat, mouse 534, 621 mg kg^{-1}, respectively (3).

LD_{50} intraperitoneal rat, mouse 390, 480 mg kg^{-1}, respectively (4).

LD_{50} intravenous mouse 260 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Oral (4 wk) rabbit 400 mg kg^{-1} day^{-1} caused weight loss, marked jaundice and fatty and hydropic degeneration of livers and kidneys (5).

Oral (6 month) dog 50 mg kg^{-1} day^{-1}, caused liver and kidney degeneration, 2 dogs also showed alterations in bone-marrow megakaryocytes (5).

Gavage (8 day) rat 200 or 400 mg kg^{-1} day^{-1}. There was a transient decrease in body weight in the lower dose

group, this was particularly observed in ♀. 400 mg kg^{-1} day^{-1} caused a very pronounced decrease in body weight, marked dorsal hair loss, early anorexia and apathy. It also induced fatty liver, an increase in total lipids and triacylglycerols in livers of ♀ rats and an increase in total cholesterol in livers of ♂ and ♀ (6).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (7).

Oral mice (114 wk) 0, 0.01, 0.03, 0.06% with 0.05% sodium ascorbate in drinking water for 60 wk. There was a significant increase of benign and malignant liver tumours in the 2 highest dose groups, there was no increase in other tumour types between ♂ and ♀ and between controls (8).

Oral rat (114 wk) 0, 0.03, 0.06% in drinking water with 0.05% sodium ascorbate for 60 wk. There was no significant increase in tumours compared to the controls (8).

Subcutaneous rat (12 month) 20 injections of 0.3 mg in saline into the axilla. No malignant tumours were observed (9).

Teratogenicity and reproductive effects

Oral mouse 500 mg kg^{-1} day^{-1} on day 9-10 of gestation caused an incidence of 59% cleft palate in the offspring (10).

Oral mouse, rat, rabbit >150 mg kg^{-1} during the period of organogenesis caused no effects on rabbit foetuses. Spina bifida in rat offspring; and spina bifida and cleft palate in mice offspring were found (2).

A study of 118 women exposed to rifampicin during pregnancy did not increase the malformation rate in the offspring (11).

Metabolism and toxicokinetics

Following oral administration of 1.25-10 mg kg^{-1} maximum blood levels were reached by 5-6 hr in dogs and 90 min in rats and mice (5).

In mice it is rapidly distributed to the tissues. The lung, myocardium, brown fat, salivary glands, gastrointestinal mucosa, pancreas and kidneys all had higher uptake levels than the blood (12).

In ♂ rats after oral administration of [^{14}C]-rifampicin after 48 hr 41% was excreted in the faeces and 21% in the urine. There were 2 metabolites identified in the liver, bile and faeces, 25-deacetylrifampicin and *N*-desmethylrifampicin (13).

Elimination from plasma was rapid in guinea pigs and rats, slower in mice and very slow in dogs (14).

In humans absorption is rapid and complete after oral administration to an empty stomach (15).

In humans after repeated oral doses of 300 mg kg^{-1} the apparent serum $t_{1/2}$ decreased with repeated administration. On day 1 $t_{1/2}$ 2.7 hr, on day 8 $t_{1/2}$ 1.5 hr(16).

In humans, it is excreted unchanged in urine as well as being metabolised. The major metabolite is deacetylrifampicin which is excreted in bile. Urinary metabolites include 3-formylrifampicin; rifampicinquinone; deacetylrifampicinquinone and 3-formyldeacetylrifampicin (6).

Given orally to humans and rats, it is more slowly absorbed, with lower blood concentrations and less bioavailability when in tablet form than as capsules (17).

Oral administration of 450 mg to humans was followed by a peak of unmetabolised rifampicin in the urine within 2 hr. The deacetyl metabolite was found in urine after 1 or 2 doses but not after repeated dosing, 3-formylrifamycin SV is found in the urine (<6 mg 24 hr^{-1}), repeated dosing did however accelerate rifampicin metabolism (18).

Readily absorbed from the gastro-intestinal tract and widely distibuted. Plasma protein binding accounts for ~80%. Crosses the placenta and occurs in human breast milk. Elimination time may decrease up to 40% from theinitial $t_{1/2}$ of 2-5 hr because rifampicin induces its own metabolism. The $t_{1/2}$ is increased in people with liver disease (19).

Sensitisation

Contact dermatitis reported in humans (20).

Genotoxicity

Salmonella typhimurium G46, TA1532 negative (metabolic activation unspecified) (21).

Escherichia coli WP2 negative (metabolic activation unspecified) (21).

In vitro whole blood cell cultures increase in chromatid breaks (22).
In vitro human leucocytes chromosomes showed no evidence of clastogenic effects (23).
Drosophila melanogaster in vivo did not increase recessive lethality (23).
In vivo mouse dominant lethal assay negative, chromosomal aberrations negative (24,25).

Other effects

Other adverse effects (human)

Administration of 1200 mg day^{-1} for 14 days to humans caused a decrease in the $t_{1/2}$ of thyroxine from 157 to 106 hr (16).
There was no increase in the frequency of chromosomal aberration in patients after treatment (26).
Thrombocytopenia, leucopenia, haemolysis/haemolytic anaemia and red cell aplasia have occurred (27-30).
Erosive gastritis and gastro-intestinal bleeding reported (31).

Any other adverse effects

Administration of rifampicin and isoniazid in equimolar doses (250 and 50 mg kg^{-1}, respectively) for 14 days increased the activities of alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase in the serum; enhanced lipid peroxidation in hepatocyte membranes and disturbed bile excretion (species unspecified) (32).

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 (33).
Production, use, toxicity and metabolism reviewed (16).
Liver failure reviewed (34).
Did not have a significant effect on murine delayed type hypersensitivity (35).

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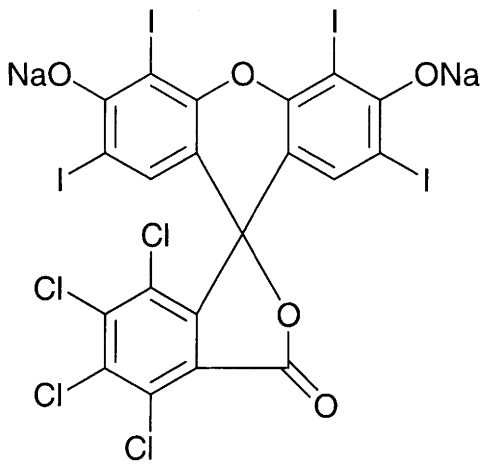
R16 Rose Bengal sodium



$C_{20}H_4Cl_4I_4Na_2O_5$ **Mol. Wt.** 1019.66 **CAS Registry No.** 632-69-9

Synonyms 4,5,6,7-tetrachloro-3′,6′-dihydroxy-2′,4′,5′,7-tetraiodospiro[isobenzofuran-1(3*H*), 9′[9*H*]xanthen]-3-one, disodium salt; 4,5,6,7-tetrachloro-2′,4′,5′,7′-tetraiodofluorescein, disodium salt; Food Red 105, sodium salt

EINECS No. 211-183-3 **RTECS No.** LM 5920000

Uses Colorant of food and external use pharmaceutical and cosmetic preparations. Diagnostic agent.

Mammalian & avian toxicity

Acute data

TD_{Lo} oral mouse 707 g kg^{-1} (1).

Carcinogenicity and chronic effects

(C57BL/6N × C3H/N)F_1 mice between 6 and 101 wk of age were given 0.125 or 0.5% Rose Bengal B in drinking water. Thyroid gland weights were significantly increased. Colloid goiters with distended follicle, lined with flattened follicular cells almost exclusively formed in the glands. There was a significantly higher incidence of follicular adenomas in ♂ thyroid glands. Iodine uptake in colloid goiters was decreased. Hepatic tumours occurred, but were not significantly greater than in controls. Fat deposits increased the body weight, particularly in ♀ animals (1).

Teratogenicity and reproductive effects

1.5 g kg^{-1} (Rose Bengal B) reduced body weight in adult rats. No malformed foetuses were found when the mother was given 0.4-1.5 g kg^{-1}. Growth was slowed in new borns for the four weeks after birth at 0.4-2.5% (2).

Metabolism and toxicokinetics
Excreted in humans via the liver in the bile (3).

Genotoxicity

Salmonella typhimurium (strains and metabolic activation unspecified) positive (Rose Bengal B) (4).
Escherichia coli positive (metabolic activation unspecified) (Rose Bengal B) (4).

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R17 rosin oil

CAS Registry No. 8002-16-2

Synonyms essential oils, rosin; oils, rosin

EINECS No. 232-300-4

Uses For soldering, surgical plasters, glues and adhesives, paper sizing, tackifiers, printing inks, emulsifiers, artists materials and as string players rosin.
Occurrence In natural resins derived from trees of the *Pinus* sp.; resin derived from these trees contains 80% rosin and 20% turpentine

Physical properties

B. Pt. >280°C **Flash point** 130°C
Solubility Water: insoluble in water. Organic solvents: ether

Occupational exposure

UN No. 1286 **HAZCHEM Code** 3YE (flash point <23°C, initial boiling point >35°C) **HAZCHEM Code** 3Y (flash point ≥23°C, ≤61°C, initial boiling point >35°C) **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Sensitisation
Particulate and gaseous emissions given off during rosin cored soldering are a significant cause of respiratory sensitisation which can lead to occupational asthma (1).

Other effects

Other adverse effects (human)
Particulate and gaseous emissions given off during rosin cored soldering are a significant cause of respiratory sensitisation which can lead to occupational asthma (1).
Occupational asthma associated with rosin soldering fumes is increasingly significant in electronics factories with 20-30 new cases per annum (2).
Using occupational type provocation tests asthma due to rosin fumes was observed in 4 workers in one study and 21 in another (total sample size unspecified) (3,4).
Contact urticaria has been reported following exposure to rosin fumes (5).

Other comments

Autoignition temperature 342°C.

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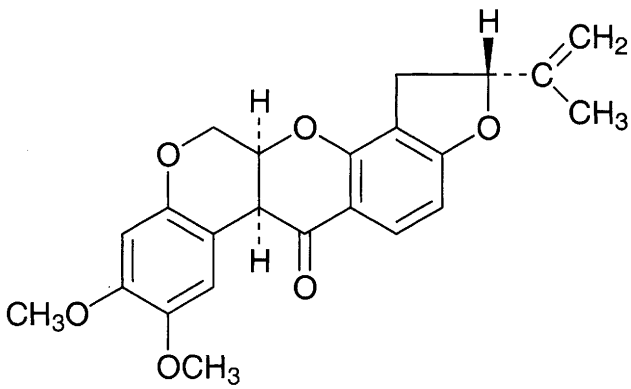
R18 rotenone



$C_{23}H_{22}O_6$ **Mol. Wt.** 394.42 **CAS Registry No.** 83-79-4

Synonyms [1]benzopyrano[3,4-*b*]furo[2,3-*h*][1]benzopyran-6 (6a*H*)-one, 1,2,12,12a-tetrahydro-8,9-dimethoxy-2-(1-methylethenyl)-, [2*R*-(2α,6aα,12aα)]-; [2*R*-(2α,6aα,12aα)]-1,2,12,12a-tetrahydro-8,9-dimethoxy-2-(1-methylethenyl)-[1]benzopyrano-[3,4- *b*]furo[2,3-*h*][1]benzopyran-6(6a*H*)-one; Derris; ENT 133; Rotacide; Chem-Fish; Noxfish; Sicid

EINECS No. 201-501-9 **RTECS No.** DJ 2800000

Uses Acaricide, ectoparasiticide, piscicide.
Occurrence In roots of species of *Derris* and *Lonchocarpus*.

Physical properties

M. Pt. 165-166°C (dimorphic form 185-186°C) **B. Pt.** 210-220°C at 0.5 mmHg **Specific gravity** 1.27 at 20°C
Partition coefficient log P_{ow} 3.88 **Volatility** v.p. $<7.52 \times 10^{-6}$ mmHg at 20°C
Solubility Water: almost insoluble in water. Organic solvents: acetone, carbon tetrachloride, chloroform, ethanol, ether

Occupational exposure

DE-MAK 5 mg m^{-3} (inhalable fraction of aerosol)
UK-LTEL 5 mg m^{-3} **UK-STEL** 10 mg m^{-3}
US-TWA 5 mg m^{-3}
Supply classification toxic

Risk phrases Toxic if swallowed – Irritating to eyes, respiratory system and skin (R25, R36/37/38)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Avoid contact with skin and eyes – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S24/25, S36, S45)

Ecotoxicity

Fish toxicity

Rainbow trout eyed eggs (32 days) 1-10 μg l^{-1} in flow-through toxicity test was not toxic, eggs hatched normally after 5 or 6 days exposure (1).
LC_{50} (48 hr) rainbow trout, carp, goldfish 26-33 μg l^{-1} (2,3).
LC_{50} (96 hr) Atlantic salmon, brown trout, northern pike, American char, rainbow trout 0.021-0.046 mg l^{-1} (4).
LC_{50} (4 day) rainbow trout, fathead minnow, longnose sucker, bluegill sunfish 5-14 μg l^{-1} (5).

Invertebrate toxicity

LC_{50} (48 hr) *Simocephalus serrulatus* 190 μg l^{-1} (6).
EC_{50} (48 hr) *Daphnia magna* 3.7 μg l^{-1} (1).
EC_{50} (21 day) *Daphnia magna* 2.1 μg l^{-1} (1).
NOEC *Daphnia magna* 1.25 μg l^{-1} (1).
LC_{50} (48 hr) *Daphnia pulex* 0.1 mg l^{-1} (6).
LC_{50} (4 day) water snail >0.040 mg l^{-1} (5).
LC_{50} (96 hr) *Gammarus lacustris* 2600 μg l^{-1} (7).
LC_{50} (96 hr) *Pteronarcys californica* 380 μg l^{-1} (8).
LD_{50} honey bee (contact) > 60 μg, (oral) > 30 μg (9).

Bioaccumulation

In fresh water mussels and crayfish residues in tissues increased for 1 wk in cold water and for 1 day in warm water then slowly declined (concentrations unspecified). Residues in fish varied between species although levels were higher in fish tissues than in water (10).

Environmental fate

Degradation studies

0.250 mg l^{-1} in cold and warm water ponds, decomposition followed 1st-order decay curve; cold water $t_{1/2}$ 10.3 days, warm water $t_{1/2}$ 0.94 days (10).

Abiotic removal

Decomposes on exposure to light and air (11).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 60-1500 and 350 mg kg^{-1}, respectively (2,11,12).
LD_{Lo} oral guinea pig, dog 100, 300 mg kg^{-1}, respectively (13,14).
LD_{50} intraperitoneal mouse, rat 2.7, 5 mg kg^{-1}, respectively (15,16).
LD_{Lo} intraperitoneal guinea pig 10 mg kg^{-1} (13).
LD_{Lo} oral human 143 mg kg^{-1} (17).

Sub-acute and sub-chronic data

Oral (14 day) rat, mouse 0-4800 ppm in diet. No compound-related toxic effects were observed in mice. Rats fed doses of ≥1200 ppm lost weight, rough hair coats were also observed (18).
Oral (13 wk) rat 0-1200 ppm in diet. ≥150 ppm caused lower body weight gain, ≥300 ppm for ♂ and ≥150 ppm for ♀ caused bone marrow atrophy and inflammation and hyperplasia of the forestomach (18).

Carcinogenicity and chronic effects

The National Toxicology Program tested rats and mice orally via feed, rats 0-75 ppm, mice 0-1200 ppm. In a 2-yr study there was equivocal evidence of carcinogenicity in ♂ rats, indicated by an increased incidence of parathyroid gland adenomas (uncommon tumours). There was no evidence of carcinogenicity in ♂, ♀ mice or ♀ rats (18,19).

Teratogenicity and reproductive effects

Wistar rats were given 0, 2.5, 5 or 10 mg kg^{-1} orally in single daily doses on gestation day 6-15. The highest dose killed 12 of the 20 dams. Listlessness and loss of body weight were signs of toxicity. Mean foetal weight was reduced but not significantly. Skeletal malformations and visceral defects were not significantly different from controls. However, skeletal aberrations including delayed ossifications of sternum, missing sternebrae and extra rib were significantly increased in the 5 mg kg^{-1} (20).

In pregnant Sprague-Dawley rats given 10-1000 ppm in diet, ovarian protein, placental protein and glycogen were decreased. No resorption of implantation sites was seen on day 12 of gestation. Absorption did not occur. Foetal survival rate was reduced in a dose-independent manner. Foetal weight on delivery was not affected (21).

Metabolism and toxicokinetics

A methoxy group is the product of the enzymically opened and cleaved furan ring in insects and rat liver. Rotenonone is the principal metabolite. Oxidation of a methyl group of the isopropenyl residue yields an alcohol as a further metabolite (11,22).

Irritancy

1% instilled into rabbits eye caused mild irritation (13).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1538 with and without metabolic activation negative (18,23).
In vitro mouse L5178Y tk^+/tk^- lymphoma assay without metabolic activation induced forward mutations (18,24).
In vitro Chinese hamster ovary cells with and without metabolic activation chromosomal aberrations negative; sister chromatid exchanges without metabolic activation negative with metabolic activation equivocal (15,25).
In vitro Chinese hamster ovary cells induced aneuploidy (hypodiploidy and hyperdiploidy), polyploidy and endoreduplication but not structural chromosomal aberrations (26).
In vitro human lymphocytes with and without metabolic activation micronuclei positive, sister chromatid exchanges negative, chromosomal aberrations negative (27).

Other effects

Other adverse effects (human)

Estimated lethal dose 0.3-0.59 g kg^{-1}, more toxic when inhaled than when ingested (12).

Any other adverse effects

Even at high concentrations (507 μmol kg^{-1}) rotenone administered intramuscularly to white leghorn roosters had neither oestrogen nor antiestrogen activity, as measured by its effect on oestrogen-related mRNA stabilising factor (28).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (29).
Included in Schedule 6 (Release into Land: 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).
WHO Class II (32).
EPA Toxicity Class III (12).

Other comments

Very toxic to pigs (12).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (33).

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R19 rubidium

Rb

Rb **Mol. Wt.** 85.47 **CAS Registry No.** 7440-17-7

EINECS No. 231-126-6 **RTECS No.** VL 8500000

Uses As a reagent in zeolite catalyst production. In photoelectric cells. Making rubidium salts. In research.
Occurrence In seawater, mineral springs and salt lakes. In rhodizite, lepidolite and rubidium carnalite. Widely distributed in very small quantities in Earth's crust: 0.0034% by weight.

Physical properties

M. Pt. 38.89°C **B. Pt.** 688°C **Specific gravity** 1.532 (solid) at 20°C; 1.475 (liquid) at 39°C
Volatility v.den. 1.475 at 39°C
Solubility Water: decomp

Occupational exposure

UN No. 1423 **HAZCHEM Code** 4W **Conveyance classification** substance which in contact with water emits flammable gas

Mammalian & avian toxicity

Acute data

LD_{50} oral rat for rubidium compounds, sulfate, carbonate, nitrate or chloride 2.6-5.0 g kg^{-1} (1).
Minimum toxic concentrations (4 hr) inhalation rat for rubidium compounds, sulfate, carbonate, nitrate or chloride 30-51 mg m^{-3} (1).
LD_{50} intraperitoneal mouse, rat 1160, 1200 mg kg^{-1}, respectively (as RbCl) (2).

Carcinogenicity and chronic effects

Not demonstrably toxic following ingestion for 3 yr by rats in drinking water (dose unspecified). Effect on the central nervous system, including increased excitability were seen. Reduced weight gain and angiogenic seizures occurred when potassium intake was restricted (3).
Sprague-Dawley rats were fed RbCl and KCl at concentrations of 121 and 75 mg l^{-1}, respectively, immediately after weaning for three generations. No differences were found compared with the control (KCl only) with respect to litter weight, deaths prior to weaning and percentage of deaths in the first year following weaning. The liver contained the most rubidium, with the brain having the least. Rb:K ratios: liver, 0.32; kidney, 0.16; lung 0.10; heart, 0.08; and brain, 0.03. The only adverse effects were related to interference wth potassium metabolism affecting the nervous system and included greater excitability and tail biting (3).

Teratogenicity and reproductive effects

Reduced survival rate of young of animals (unspecified) fed 0.1% in diet (3).

Metabolism and toxicokinetics

For a 70 kg man the normal total body level is 360 mg (4).
Average levels in human (μg ml^{-1}): 4.18, red blood cells; 0.16, plasma; and 1.52, urine (5).
Content of human backbone in Australian study was 25 ppm (range 16-45 ppm). The highest values were found in the newborn and in 1-9 yr olds, the trend with age was seen after this age (6).
Rapidly absorbed from the intestine and accumulates in muscle, where it is retained at the expense of potassium (7).
Replaced 50% or more of the muscle potassium in chronic feeding studies when given with equivalent amounts of potassium in the rats (7).
The major excretion route is via the urine. When intravenously administered it was rapidly cleared from the blood, with only 7% remaining after 1 hr. Urinary excretion accounted for 14% within 12 days (species unspecified) (8).
$t_{1/2}$ in man, 50-60 days (estimated) (9).

Sensitisation

Non-sensitising to guinea pigs (10).

Other effects

Other adverse effects (human)

Destructive to the tissues of the upper respiratory tract and inhalation may cause dyspnoea, headache and coughing (3).

Any other adverse effects

Animal studies, including those in monkeys, have shown increased levels of alertness and activity and a shift of the electroencephalogram to higher frequencies (11-13).

Other comments

Exchanges with potassium in blood, plasma and tissue (3).
Ignites spontaneously in oxygen; when molten ignites in air.

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R20 rubidium hydroxide

RbOH

HORb **Mol. Wt.** 102.48 **CAS Registry No.** 1310-82-3

Synonyms rubidium hydroxide (RbOH)

EINECS No. 215-186-0 **RTECS No.** VL 8750000

Uses Catalyst in oxidative chlorination.

Physical properties

M. Pt. 300°C **Specific gravity** 3.203 at 11°C
Solubility Water: 1800 g l^{-1} cold water. Organic solvents: ethanol

Occupational exposure

UN No. 2677 **HAZCHEM Code** 2X **HAZCHEM Code** 2R (solution)
Conveyance classification corrosive substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 586, 900 mg kg^{-1}, respectively (1,2).
Minimum toxic concentration via inhalation human, rat (duration unspecified) 5.75, 39 mg m^{-3}, respectively (3).
LD_{50} intragastric rat 1.6 g kg^{-1} (3).

Irritancy

5% solution was mildly irritating to abraded but not intact rabbit skin and extremely irritating and corrosive to the rabbit eye causing corneal turbidity, ulceration of the lower lid mucous membrane and purulent formation in the conjunctival sac (4).

Sensitisation
Non-sensitising to guinea pig skin (1).

Other effects

Any other adverse effects
Lethal doses resulting in death of rats within 72 hr caused haemorrhages to the stomach and intestine with necrotisation and thinning of the walls and adhesions of the abdominal organs. Death was related to the degree of blockage of the gastro-intestinal tract from adhesions and/or the leakage of bloody fluid exudate into the peritoneal cavity. Survivors showed hyperexcitability followed by apathy and weakness, increased respiration rate, eyeclosing and huddling together (4).

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R21 ruthenium

Ru

Ru **Mol. Wt.** 101.07 **CAS Registry No.** 7440-18-8

EINECS No. 231-127-1

Uses Substitute for platinum in jewellery. In pen nibs. As hardner for electrical contact alloys.
Occurrence Found in the minerals osmiridium, laurite, in platinum ores, in some copper-nickel ores. constitutes about 0.4 ppb of Earth's crust.

Physical properties

M. Pt. ~2450°C **B. Pt.** ~4150°C **Specific gravity** 12.45 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Acute data
LD_{50} (route unspecified) mouse 132 mg kg^{-1} (as Ru^{3+} ammine complex) (1).

Metabolism and toxicokinetics
In ^{106}Ru-label experiments retention from oral administration was very much less than from intraperitoneal injection in mice and rats. Whole-body retention was 4% of the dose at 450 days following intraperitoneal injection, whereas by oral route activity was undetectable beyond 23 and 33 days in rats and mice, respectively. Dogs still retained a proportion of the dose at 1000 days following intravenous administration. ~40% of a parenteral dose was lost with a $t_{1/2}$ of ~1 wk in rat, mouse, monkey and dog (2).
Absorption from the gastro-intestinal tract decreases with age (species unspecified) (3).
An effective $t_{1/2}$ in the chest of human following accidental exposure to a volatile ^{103}Ru compound was 26.6 days (4).

Other effects

Other adverse effects (human)
Accidental exposure to ^{103}Ru has occurred without serious consequences (5,6).

Other comments

Has anticancer and immunosuppressive properties (1).

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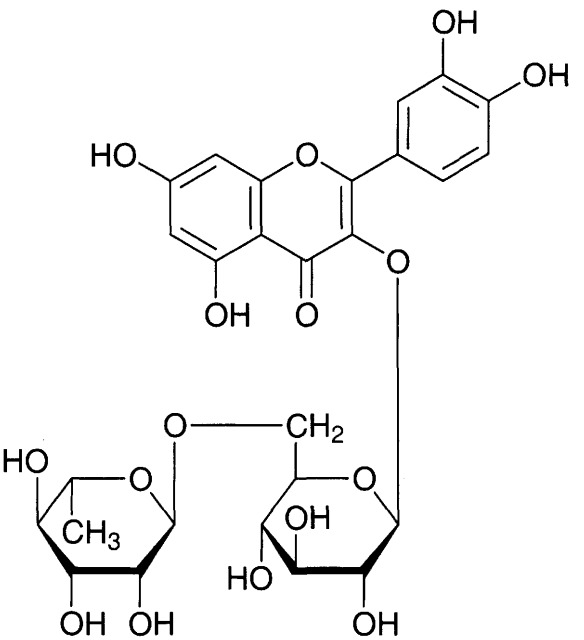
R22 rutin



$C_{27}H_{30}O_{16}$ **Mol. Wt.** 610.53 **CAS Registry No.** 153-18-4

Synonyms 4*H*-1-benzopyran-4-one, 3-[[6-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyrano syl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-; rutoside; myrticolorin; osyritrin; quercetin 3-rutinoside; violaquercitin; C.I. 75730

EINECS No. 205-814-1 **RTECS No.** VM 2975000

Uses Capillary protectant.

Occurrence Many plant species, especially buckwheat plant.

Physical properties

Solubility Water: 1 g in 8 l. Organic solvents: acetone, ethanol, ethyl acetate, formamide, pyridine

Ecotoxicity

Invertebrate toxicity

Cultured cell-free microbial extracts from human faeces (fecalase) and saliva (salivase), rutin was inhibitory to fecalase but was not inhibitory to salivase (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >100 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (3).
LD_{50} intraperitoneal rat, guinea pig 2000 mg kg^{-1} (4).
LD_{50} intravenous mouse 950 mg kg^{-1} (5).

Metabolism and toxicokinetics

In humans 4 metabolites were detected following oral administration: 3,4-dihydroxytoluene, 3-hydroxyphenylacetic acid, 3,4-dihydroxyphenylacetic acid and 3-methoxy-4-hydroxyphenylacetic acid. These metabolites increased 4-8 hr after administration and had reached a maximum by 8-12 hr, after which blood levels declined to the original level by 20-35 hr post administration. $t_{1/2}$ 11 hr (for sum of metabolites). Total urinary excretion of the metabolites was 50.5% of dose within 48 hr (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 with and without metabolic activation positive (7).

Other effects

Any other adverse effects

Enzymic hydrolysis results in the formation of quercetin which is mutagenic in the Ames test (1).
Showed antibacterial activity to *Staphylococcus aureus, Staphylococcus albus, Bacillus subtilis* and *Bacillus anthracoides* (8).

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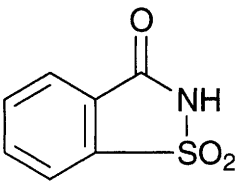
S1 saccharin



$C_7H_5NO_3S$ **Mol. Wt.** 183.19 **CAS Registry No.** 81-07-2

Synonyms benzosulfimide; *o*-sulfobenzimide; 1,2-dihydro-2-ketobenzisosulfonazole; 2,3-dihydro-3-oxobenzisosulfonazole; *o*-sulfobenzoic acid imide; 1,2-benzisothiazolin-3(2*H*)-one 1,1-dioxide; Supasac; Sweeta; Syncal SDI; Unisweet SAC

EINECS No. 201-321-0 **RTECS No.** DE 4200000

Uses Non-caloric sweetening agent. Food additive. Formulation for electroplating bath brightness. Normally used as sodium (RN 128-44-9) or calcium (RN 6485-34-3) salt.

Physical properties

M. Pt. 229°C **Specific gravity** 0.828

Solubility Water: 3.4 g l^{-1} at 25°C. Organic solvents: acetone, ethanol, glycerol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 18.3 g l^{-1} (salt) (1).

Bioaccumulation

Bioconcentration factors of 1.58 and 2.1 based on a water solubility of 4000 mg l^{-1} at 25°C and log P_{ow} of 0.91 suggests bioconcentration in aquatic organisms is unlikely (2).

Environmental fate

Abiotic removal

Respective acid and alkaline hydrolysis products are *o*-sulfamoylbenzoic acid and ammonium *o*-sulfolbenzoic acid (3).

Stable enough in aqueous solution for most normal food applications, especially beverages, therefore suggesting hydrolysis in environmental media is unlikely (4).

Atmospheric $t_{1/2}$ 6.5 hr (4).

Adsorption and retention

Calculated solid adsorption coefficient from 45-75 indicate high mobility in soil. It should not partition from the water column to organic matter contained in sediments and suspended solids (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 17 g kg^{-1} (6).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (7).

Dose-related increase in bladder tumours in F_1 ♂ rats fed sodium saccharin at 5-7.5% in two-generation studies. Increased incidence of bladder tumours in mice (7).

1969 study of 10:1 mixture of cyclamates and saccharin found bladder tumours in rats which led to a ban on cyclamates in the US and a ban on saccharin in Canada. However, with normal ingestion there is little or no risk of bladder cancer. It should be noted that the equivalent to a daily intake by humans would be 500 g day^{-1} and that foods containing such doses would be inedible (1,8).
Albino mice (1 yr) 0-1.5 g kg^{-1} day^{-1} in diet. A marked decrease in total erythrocyte count, haemoglobin content and packed cell volume, at 1 and 1.5 g kg^{-1} day^{-1} suggesting occurrence of anaemia. Differential leukocyte count revealed an increase in the number of polymorphonuclear neutrophils (8).

Teratogenicity and reproductive effects
Intraperitoneal, intragastric and oral ingestion mice 2000 mg kg^{-1}, no teratogenic effects reported (9).

Metabolism and toxicokinetics
Transplacental transfer following intravenous infusion to rhesus monkeys in late pregnancy was rapid, but slight. Clearance was slower from foetal than maternal blood. Distributed in all foetal tissues examined with limited biotransformation and rapid excretion (10).
In three volunteers, 85-92% of 1 g doses administered orally for 21 days was excreted unchanged in the urine within 24 hr; no metabolites were found. Within 48 hr, 92.3% of a 500 mg dose was excreted in the urine and 5.8% in the faeces (11).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (12).
Failed to induce micronuclei in bone marrow cells of mice, caused DNA strand breaks in rat hepatocytes but no chromosome aberrations in Chinese hamster cells, did not induce sister chromatid exchange in cultured human lymphocytes (7).
HeLa S3 DI_{50} (concentration of agent which inhibits DNA synthesis by 50%) 140 mM (13).
In human RSa cells, 10-22.5 mg ml^{-1} induced a dose-dependent increase in the number of mutations to ouabain resistance, which is the first reporting of mutagenic activity in human cells (14).

Other effects

Other adverse effects (human)
A number of case-control studies have been carried out on populations in the US, UK, Canada and Denmark. A US study using 3010 patients with bladder cancer and 5783 controls found the relative risk for bladder cancer associated with the use of artificial sweetners was 1.0 in men and 1.1 in women. Significant trends of increasing risk with increasing average daily consumption were found in certain subgroups examined *a priori* on the basis of results in animal experiments; these subgroups were ♀ nonsmokers and ♂ heavy smokers (15).
Independent re-analysis of the same data confirmed the original findings but cast doubt on the significance of the findings in the two subgroups (16).
Three other studies also showed increased risks among subgroups. In a simultaneous study carried out in Japan, the UK and the US, the relative risks among women in the US study associated with diet drinks and sugar substitutes showed a marginal increase in risk, however in Japan and the UK a history of the use ofsugar substitutes, primarily saccharin, was not associated with an elevated bladder cancer risk (17,18).
A second study in the UK found elevated risk in saccharin takers who were non-smokers (19).
A third study carried out in Denmark found a relative risk of 2.5 for saccharin consumption in men and women combined. The risk was not reduced after controlling for tobacco use and industrial work (20).
Two further studies in Denmark, one in the US and one in Canada gave negative results (21-23).
In the US, a study of 1862 patients hospitalised for cancer and of 10874 control patients, a greater proportion of artificial sweetner users was found only among women with cancer of the stomach. No overall association was found between artificial sweetner use and cancer (24).

Other comments

In 1976, 23% of all saccharin consumed in the US was added to non-food items. In particular, 10% was used in cosmetics such as toothpaste, mouthwash and lipstick, 7% in pharmaceuticals such as pill coatings, 2% in smokeless tobacco products such as chewing tobacco and snuff, 2% in electroplating, 1% in cattle feed and 1% in miscellaneous uses (25).
Toxicology and carcinogenicity reviewed (26-28).
Reviews on human health effects and experimental toxicology listed (29).
Soluble in alkali carbonates.

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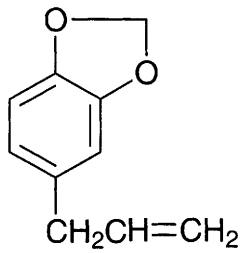
S2 safrole



$C_{10}H_{10}O_2$ **Mol. Wt.** 162.19 **CAS Registry No.** 94-59-7

Synonyms 5-(2-propenyl)-1,3-benzodioxole; 4-allyl-1,2-methylenedioxybenzene; allylcatechol methylene ether; allyldioxybenzene methylene ether; *m*-allylpyrocatechin methylene ether

EINECS No. 202-345-4 **RTECS No.** CY 2800000

Uses Topical antiseptic; in perfumery; for denaturing fats in soap manufacture; in manufacture of heliotropin.
Occurrence Constituent of several essential oils, notably sassafras.

Physical properties

M. Pt. 11°C **B. Pt.** 232-234°C **Specific gravity** 1.096 at 20°C **Volatility** v.p. 1 mmHg at 63.8°C
Solubility Organic solvents: ethanol

Occupational exposure

Supply classification toxic
Risk phrases May cause cancer – Harmful if swallowed – Possible risk of irreversible effects (R45, R22, R40)
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 1950, 2350 mg kg^{-1}, respectively (1).
LD_{50} subcutaneous mouse 1020 mg kg^{-1} (2).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (3).
120 μg g^{-1} was administered intragastrically to mice on days 12, 14, 16 and 18 of pregnancy, every other day during lactation or 2 × wk^{-1} for 90 wk to neonates. *In utero* exposure resulted in renal epithelial tumours in 7% of ♀ offspring, and exposure via lactation resulted in hepatocellular tumours in 34% of ♂ offspring. Direct administration to neonates caused hepatocellular tumours in 48% of ♀ (mainly carcinomas with a high rate of pulmonary metastases) and 8% in ♂ (4).
Oral ♂ and ♀ (C57BL/6×C3H/Anf)F_1 or (C57BL/6×AKR)F_1 mice (82 wk) 464 mg kg^{-1} body weight at 7 days of age daily until 28 days old, then administered at 112 mg kg^{-1} diet. Liver cell tumours occurred in 11/17 ♂ and 16/16 ♀, and 3/17 ♂ and 16/17 ♀, respectively (5).
Oral ♂ CD1 mice (13 months), 4000 or 5000 mg kg^{-1} diet. 23/87 mice surviving 12-16 months developed hepatocellular carcinomas compared with 7/70 controls (6).
Oral 48 ♂ CD rats (26 months) 5000 mg kg^{-1} diet for 10 months and then a control diet for 16 months. Two developed hepatocellular carcinomas and one a benign tumour liver adenoma. No liver tumours occurred in 48 controls (6).
Subcutaneous ♂ CD rats (18 months) 20 twice wkly injections of 3 mg $animal^{-1}$, no local tumours were observed (6).

Intraperitoneal 15 ♂ and 15 ♀ A/He mice (24 wk) 12 injections of safrole in tricaprylin twice wkly, total doses 0.9 and 4.5 g kg^{-1} body weight. All surviving animals were killed, 2/14 ♂ and 4/13 ♀ and 1/10 ♂ and 2/10 ♀ at the two dose levels developed lung tumours. Of controls injected with tricaprylin 22/77 ♂ and 15/77 ♀ developed lung tumours (7).

Teratogenicity and reproductive effects

Did not induce sperm abnormalities in mice after intraperitoneal injection of 12.5-200 μg kg^{-1} (8).

Metabolism and toxicokinetics

Metabolised by demethylenation of the methylenedioxy moiety to 4-allyl-1,2-dihydroxybenzene, which accounts for 77% of urinary metabolites in rats. Other metabolic pathways include hydroxylation and the epoxide-diol pathway (9).

Other urinary metabolites in rats and guinea pigs are 1,2-methylenedioxy-4-(1-hydroxyallyl)benzene, 1,2-methylenedioxy-4-(2,3-dihydroxypropyl)benzene, 1,2-dihydroxy-4-(2,3-dihydroxypropyl)benzene, 2-hydroxy-3-(3,4-methylenedioxyphenyl)propanoic acid and 3,4-methylenedioxybenzoylglycine (10).

In guinea pigs after oral or intraperitoneal administration 3′-*N*,*N*-dimethylamino-1′-(3,4-methylenedioxyphenyl)-1′-propane is a major urinary metabolite, unlike rats in which it is only a minor metabolite (11).

Irritancy

500 mg applied to rabbit skin for 24 hr caused moderate irritation (12).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (13).

Salmonella typhimurium TA1535 *umu* test with and without metabolic activation negative (14).

Saccharomyces cerevisiae C658-K42 with and without metabolic activation negative (15).

Induced morphological transformation in C3H/10$T_{1/2}$ CL8 mouse embryo fibroblasts (16).

Induced unscheduled DNA synthesis in HeLa S3 cells (17).

Mouse lymphoma L5178 cell assay with metabolic activation positive (18).

Did not induce sex-linked recessive lethal mutations in *Drosophila melanogaster* (19).

Chinese hamster lung cells with metabolic activation induced sister chromatid exchange and chromosomal aberrations (20).

Gastric intubation F344 rats induced chromosome aberrations, sister chromatid exchanges and the formation of DNA-adducts in hepatocytes (21).

Legislation

Land disposal prohibited by US Federal Resource Conservation and Recovery Act (22).

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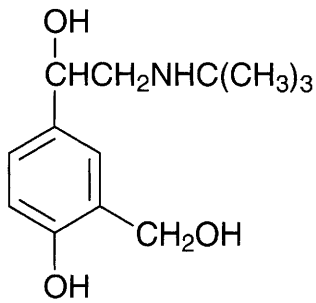
S3 salbutamol



$C_{13}H_{21}NO_3$ **Mol. Wt.** 239.31 **CAS Registry No.** 18559-94-9

Synonyms albuterol; α^1-[[(1,1-dimethylethyl)amino]methyl]-4-hydroxy-1,3-benzenedimethanol; α^1-[(*tert*-butylamino)methyl-4-hydroxy-*m*-xylene-α,α'-diol; 2-(*tert*-butylamino)-(4-hydroxy-3-hydroxymethylphenyl)ethanol; Proventil Inhaler; Salbulin Inhaler

EINECS No. 242-424-0 **RTECS No.** ZE 4400000

Uses Direct acting sympathomimetic with a relatively selective action on beta$_2$-adrenoreceptors, used as a bronchodilator in asthma treatment.

Physical properties

M. Pt. 151°C
Solubility Water: 1 in 70 parts. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 660 mg kg^{-1} (1).
TD_{Lo} oral human child 1850 μg kg^{-1} (2).
TC_{Lo} (6 hr) inhalation human 36 μg kg^{-1} (3).
TD_{Lo} intravenous human 6 μg kg^{-1} (4).
LD_{50} intraperitoneal mouse, rat 239, 295 mg kg^{-1}, respectively (5).

Metabolism and toxicokinetics
Readily absorbed from the human gastro-intestinal tract, is subject to first-pass metabolism in liver and gut wall, and 50% is excreted as an inactive sulfate conjugate in urine following oral administration. It does not appear to be metabolised by the lung. Plasma $t_{1/2}$ 2-7 hr; half life depends on route of administration, increasing in the order intravenous < oral < inhalation (6).

Administered to healthy volunteers intravenously and orally. After intravenous injection terminal $t_{1/2}$ 3.8 hr. After oral administration peak plasma concentrations of 10-20 ng ml^{-1} occurred 1-3 hr after administration, absorption bioavailability 44% (7).

Other effects

Other adverse effects (human)

Adverse effects are those of adrenergic stimulation; it may cause fine tremor, palpitations and muscle cramp. Slight tachycardia, tenseness, headache and peripheral vasodilation have been reported after large doses. Nausea, vomiting, cardiac and metabolic effects have been reported after intravenous use to delay labour (6).
Myocardial ischaemia has been reported after withdrawal of salbutamol for pre-term labour. Congestive heart failure, pulmonary oedema and metabolic acidosis have been reported during use in pregnancy (6).
Decreased human sperm motility and velocity *in vitro* (8).
Salbutamol inhalers have been abused (9).

Other comments

Pharmacokinetics reviewed (10,11).

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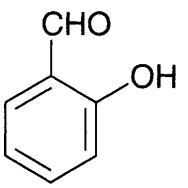
S4 salicylaldehyde



$C_7H_6O_2$ **Mol. Wt.** 122.12 **CAS Registry No.** 90-02-8

Synonyms *o*-hydroxybenzaldehyde; 2-hydroxybenzaldehyde; salicylic aldehyde; 2-formylphenol; Salicylal

EINECS No. 201-961-0 **RTECS No.** VN 5250000

Uses Analytical chemistry, perfumery, coumarins synthesis, gasoline additives.

Physical properties

M. Pt. –7°C **B. Pt.** 196°C **Specific gravity** 1.167 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.81 **Volatility** v.p. 1 mmHg at 33°C
Solubility Water: slightly soluble. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) *Salmo gairdneri* 1.35 mg l^{-1} (1).

Invertebrate toxicity

LOEC *Microcystis aeruginosa* 1.6 mg l^{-1} (2).
NOEC *Selenastrum capricornutum* 5.5 mg l^{-1} (1).
LC_{50} (48 hr) *Daphnia pulex* 5.4 mg l^{-1} (3).
LOEC *Entosiphon sulcatum* 1.4 mg l^{-1} (4).
EC_{50} (5-15 min) *Photobacterium phosphoreum* 14.3 ppm Microtox test (5).
LOEC *Pseudomonas putida* 10 mg l^{-1} (4).
LC_{50} (48 hr) clawed toad 7.7 mg l^{-1} (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 520 mg kg^{-1} (7).
LD_{50} dermal rat, rabbit 600, 3000 mg kg^{-1}, respectively (7).
LD_{50} subcutaneous rat 900 mg kg^{-1} (7).

Teratogenicity and reproductive effects

Increased incidence of resorption, dead foetuses and malformations (cleft lip and polydactylia) reported in rats following subcutaneous administration of 400 mg kg^{-1} on day 11 of pregnancy (8).

Irritancy

500 mg applied to rabbit skin for 24 hr caused moderate irritation (7).

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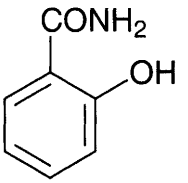
S5 salicylamide



$C_7H_7NO_2$ **Mol. Wt.** 137.14 **CAS Registry No.** 65-45-2

Synonyms 2-hydroxybenzamide; Salamid; Cidal; Novecyl; Dolomide; Urtosal

EINECS No. 200-609-3 **RTECS No.** VN 6475000

Uses Analgesic and antipyretic.

Physical properties

M. Pt. 140°C

Solubility Water: 0.2% at 30°C. Organic solvents: diethyl ether, ethanol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 300, 980 mg kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal mouse, rat 180, 600 mg kg^{-1}, respectively (3,4).

LD_{50} intravenous mouse 313 mg kg^{-1} (5).

Teratogenicity and reproductive effects

Potent spermicide against human spermatozoa *in vitro*, 5 mg ml^{-1} immobilising sperm within 20 sec (6).

Increased incidence of foetal resorptions and induced malformations in rats fed 2% in the diet on days 5-11 of pregnancy (7).

Salicylamide has been used as a model compound to test whether drugs yielding an arylsulfate as a major urinary metabolite may create a sulfate deficit in pregnant animals which adversely affects foetal sulfate utilisation for skeletal development (7).

Metabolism and toxicokinetics

Readily absorbed from the human gastro-intestinal tract and almost completely metabolised to inactive metabolites during absorption and first pass through the liver. It is distributed to most body tissues and rapidly excreted in urine, mainly as glucuronide and sulfate conjugates (8).

Metabolised to gentisamide 5-glucuronide in single pass *in situ* perfused rat liver (9).

Irritancy

100 mg instilled into rabbit eye caused moderate irritation (10).

10 mg ml^{-1} in 8% dimethyl sulfoxide instilled into rabbit eyes caused no significant conjunctival irritation (6).

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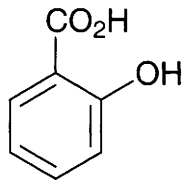
S6 salicylic acid



$C_7H_6O_3$ **Mol. Wt.** 138.12 **CAS Registry No.** 69-72-7

Synonyms *o*-hydroxybenzoic acid; 2-hydroxybenzoic acid

EINECS No. 200-712-3 **RTECS No.** VO 0525000

Uses Food preservative (use prohibited in some countries). In manufacture of methyl salicylate and other salicylates and dyes. Analytical reagent. Topical keratolytic. Veterinary antiseptic and antifungal agent.
Occurrence In wintergreen leaves and sweet birch bark (as the ester).

Physical properties

M. Pt. 158-160°C **B. Pt.** 211°C at 20 mmHg **Flash point** 157°C **Specific gravity** 1.443 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.35 **Volatility** v.p. 5 mmHg at 136°C
Solubility Water: 1 g 460 ml^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (5 min) *Photobacterium phosphoreum* 214 ppm Microtox test (1).

Environmental fate

Degradation studies
Decomposed by soil microflora in 2 days (2).
In adapted activated sludge at 20°C with salicylic acid as sole carbon source 98.8% COD removal at 95 mg COD g^{-1} dry inoculum hr^{-1} (3).
BOD_5 0.95 mg O_2 l^{-1} (standard diluted sewage), 0.97 mg O_2 l^{-1} (standard diluted acclimated sewage) 41% ThOD (4-6).
BOD_{20} 1.25 mg O_2 l^{-1} (7).
COD 1.58 mg O_2 l^{-1} (5), 100% ThOD (6).
ThOD 1.623 (7).
Waste water treatment, coagulation: 17% BOD reduction with 360 mg l^{-1} alum (8).
20-30% of an initial concentration of 100 ppm was removed by activated-sludge process at 20°C at 120 hr (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 400-800, 1312 mg kg^{-1}, respectively (10,11).
TD_{Lo} dermal human 57 mg kg^{-1} (12).
LD_{50} intravenous, intraperitoneal mouse 180, 300 mg kg^{-1}, respectively (13,14).

Metabolism and toxicokinetics
Readily absorbed through human skin and excreted slowly in urine. Excessive application to large areas of skin may cause acute systemic salicylate poisoning and fatalities have been reported (14).
In volunteers given 1 g salicylic acid, urinary hourly excretion ratio of salicylurate to salicylglucuronic acid was >1 in ♀ and <0.5 in ♂ (15).

Irritancy
100 mg instilled into rabbit eye caused severe irritation (16).
500 mg applied to rabbit skin for 24 hr caused mild irritation (16).
10 mg ml^{-1} in 8% dimethyl sulfoxide instilled into rabbit eyes caused no significant conjunctival irritation (11).
Mild skin irritant in humans, may cause dermatitis (14).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537, TA1535 with and without metabolic activation negative (10).
Saccharomyces cerevisiae rad 18 positive (mutagenicity was strongly temperature-dependent and mutations were only induced when lethality reached 95-99%) (17).
Did not inhibit testicular DNA synthesis in mice after administration of 100 mg kg^{-1} (18).

Other effects

Other adverse effects (human)
3 mg ml^{-1} immobilised human sperm within 20 sec *in vitro* (11).

Other comments

Hazards reviewed (19).

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S7 samarium

Sm

Sm **Mol. Wt.** 150.36 **CAS Registry No.** 7440-19-9

EINECS No. 231-128-7

Uses In production of sintered permanent magnets.
Occurrence In samarskite, cerite, orthite, ytterbite, monazite and fluorspar. Forms 4.5-7 ppm of the Earth's crust.

Physical properties

M. Pt. 1072°C **Specific gravity** 7.536

Genotoxicity

Inhibited DNA synthesis in HeLa cells (1).

Other comments

Moderately fibrogenic.

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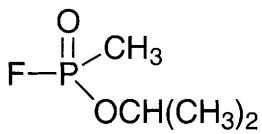
S8 sarin



$C_4H_{10}FO_2P$ **Mol. Wt.** 140.09 **CAS Registry No.** 107-44-8

Synonyms methylphosphonofluoridic acid, 1-methylethyl ester; isopropoxymethylphosphoryl fluoride; isopropyl methylphosphonofluoridate; isopropyl methylphosphofluoridate

RTECS No. TA 8400000

Uses Organophosphorus nerve agent, cholinesterase inhibitor.

Physical properties

M. Pt. –57°C **B. Pt.** 147°C **Specific gravity** 1.10 at 20°C
Solubility Water: miscible and hydrolysed

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 550 μg kg^{-1} (1).
LC_{Lo} (duration unspecified) inhalation human 70 mg m^{-3} (2).
LC_{50} (10 min) inhalation dog, monkey, rat 100-150 mg m^{-3} (1).
LD_{Lo} dermal human 28 mg kg^{-1} (2).
LD_{50} dermal mouse 1080 μg kg^{-1} (1).
LD_{50} intraperitoneal rat 303 μg kg^{-1} (3).
LD_{50} intraperitoneal mouse 0.42 mg kg^{-1} (4).
LD_{50} intramuscular, subcutaneous rat 108, 113 μg kg^{-1}, respectively (3,5).

Sub-acute and sub-chronic data

♀ mice exposed to 5 mg m^{-3} 20 min day^{-1} for 10 days suffered from a delayed neurotoxic effect, including muscular weakness of the limbs and ataxia 14 days after exposure began (6).

Teratogenicity and reproductive effects

Oral rat and rabbit (days 6-15 and 6-19 of gestation, respectively) 0, 100, 240 or 380 and 0, 5, 10 or 15 μg kg^{-1} body weight day^{-1}. Both species in the high-dose groups showed significant maternal toxicity, however results showed no evidence of developmental toxicity (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 (metabolic activation unspecified) negative (8).
Did not induce sister chromatid exchanges in Chinese hamster ovary cells *in vitro* (8,9).
Did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro* (8).
Did not induce sister chromatid exchanges in lymphocytes of mice exposed *in vivo* (8).

Other effects

Other adverse effects (human)

Induces organophosphate-induced delayed neurotoxicity; ataxia followed by paralysis occurs 4-21 days after exposure (6).
Short-term effects include miotic pupils and reduced visual field (10,11).

Other comments

Pharmacology and pharmacokinetics in organophosphate therapy in Alzheimer's disease reviewed (12).

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S9 schradan

$$[(CH_3)_2N]_2P(=O)O(=O)P[N(CH_3)_2]_2$$

$C_8H_{24}N_4O_3P_2$ **Mol. Wt.** 286.25 **CAS Registry No.** 152-16-9

Synonyms octamethyldiphosphoramide; octamethylpyrophosphoramide; bis[bisdimethyl aminophosphorus] anhydride; bis-*N,N,N',N'*-tetramethylphosphorodiamidic anhydride; octamethylpyrophosphoric tetramide

EINECS No. 205-801-0 **RTECS No.** UX 5950000

Uses Superseded insecticide.

Physical properties

M. Pt. 14-20°C **B. Pt.** 120-125°C at 0.5 mmHg **Specific gravity** 1.137 at 20°C
Volatility v.p. 1×10^{-3} mmHg at 25°C
Solubility Water: miscible. Organic solvents: soluble in most organic solvents

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 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)

Mammalian & avian toxicity

Acute data
LD_{50} oral starling 11-12 mg kg^{-1} (1).
LD_{50} oral rat 5 mg kg^{-1} (2).
LC_{Lo} (4 hr) inhalation rat 8 mg m^{-3} (3).
LD_{50} dermal rat 15 mg kg^{-1} (4).
LD_{50} subcutaneous mouse 14 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Intraperitoneal rat (>60 day) 1.0, 1.5, 2.0 mg kg^{-1} day^{-1} caused progressive cholinesterase activity depletion and cumulative toxic action, but 0.25, 0.5 mg kg^{-1} caused no adverse effect (6).

Metabolism and toxicokinetics
Absorbed from the gastro-intestinal tract, peritoneal cavity and skin and metabolised primarily in the liver (7). Hydroxymethylamide is the active metabolite (8).

Other effects

Other adverse effects (human)
Following oral doses to five men, plasma cholinesterase activity decreased 11% after 16 days but increased at 39 days and red cell activity decreased 15% at the lower dose (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).

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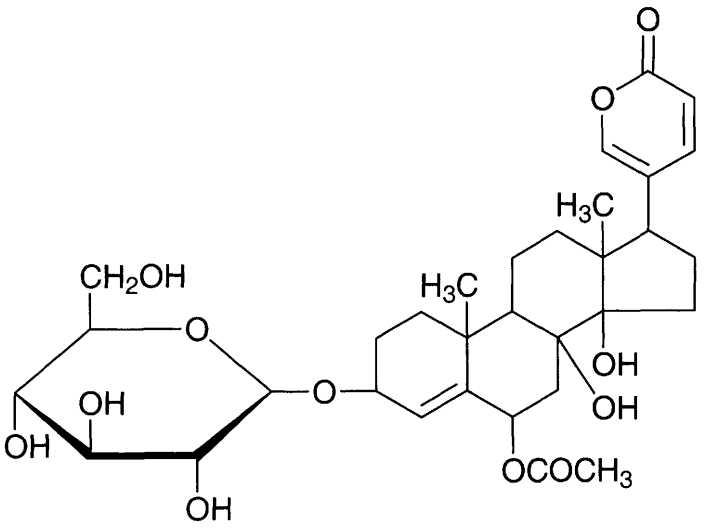
S10 scilliroside



$C_{32}H_{44}O_{12}$ **Mol. Wt.** 620.69 **CAS Registry No.** 507-60-8

Synonyms (3β,6β)-6-(acetyloxy)-3-(β-D-glucopyranosyloxy)-8,14-dihydroxybufa-4,20,22-trienolide

EINECS No. 208-077-4 **RTECS No.** VR 3520000

Uses Superseded rodenticide.

Occurrence Glycoside in red squill bulb, *Urginea maritima*.

Physical properties

M. Pt. 168-170°C (hemihydrate)

Solubility Water: slightly soluble. Organic solvents: dioxane, ethanol, ethylene glycol

Occupational exposure

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) – 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)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 440 μg kg^{-1} (1,2).

LD_{50} subcutaneous mouse 471 μg kg^{-1} (1).

LD_{50} intravenous cat 130 μg 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).

Other comments

Among the 21 pesticides released into the river Rhine by the 1986 Sandoz warehouse fire (6).

References

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S11 sebacic acid

$$HO_2C(CH_2)_8CO_2H$$

$C_{10}H_{18}O_4$ **Mol. Wt.** 202.25 **CAS Registry No.** 111-20-6

Synonyms decanedioic acid; 1,8-octanedicarboxylic acid

EINECS No. 203-845-5 **RTECS No.** VS 0875000

Uses In manufacture of alkyd or polyester resins, non-migrating plasticisers, polyester rubbers and polyamide-type synthetic fibres. As an emolient in preparations used to protect damaged skin.

Physical properties

M. Pt. 134.5°C **B. Pt.** 294.5°C at 100 mmHg **Specific gravity** 1.207 at 20°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 183°C
Solubility Water: 1 g l^{-1} at 20°C. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 3400, 6000 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal mouse 500 mg kg^{-1} (3).

Metabolism and toxicokinetics

Increased amounts of 3-oxohexanedioic acid, 3-oxooctanedioic acid and 3-oxodecanedioic acid were excreted in human urine after ingestion of sebacic acid (4).

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S12 selenic acid

H_2SeO_4

H_2O_4Se **Mol. Wt.** 144.97 **CAS Registry No.** 7783-08-6

EINECS No. 231-979-4 **RTECS No.** VS 6575000

Physical properties

M. Pt. 58°C **B. Pt.** 260°C **Specific gravity** 2.9508 at 15°C with respect to water at 4°C
Solubility Water: very soluble (deliquescent)

Occupational exposure

JP-OEL 0.1 mg m^{-3} (as Se)
SE-LEVL 0.1 mg m^{-3} (as Se)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 1905 **Conveyance classification** corrosive substance
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

Carcinogenicity and chronic effects
Available animal data are insufficient to allow an evaluation of the carcinogenicity of selenium compounds (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1} (2).

Other comments

Data used in setting UK occupational exposure limits summarised (3).

References

1. *IARC Monograph* 1975, **9**, 245-260.
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. *Occupational exposure limits: criteria document summaries* 1993, HMSO, London, UK

S13 selenious acid

H_2SeO_3

H_2O_3Se **Mol. Wt.** 128.97 **CAS Registry No.** 7783-00-8

Synonyms selenous acid; monohydrated selenium dioxide

EINECS No. 231-974-7 **RTECS No.** VS 7175000

Uses Reagent for alkaloid estimations. Oxidising agent. Used as a source of selenium for patients with deficiency states following prolonged parenteral nutrition.

Physical properties

Specific gravity 3.004 at 15°C with respect to water at 4°C **Volatility** v.p. 2 mmHg at 15°C
Solubility Water: 900 mg l^{-1} at 0°C. Organic solvents: ethanol

Occupational exposure

JP-OEL 0.1 mg m^{-3} (as Se)
SE-LEVL 0.1 mg m^{-3} (as Se)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 3283 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
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
LD_{Lo} oral rat 25 mg kg^{-1} (1).
LD_{Lo} intraperitoneal rat 10 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Available animal data are insufficient to allow an evaluation of the carcinogenicity of selenium compounds (2).

Metabolism and toxicokinetics
Selenious acid aerosol (particle size 0.5-0.7 μm) was absorbed by dogs in nose-only inhalation studies; for the first 32 days after exposure, urine accounted for 79% of excretion (3).

Irritancy
Selenious acid causes skin burns in humans, but pain and visible damage is delayed; 4 hr after exposure to a 50% solution, intense pain begins, small petechial areas and a faint orange coloration occur, and if untreated the burn may ulcerate (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1} (5).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).
Toxicity reviewed (4,7).
Data used in settings UK occupational exposure limit summarised (8).

References

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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.
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S14 selenium

Se

Se **Mol. Wt.** 78.96 **CAS Registry No.** 7782-49-2

Synonyms colloidal selenium; Vandex; C.I. 77805

EINECS No. 231-957-4 **RTECS No.** VS 7700000

Uses Decoloriser for glass and ceramics, in photoelectric cells, vulcanising agent in rubber manufacture, catalyst, in photographic toning baths, rectifier in radios and televisions, in electrodes.

Occurrence In sulfide ores of heavy metals. Exists in several allotropic forms: amorphous, crystalline or red, and grey or metallic. Constitutes ~0.09 ppm of the Earth's crust.

Present in foods, mainly as the amino acids selenomethionine and selenocysteine and derivatives.

Essential trace element and integral part of the peroxidase enzyme system.

Physical properties

M. Pt. 170-217°C **B. Pt.** 690°C **Specific gravity** 4.81-4.26 **Volatility** v.p. 1 mmHg at 356°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable fraction of aerosol)
JP-OEL 0.1 mg m^{-3}
SE-LEVL 0.1 mg m^{-3}
UK-LTEL 0.1 mg m^{-3}
US-TWA 0.2 mg m^{-3}

UN No. 2658 (powder) **HAZCHEM Code** 2Z (powder) **Conveyance classification** toxic substance (powder)
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)

Ecotoxicity

Bioaccumulation
Average selenium uptake 13.6% by heterotrophic bacteria (1).

Environmental fate

Degradation studies

Bacillus megaterium isolated from soil will oxidise elemental selenium to selenite and traces of selenate (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6700 mg kg^{-1} (form unspecified) (3).

LD_{50} intravenous rat 6 mg kg^{-1} (form unspecified) (4).

Rats, guinea pigs and rabbits exposed to ~30 mg m^{-3} selenium dust (particle diameter 1.2 μm) for 16 hr suffered mild interstitial pneumonitis (5).

Intratracheal injection of a suspension containing 50 mg highly dispersed elemental selenium dust caused morphological and biochemical changes in the respiratory tract of rats (6).

Carcinogenicity and chronic effects

Available animal data are insufficient to allow an evaluation of the carcinogenicity of selenium compounds (7). Further evaluation by the IPCS/WHO felt this was still valid in 1987 (8).

Metabolism and toxicokinetics

Elemental selenium aerosol (particle size 0.5-0.7 μm) was absorbed by dogs in nose-only inhalation studies; for the first 32 days after exposure, urine accounted for 66% of excretion (9).

^{75}Se (as selenious acid) was injected into the wing of ♀ mallard ducks and tissue samples taken up to 24 hr post-injection. Visceral tissues exhibited a triphasic pattern of uptake with a rapid rise, a decline followed by an increase in levels between the last two time points. Brain uptake was continuous over the 24 hr. Plasma levels rose rapidly and then declined to a constant level. Ovaries showed the greatest relative increase, suggesting accumulation that could lead to teratogenicity (10).

Sensitisation

Occupational exposure to selenium fumes may cause allergic dermatitis (8).

Other effects

Other adverse effects (human)

Rhinitis, nose bleeds, headaches, irritability and pain in the extremities have been reported following prolonged occupational exposure to selenium aerosols containing 0.35-24.8 mg m^{-3} elemental selenium (8).

Other symptoms reported in workers exposed to selenium for 3-16 yr include pain in the right hypochondrium, dyspeptic phenomena, fatigue, dyspnoea, weakness, cough, sleeplessness, chronic bronchitis, emphysema, hyperthyroidism, skin pigmentation, an astheno-vegetative syndrome, and liver and gastro-intestinal impairments (8).

Any other adverse effects

Three types of farm animal diseases are associated with high selenium intake: acute; chronic, blind staggers type; and chronic, alkali disease type (8).

Intraperitoneal administration of 3.0 mg kg^{-1} of selenium (as sodium selenite) into the striatum of ♂ rats caused a 70% increase in dopamine overlfow. Direct perfusion of 10 mM of selenium (as sodium selenite) caused increased dopamine levels in both the striatum and the nucleus accumbens (11).

Legislation

Land disposal prohibited by US Federal Resource Conservation and Recovery Act (12).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1} (13).

Other comments

Experiments on B6C3F1 mice maintained for 28 days on a diet deficient, sufficient, or excessive in selenium content and then administered sodium arsenate (5 mg kg^{-1} As) by gavage provided suggestive evidence that dietary selenium status alters arsenate metabolism and disposition (14).
Dietary selenium deficiency had been associated with Keshan disease, Kashin-Beck disease and ischaemic heart disease, but is likely to be only one of the causative factors in diseases with complex multiple etiopathogenesis.
IPCS/WHO reviewed apparent negative correlations between selenium status and cancer death rate and conclude that the data are as yet insufficient. Similarly, an association between high selenium intake and dental caries reported in an animal study has not been confirmed in humans (8).
Hazards reviewed (15).
Environmental effects reviewed (16,17).
Toxicity and dietary deficiency reviewed (18-22).
Role in cancer prevention reviewed (23-29).
Role in carcinogenesis reviewed (30-32).
Clinical use and toxicology reviewed (33).
Biochemistry reviewed (34-36).
Data used in setting UK occupational exposure limit summarised (37).
UK recommended dietary reference value for adult ♂ and ♀ 75 and 60 μg day^{-1}, respectively.

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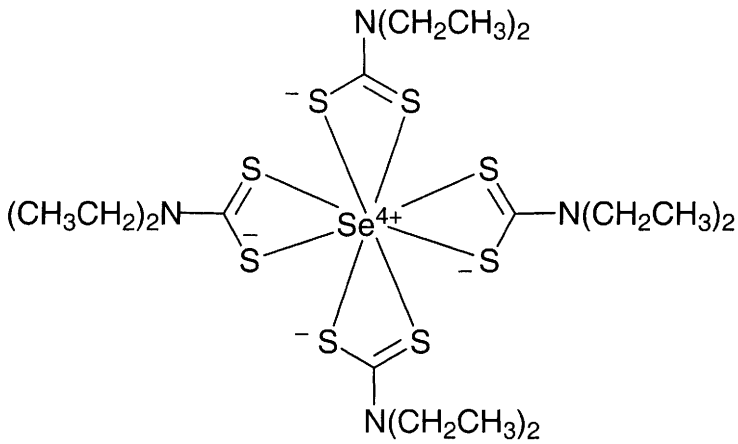
S15 selenium diethyldithiocarbamate



$C_{20}H_{40}N_4S_8Se$ **Mol. Wt.** 672.05 **CAS Registry No.** 5456-28-0

Synonyms selenium tetrakis(diethyldithiocarbamate); tetrakis(diethylcarbamodithioato-*S*,*S'*)selenium

EINECS No. 226-713-9 **RTECS No.** VT 0700000

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Se) (inhalable dust fraction)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 3283 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
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

Carcinogenicity and chronic effects
Available animal data are insufficient to allow an evaluation of the carcinogenicity of selenium compounds (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1} (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3).
Data used in setting UK occupational exposure limits summarised (4).

References

1. *IARC Monograph* 1975, **9**, 245-260.
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. *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. *Occupational exposure limits: criteria document summaries* 1993, HMSO, London, UK

S16 selenium dioxide

SeO_2

O_2Se **Mol. Wt.** 110.96 **CAS Registry No.** 7446-08-4

Synonyms selenium oxide; selenious anhydride; selenium(IV) dioxide

EINECS No. 231-194-7 **RTECS No.** VS 8575000

Uses In production of other selenium compounds, oxidising agent for organics and pharmaceuticals, reagent for alkaloid estimations.

Physical properties

M. Pt. 340-350°C (subl.) **B. Pt.** sublimes at 315°C **Specific gravity** 3.95 at 15°C with respect to water at 15°C
Volatility v.p. 1 mmHg at 157°C
Solubility Water: 38.4 parts in 100 parts water at 14°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Se) (inhalable dust fraction)
JP-OEL 0.1 mg m^{-3} (as Se)
SE-LEVL 0.1 mg m^{-3} (as Se)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 3283 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
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} (20 min) inhalation rabbit 5890 mg m^{-3} (1).
LD_{50} subcutaneous rabbit 4 mg kg^{-1} (2).
LD_{Lo} subcutaneous gerbil 7500 μg kg^{-1} (3).

Sub-acute and sub-chronic data

Decreased blood catalase activity, and total and reduced glutathione levels were reported in rabbits exposed to 10 $\mu g\ l^{-1}$, 2 hr day^{-1} for 1-12 wk (4).

Carcinogenicity and chronic effects

Selenium dioxide had an antitumorigenic effect on B16 melanoma cells transplanted into mice (5).

7-10 intraperitoneal doses of 7.5-30 μg Se day^{-1} given every other day inhibited transplanted tumour growth in mice (6).

Given in drinking water at up to 6 mg Se l^{-1} for 1 yr, selenium dioxide reduced the incidence of mammary tumours in mice (7).

Teratogenicity and reproductive effects

Testicular degeneration and atrophy occurred in ♂ rats administered 10 $\mu g\ rat^{-1}\ day^{-1}$ intraperitoneally for 90 days (8).

Given in drinking water at up to 6 mg Se l^{-1} for 1 yr, selenium dioxide had no effect on reproductive function in mice (9).

5.6 mg kg^{-1} injected subcutaneously into ♂ gerbils caused reduction of testicular weight and atrophy of Leydig cells and seminiferous tubules a week after injection (3).

Irritancy

Causes skin burns and dermatitis in humans (10).

Occasionally a true urticarial generalised body rash occurs after occupational exposure, and 'rose eye', a pink discoloration of the skin of the eyelids, which also become puffy, may occur (11).

Several cases of dermatitis and acutely painful paronychia have been reported from contact with dry selenium dioxide. The burns are caused by selenious acid formed on the skin due to moisture (9).

Genotoxicity

Induced *umu* gene expression in *Salmonella typhimurium* TA1535 (12).

Bacillus subtilis rec assay positive (13).

Did not induce sister chromatid exchanges in Chinese hamster Don cells *in vitro* (14).

Induced sister chromatid exchanges in human whole blood cultures (15).

Selenium dioxide has an antimutagenic effect in *Salmonella typhimurium*, reducing the number of revertants in TA100 induced by dimethylbenzanthracene and its metabolites (16,17).

Other effects

Other adverse effects (human)

Acute local effects of occupational exposure to selenium dioxide involve the lungs, gastric mucosa, skin, nails and eyes. Sudden inhalation of large amounts causes pulmonary oedema. Symptoms include garlicy-smelling breath, metallic taste on the tongue, and indefinite sociopsychological effects (11).

Rhinitis, nose bleeds, weight loss, irritability and pain in the extremities have been reported after long exposure to selenium aerosols containing 0.11-0.78 mg m^{-3} selenium dioxide (9).

Other symptoms reported in workers exposed to selenium dioxide for 3-16 yr include pain in the right hypochondrium, dyspeptic phenomena, fatigue, weakness, dyspnoea, cough, sleeplessness, chronic bronchitis, emphysaema, hyperthyroidism, skin pigmentation, an astheno-vegetative syndrome, and liver and gastro-intestinal impairments (9).

Legislation

Land disposal prohibited under US Federal Resource Conservation Act (18).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 $\mu g\ l^{-1}$ (19).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (20).
Data used in setting UK occupational exposure limit summarised (21).

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S17 selenium disulfide

SeS_2

S_2Se **Mol. Wt.** 143.09 **CAS Registry No.** 7488-56-4

Synonyms selenium sulfide (SeS_2); Selsun blue

EINECS No. 231-303-8 **RTECS No.** VS 8925000

Uses In shampoos as antidandruff agent; antifungal agent.

Physical properties

M. Pt. <100°C **B. Pt.** decomposes
Solubility Organic solvents: chloroform, diethyl ether

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Se) (inhalable dust fraction)
JP-OEL 0.1 mg m^{-3} (as Se)
SE-LEVL 0.1 mg m^{-3} (as Se)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 2657 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
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
LD_{50} oral rat 138 mg kg^{-1} (1).

Metabolism and toxicokinetics
Only traces are absorbed through intact human skin, but systemic toxicity has been reported following prolonged use on broken skin (2).

Irritancy
Topical application in humans can cause irritation of the conjunctiva, scalp and skin, especially in the genital area and skin folds (2).

Other effects

Other adverse effects (human)
Oiliness or dryness of hair or scalp, hair discoloration and hair loss reported after topical use in humans (2). Anorexia, abdominal pain, vomiting, tremors and reported sweating reported in a woman following use of a selenium disulfide-containing shampoo for 8 months (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1} (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5). Toxicity reviewed (6).

References

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S18 selenium hexafluoride

SeF_6

SeF_6 **Mol. Wt.** 192.95 **CAS Registry No.** 7783-79-1

Synonyms selenium fluoride (SeF_6)

RTECS No. VS 9450000

Uses Gaseous electric insulator.

Physical properties

M. Pt. –50.8°C **B. Pt.** –63.8°C (subl.) **Specific gravity** 3.25 at –28°C **Volatility** v.p. 651 mmHg at –48.7°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Se) (inhalable dust fraction)
FR-VME 0.05 ppm (0.2 mg m^{-3}) (as Se)
JP-OEL 0.1 mg m^{-3} (as Se)
SE-LEVL 0.1 mg m^{-3} (as Se)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.05 ppm (0.16 mg m^{-3}) (as Se)

UN No. 2194 **Conveyance classification** toxic gas, corrosive
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_{Lo} (3 hr) inhalation mouse 10 ppm (1).
LC_{Lo} (1 hr) inhalation guinea pig 10 ppm (1).
LC_{Lo} (1 hr) inhalation rat 10 ppm (1).
Rabbits, rats, mice and guinea pigs exposed to 5 ppm for 4 hr suffered pulmonary oedema but there were no fatalities (1).

Carcinogenicity and chronic effects

Available animal data are insufficient to allow on evaluation of the carcinogenicity of selenium compounds (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1} (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).
Data used in setting UK occupational exposure limits summarised (5).

References

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5. *Occupational exposure limits: criteria document summaries* 1993, HMSO, London, UK

S19 selenium oxychloride

$SeOCl_2$

Cl_2OSe **Mol. Wt.** 165.86 **CAS Registry No.** 7791-23-3

Synonyms seleninyl chloride

EINECS No. 232-244-0 **RTECS No.** VS 7000000

Physical properties

M. Pt. ~5°C (solidifies) **B. Pt.** 180°C **Specific gravity** 2.44 at 16°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 34.8°C
Solubility Water: decomposes. Organic solvents: benzene, carbon disulfide, carbon tetrachloride, chloroform, toluene

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Se) (inhalable dust fraction)
JP-OEL 0.1 mg m^{-3} (as Se)
SE-LEVL 0.1 mg m^{-3} (as Se)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 2879 **HAZCHEM Code** 2XE **Conveyance classification** corrosive substance, toxic
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
TD_{Lo} dermal human 710 μg kg^{-1} (1).
LD_{50} dermal rabbit 2 mg kg^{-1} (2).
LD_{50} subcutaneous rabbit 7 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Available animal data are insufficient to allow an evaluation of the carcinogenicity of selenium compounds (3).

Irritancy
<5 μg on the skin of a human hand caused a painful reaction within minutes, erythema surrounding a central necrotic area (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1} (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).
Toxicity reviewed (6).
Data used in setting UK occupational exposure limits summarised (7).

References

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S20 selenium sulfide

SeS

SSe **Mol. Wt.** 111.03 **CAS Registry No.** 7446-34-6

Synonyms selenium monosulfide; sulfur selenide

RTECS No. VT 0525000

Uses Used to treat seborrheic dermatitis, dandruff, eczema, and non-specific dermatoses.

Physical properties

M. Pt. 111.03°C **B. Pt.** 118-119°C (decomp.) **Specific gravity** 3.056 at 0°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (as Se) (inhalable dust fraction)
JP-OEL 0.1 mg m^{-3} (as Se)
SE-LEVL 0.1 mg m^{-3} (as Se)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 3283 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
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

LD_{50} oral rat, mouse 38, 370 mg kg^{-1}, respectively (1,2).

Carcinogenicity and chronic effects

Clear evidence of carcinogenicity in ♂ and ♀ rats and ♀ mice after administration by gavage (3).
Increased incidence of primary liver and lung tumours in ♀ mice, a marginal increase in incidence of these tumours in ♂ mice, and increased incidence of primary liver tumours in ♂ and ♀ rats exposed to 15 mg kg^{-1} by gavage, 5 days wk^{-1} for 103 wk. The commercial selenium sulfide used in this assay contained primarily the monosulfide (3).
Not carcinogenic in ♂ or ♀ mice after dermal application (4).

Genotoxicity

Salmonella typhimurium TA97 with and without metabolic activation positive; TA100 with metabolic activation positive; TA1535, TA98 with and without metabolic activation negative (5).
Mouse lymphoma L5178Y cell assay without metabolic activation positive (6).
Induced sister chromatid exchanges with and without metabolic activation, and chromosome aberrations without metabolic activation in Chinese hamster ovary cells *in vitro* (6,7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 $\mu g\ l^{-1}$ (8).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).
Toxicity reviewed (10).
Data used in setting UK occupational exposure limit summarised (11).

References

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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.
10. *Environmental Health Criteria No. 58. Selenium* 1987, WHO, Geneva, Switzerland.
11. *Occupational exposure limits: criteria document summaries* 1993, HMSO, London, UK

S21 selenourea

$$(NH_2)_2CSe$$

CH_4N_2Se **Mol. Wt.** 123.02 **CAS Registry No.** 630-10-4

Synonyms carbamimidoselenoic acid; isoselenourea; selenouronium; 2-selenourea

EINECS No. 211-129-9 **RTECS No.** YU 1820000

Physical properties

M. Pt. 200°C

Occupational exposure

UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 3283

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 50 mg kg^{-1} (1).
LD_{50} intravenous mouse 56 mg kg^{-1} (2).

Other effects

Any other adverse effects

Buffalo calf, 0.15 mg kg^{-1} produced symptoms of chronic selenosis. Oedema of fetlock region, tips of tail and ears were the first symptoms followed by wound formation and necrosis. Symptoms developed 5-20 days after administration and resembled the reported Degnala disease (3).

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S22 semicarbazide hydrochloride

$$H_2NC(O)NHNH_2{\cdot}HCl$$

CH_6ClN_3O **Mol. Wt.** 111.53 **CAS Registry No.** 563-41-7

Synonyms semicarbazide monohydrochloride; hydrazinecarboxamide monohydrochloride; amidourea hydrochloride; aminourea hydrochloride; carbamylhydrazine hydrochloride

EINECS No. 209-247-0 **RTECS No.** VT 3500000

Uses Reagent in determination of aldehydes and ketones and in isolation of hormones and fractions from essential oils.

Physical properties

M. Pt. 175-177°C (decomp.)
Solubility Water: soluble

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 176 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 123 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 145 mg kg^{-1} (2).

Carcinogenicity and chronic effects

No adequate data on carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (3).
Increased incidence of lung tumours occurred in mice fed a diet containing 0.1% for 7 months (4).
Increased incidence of lung tumours occurred in ♂ but not ♀ mice given 0.0625% in drinking water for life (5).

Teratogenicity and reproductive effects

Facial abnormalities reported in rats after oral administration (dose unspecified) during pregnancy (6).
High incidence of resorptions and cleft palate occurred in rats given 50-100 mg day^{-1} (route unspecified) on days 10-16 of pregnancy (7).
Intraperitoneal injection of 17 mg kg^{-1} day^{-1} to rats throughout pregnancy reduced numbers of implantations and live foetuses, and caused brain, kidney, gastro-intestinal and skeletal abnormalities. A single intraperitoneal injection of 50-150 mg kg^{-1} on day 5, 7, 10, 13 or 15 of pregnancy resulted in high postnatal mortality (8).

Genotoxicity

Induced chromosomal aberrations in spermatocyte chromosomes of the grasshopper *Spathosternum prasiniferum in vivo* (9).
Induced chromosomal aberrations in mouse bone marrow *in vivo* (10).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (11).

References

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2. *Farmakol. Toksikol. (Moscow)* 1961, **24**, 623.
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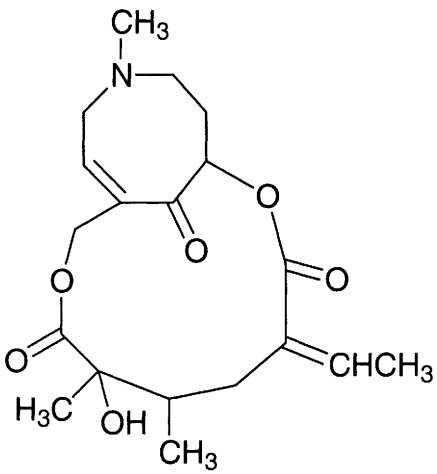
S23 senkirkine



$C_{19}H_{27}NO_6$ **Mol. Wt.** 365.43 **CAS Registry No.** 2318-18-5

Synonyms *trans*-15-ethylidene-12β-hydroxy-4,12α,13β-trimethyl-8-oxo-4,8-secosenec-1-enine; 12-hydroxy-4-methyl-4,8-secosenecionan-8,11,16-trione

RTECS No. VT 5960000

Uses Plants in which it occurs are used in Japanese folk medicine to treat eczema.

Occurrence Pyrrolizidine alkaloid occurring in plants belonging to the Compositae, such as coltsfoot (*Tussilago farfara*) and *Senecio* spp.

Physical properties

M. Pt. 198°C

Solubility Organic solvents: chloroform, ethyl acetate

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 200 mg kg^{-1} (1).

LD_{50} intraperitoneal rat 220 mg kg^{-1} (2).

Carcinogenicity and chronic effects

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

Liver adenomas, myeloid leukaemia and an interstitial tumour of the testis reported in ♂ rats given intraperitoneal injection of 22 mg kg^{-1} 2 × wk^{-1} for 4 wk, then 22 mg kg^{-1} 1 × wk^{-1} for 52 wk (2).

Metabolism and toxicokinetics

In general, ingested toxic pyrrolizidine alkaloids are rapidly metabolised and excreted in mammals; major metabolic routes are hydrolysis, *N*-oxidation and dehydrogenation (4).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation positive, TA92, TA1535, TA1537, TA98 with or without metabolic activation negative (5).

Induced sister chromatid exchanges in V79 Chinese hamster cells with metabolic activation (6).

Mutagenic in hepatocyte primary culture/DNA repair test and *Drosophila melanogaster* (experimental details unspecified) (5).
DNA repair test in hamster and mouse hepatocytes positive (7).
Induced sex-linked recessive lethal mutations in *Drosophila melanogaster* (8).

Other comments

Hepatotoxic, like most pyrrolizidine alkaloids. Toxicity of plants containing senkirkine among other pyrrolizidine alkaloids, reviewed (4).

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S24 DL-serine

$$H_2NCH(CH_2OH)CO_2H$$

$C_3H_7NO_3$ **Mol. Wt.** 105.09 **CAS Registry No.** 302-84-1

Synonyms 2-amino-3-hydroxypropanoic acid

EINECS No. 206-130-6

Physical properties

M. Pt. 246°C (decomp.)
Solubility Water: 50.2 g l^{-1} at 25°C

Environmental fate

Degradation studies
Wastewater treatment: activated sludge after 6, 12 and 24 hr 8.6%, 21% and 29% ThOD, respectively (1).

Other comments

Aliphatic amino acid.

References

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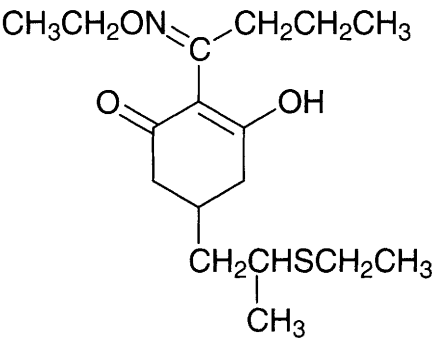
S25 sethoxydim



$C_{17}H_{29}NO_3S$ **Mol. Wt.** 327.49 **CAS Registry No.** 74051-80-2

Synonyms ±-(*EZ*)-2-(1-ethoxyiminobutyl)-5-[(2-ethylthio)propyl]-3-hydroxycyclohex-2-enone

EINECS No. 277-682-3 **RTECS No.** GW 7191000

Uses Selective systemic herbicide used to control annual and perennial grasses in broad-leaved crops.

Physical properties

B. Pt. >90°C at 3×10^{-5} mmHg **Specific gravity** 1.043 at 25°C **Partition coefficient** log P_{ow} 1.65 at pH 7, 4.51 at pH 5 **Volatility** v.p. $<7.50 \times 10^{-7}$ mmHg at 20°C

Solubility Water: 4.7 g l^{-1} at 20°C and pH 7, 25 mg l^{-1} at 20°C and pH 5. Organic solvents: acetone, benzene, ethyl acetate, hexane, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) carp, trout 1.6, 30 mg l^{-1}, respectively (1).

Invertebrate toxicity

LC_{50} (3 hr) *Daphnia magna* 1.5 mg l^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil ~25 days; degradation is via oxidation and conjugation (1).

Abiotic removal

Photodecomposition of a 10 mg l^{-1} solution illuminated with a xenon lamp 12 hr day^{-1}; $t_{1/2}$ 5.5 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♀, ♂ rat 2676, 3200 mg kg^{-1}, respectively (1).

LD_{50} oral ♂, ♀ mouse 5600, 6300 mg kg^{-1}, respectively (1).

LC_{50} (4 hr) inhalation rat >6.28 mg l^{-1} (1).

LD_{50} dermal rat, mouse >5000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No-effect level in 2-yr feeding trials in mice and rats was 12 and 17.2 mg kg^{-1} day^{-1}, respectively (1).

Metabolism and toxicokinetics
Excreted in urine (78.5%) and faeces (20.1%) 48 hr after oral administration to rats (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).
Log P_{ow} exceeds the European Union recommended limit of 3.0 (4).
WHO Toxicity Class III (5).
EPA Toxicity Class III (formulation) (6).

Other comments

Metabolic pathways reviewed (7).

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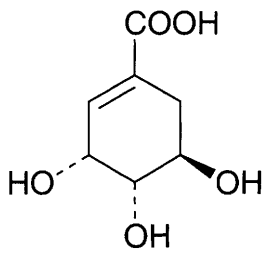
S26 shikimic acid



$C_7H_{10}O_5$ **Mol. Wt.** 174.15 **CAS Registry No.** 138-59-0

Synonyms [3*R*(3α,4α,5β)]-3,4,5-trihydroxy-1-cyclohexene-1-carboxylic acid; 3,4,5-trihydroxy-1-cyclohexene-1-carboxylic acid

EINECS No. 205-334-2 **RTECS No.** GW 4600000

Occurrence Isolated from the fruit of the oriental plant *Illichium anisatum* (*I. religiosum*).
Occurs in bracken fern at 1440 mg kg^{-1} (1).

Physical properties

M. Pt. 183-184.5°C (needles from methanol/ethyl acetate)
Solubility Water: ~180 g l^{-1}. Organic solvents: 22.5 g l^{-1} in absolute alcohol at 23°C, 0.15 g l^{-1} in anhydrous ether at 23°C, practically insoluble in benzene, chloroform and petroleum ether

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 1000 mg kg^{-1} (2).
LD_{50} oral redwinged blackbird >100 mg kg^{-1} (3).

Carcinogenicity and chronic effects
There is inadequate evidence for the carcinogenicity of shikimic acid derived from bracken fern in experimental animals (4).
Ten ♂ and 3 ♀ TF1 mice injected with a single intraperitoneal dose 1-30 mg shikimic acid. After 70 wk 6 mice had developed neoplasms of the glandular stomach, 3 reticular-cell leukaemia and 1 lymphocytic leukaemia. No such tumours were seen in the control mice (5).
Six ♂ and 6 ♀ ACI rats received 0.1% shikimic acid (derived from bracken fern) in the diet for 142 days and were fed a basal diet for 70 wk. Neither dosed nor control animals developed tumours (1).

Genotoxicity

Intraperitoneal mouse 1000 mg kg^{-1} dominant lethal test positive (5).
Oral mouse 3000 mg kg^{-1} dominant lethal test positive (5).
BHK 21 cell transformation test positive (6).
Intraperitoneal mouse 500 mg kg^{-1} once a wk for 8 successive wk or once only before mating to 3 ♀ for either 2 or 8 wk, respectively, dominant lethal effect and evidence of heritable translocation negative (7).
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with or without metabolic activation negative (8,9).
Induction of chromosomal aberrations in cultured Chinese hamster CHL cells negative (10).

Other comments

Shikimic acid is a major biosynthetic precursor of phenylalanine, tyrosine and tryptophan. It is involved in the biosynthesis of lignins, flavonoids and other aromatic compounds in plants and micro-organisms.
Known and proposed metabolites of shikimic acid showed no mutagenic activity whereas shikimic acid itself was active in the BHK 21 cell transformation assay. It seems unlikely that shikimic acid is a neoplasm initiating agent, but it may act as a carcinogen-promoting agent in the bracken fern (*Pteridium aquilinum*) (6).

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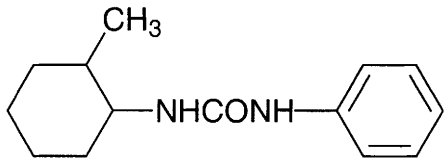
S27 siduron



$C_{14}H_{20}N_2O$ **Mol. Wt.** 232.33 **CAS Registry No.** 1982-49-6

Synonyms 1-(2-methylcyclohexyl)-3-phenylurea; *N*-(2-methylcyclohexyl)-*N'*-phenylurea

EINECS No. 217-844-2 **RTECS No.** YT 7350000

Uses Selective herbicide.

Physical properties

M. Pt. 133-138°C **Specific gravity** 1.08 at 25°C **Partition coefficient** log P_{ow} 3.8

Volatility v.p. 4.0×10^{-9} mmHg at 25°C

Solubility Water: 18 mg l^{-1} at 25°C. Organic solvents: dimethylacetamide, dimethylformamide, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 18 mg l^{-1}, Japanese goldfish 10-40 mg l^{-1} (1).

Environmental fate

Degradation studies

Resists leaching in soil; not decomposed by sunlight. $t_{1/2}$ ~120-150 days; microbial degradation occurs (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >7500 mg kg^{-1} (1).

LD_{50} dermal rabbit >5500 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No-effect level in 2-yr feeding trials in rats and dogs was 500 and 2500 mg kg^{-1} diet, 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).

Log P_{ow} exceeds the European Union recommended limit of 3.0 (4).

WHO Toxicity Class Table 5 (5).

EPA Toxicity Class III (formulation) (6).

ADI 0.14 mg kg^{-1} (6).

Other comments

Metabolic pathways reviewed (7).

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S28 silane

SiH_4

H_4Si **Mol. Wt.** 32.12 **CAS Registry No.** 7803-62-5

Synonyms silicon tetrahydride; silicane; monosilane

EINECS No. 232-263-4 **RTECS No.** VV 1400000

Uses Source of hyperpure silicon for semiconductors.

Physical properties

M. Pt. –185°C **B. Pt.** –112°C **Specific gravity** 0.68 at -185°C
Solubility Water: decomposes

Occupational exposure

FR-VME 5 ppm (7 mg m^{-3})
JP-OEL ceiling limit 100 ppm (130 mg m^{-3})
UK-LTEL 0.5 ppm (0.67 mg m^{-3}) **UK-STEL** 1 ppm (1.3 mg m^{-3})
US-TWA 5 ppm (6.6 mg m^{-3})

UN No. 2203 **Conveyance classification** flammable gas
Supply classification toxic
Risk phrases Toxic by inhalation and if swallowed – Danger of cumulative effects (R23/25, R33)
Safety phrases When using do not eat, drink or smoke – After contact with skin, wash immediately with plenty of water (S20/21, S28)

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) rat, mouse 9600 ppm (1).

Other effects

Any other adverse effects
Mice exposed to a mixture of 2500-10,000 ppm silane for 30 min and 1000 ppm tetraethoxysilane for 1-8 hr suffered renal necrosis and splenic atrophy (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3).

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S29 silica

SiO_2

O_2Si **Mol. Wt.** 60.08 **CAS Registry No.** 7631-86-9

Synonyms amorphous: diatomaceous earth; fused silica; silica gel; silica glass; vitreous silica; opal; crystalline: silica sand; quartz; chert; flint; chalcedony; jasper

EINECS No. 231-545-4

Uses Silica sand is used in glass manufacture, ceramics, foundry castings and hydraulic fracturing. Pure quartz is used in electronics. Diatomite is used in filtering water, beverages and pharmaceuticals.
Occurrence Quartz constitutes 12% of continental land masses. 25% of the Earth's surface is made up of crystalline rocks, the most common being igneous.

Occupational exposure

DE-MAK 4 mg m^{-3} (inhalable fraction of aerosol)
UK-LTEL 6 mg m^{-3} (amorphous total inhalable dust); 2.4 mg m^{-3} (amorphous respirable dust); 0.08 mg m^{-3} (fused respirable dust); MEL 0.3 mg m^{-3} (crystalline respirable dust)
US-TWA diatomaceous earth 10 mg m^{-3} (inhalable particulate), 3 mg m^{-3} (respirable particulate); fused 0.1 mg m^{-3}; fume 2 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat 15 mg kg^{-1} (amorphous), 500 mg kg^{-1} (quartz) (1).
Rats were administered 50 mg kg^{-1} silica dust intratracheally. The dust particles averaged <5 μm in diameter. Bronchoalveolar lavage was performed 24 hr later. Production of inducible nitric oxide synthase mRNA and levels of acellular lavageable lung protein were increased. Alveolar neutrophil numbers increased, indicating an inflammatory response (2).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity of amorphous silica to humans and animals, IARC classification group 3; limited evidence for carcinogenicity of crystalline silica to humans, sufficient evidence for carcinogenicity of crystalline silica to animals, IARC classification group 2A (3).
Fibrosis and enlarged mediastinal lymph nodes reported in rats inhaling 10 mg m^{-3} for 1 yr (4).
Lung carcinomas reported in rats exposed to 51.6 mg m^{-3} quartz 6 hr day^{-1}, 5 days wk^{-1} for 2 yr (5).
Lung tumours reported in rats after intratracheal administration of 7 mg wk^{-1} quartz for 10 wk (6).
Malignant reticulothelial tumours reported in rats following intrapleural injection of 20 mg quartz (7,8).
Malignant lymphomas reported in rats following intraperitoneal injection of 20 mg quartz (7).
No increased incidence of tumours was reported when amorphous silica (usually as diatomaceous earth) was

administered orally to rats (20 mg day^{-1} for life), by inhalation in mice (0.5 g day^{-1}, 5 days wk^{-1} for 1 yr), by intratracheal administration of 3 mg to hamsters, by subcutaneous or intraperitoneal administration of 20 mg to mice, or intrapleural administration of 40 mg to rats (9).
Silicotic nodules reported in rats exposed to 30,000 particles ml^{-1} quartz dust, 18 hr day^{-1}, 5 days wk^{-1} for 420 days (9).
These nodules also develop after intratracheal injection of 50 mg quartz to rats (9).
Not all forms of silica are equally pathogenic: the relatively insoluble forms of amorphous silica are fibrogenic, but less so than pure crystalline silica. Nodules occurred in rabbits following injection of 200 mg amorphous or crystalline silica, although nodules due to crystalline silica were larger. Differences in pathogenic effects also exist between individual crystalline varieties (9).
Substantial exposure-related mortality from silicosis has been reported in workers in ore mining, quarrying granite and stone industries (9).
Increased risk of lung cancer was reported in workers in ceramics, glass and related industries, foundries and metallurgical industries (9).
Two studies found an association between silicosis and lung cancer in humans (9).
There is some evidence that exposure to silica dust and smoking act synergistically in causing chronic obstructive lung disease (10).

Metabolism and toxicokinetics

In rats exposed to 109 mg m^{-3} crystalline silica for 3 hr, 82% had been cleared from alveolar duct surfaces within 24 hr (11).
In general, long-term pulmonary clearance of quartz is slow and biphasic; soluble amorphous silica dusts of small particle size are more rapidly cleared (9).
Quartz is slightly soluble in body fluids, forming silicic acid, and is readily excreted via the kidneys (9).
Autopsy results from humans showed lungs do not accumulate >5 g quartz, even in severe silicosis (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (12,13).
Escherichia coli WP2 *uvr*A with or without metabolic activation negative (12,13).
Bacillus subtilis rec assay negative (14).
Did not induce sister chromatid exchanges in Chinese hamster V79-4 cells (15).
Induced micronuclei in Syrian hamster embryo cells (5).
Equivocal results for sister chromatid exchanges induction in cultured human lymphocytes (16).
Did not induce micronuclei in bone marrow cells of mice *in vivo* (17).

Other effects

Other adverse effects (human)

Silicosis (nodular pulmonary fibrosis) is caused by deposition of fine particles of crystalline silica in the lungs, and is rarely observed after exposure to amorphous silica. The typical course is decades long (9).
284 subjects with silicosis were examined for hereditary polymorphism including HLA system and compared with 431 healthy individuals. The results provided genetic factors showing propensity to and resistance against silicosis (18).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC (19).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (20).
Data used in setting UK occupational exposure limits summarised (21).
Diseases caused by silica exposure reviewed (22).
Mutagenicity and carcinogenicity reviewed (23).

Amorphous silica: health effects from inhalation exposure with particular reference to cancer reviewed (24). Etiopathogeny of silicosis reviewed (25).
The pure, unaltered form is non-toxic but some deposits contain small amounts of crystalline quartz which is therefore fibrogenic. Currently being tested for biochemical, tissue and cellular effects, immunologic toxicity, pulmonary toxicity and epidemiology at Tulane University and the University of Vermont, USA under the National Heart, Lung and Blood Institute Lung Diseases Program.

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S30 silicon

Si

Si **Mol. Wt.** 28.09 **CAS Registry No.** 7440-21-3

EINECS No. 231-130-8 **RTECS No.** VW 0400000

Uses Used in making silanes and silicones, in the manufacture of semiconductors, alloys such as ferrosilicon and as a reducing agent in high temperature reactions.

Occurrence Occurs in nature as silica (quartz and sand) and silicates such as feldspar, orthoclase and kaolinite; it is the second most abundant element on Earth, constituting 27.6% of the Earth's crust.

Physical properties

M. Pt. 1410°C **B. Pt.** 2600°C **Specific gravity** 2.33 at 25°C **Volatility** v.p. 1 mmHg at 1724°C
Solubility Water: insoluble in water

Occupational exposure

FR-VME 10 mg m^{-3}
UK-LTEL 10 mg m^{-3} (total inhalable dust); 4 mg m^{-3} (respirable dust)
US-TWA 10 mg m^{-3}

UN No. 1346 (powder, amorphous) **HAZCHEM Code** 1Z (powder, amorphous)
Conveyance classification flammable solid (powder, amorphous)

Mammalian & avian toxicity

Metabolism and toxicokinetics
Renal silicon handling was investigated in healthy adult humans. Mean urinary silicon excretion was 33.1 mg day^{-1} and the mean fractional excretion of silicon was 86.35%. Urinary silicon was found to be highly correlated to urinary magnesium and sodium and urinary osmolality (1).

Other effects

Any other adverse effects
In rats and chicks, silicon deficiency produced defective collagenous connective tissue formation and defects in growth of bone. Growth was significantly retarded (25-40%) in silicon deficiency and was restored upon the addition of silicon to the diet – up to 500 mg silicate kg^{-1} (2,3).

Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (4).
Potential toxicity is reviewed with special reference to Alzheimer's disease (5).

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S31 silicon carbide

SiC

CSi **Mol. Wt.** 40.10 **CAS Registry No.** 409-21-2

Synonyms carbogran; carbon silicide; carborundum; silicon monocarbide

EINECS No. 206-991-8 **RTECS No.** VW 0450000

Uses Polishing glass and granite. Smoothing bisque ware. In sharpening-stones. Abrasive. Porcelain manufacture. Used during the manufacture of 'emery' paper and wheels, shoe soles, refractory brick, furnace linings and antiskid pavements. In semiconductor technology.

Physical properties

M. Pt. 2600°C **B. Pt.** >2700°C **Specific gravity** 3.23

Occupational exposure

DE-MAK 4 mg m^{-3} (without fibres) (respirable fraction or aerosol)
FR-VME 10 mg m^{-3}
UK-LTEL 10 mg m^{-3} (total inhalable dust, not whiskers); 4 mg m^{-3} (respirable dust, not whiskers)
US-TWA 10 mg m^{-3} (inhalable particulate matter containing no asbestos and <1% crystalline silica)

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Increased lung weight reported in rats exposed to 60.5 mg m^{-3}, 6 hr day^{-1}, 5 days wk^{-1} for 13 wk. In rats exposed to 3.93, 10.7 or 60.5 mg m^{-3}, 6 hr day^{-1}, 5 days wk^{-1} for 13 wk, inflammatory lung lesions; bronchiolar, alveolar and pleural wall thickening; focal pleural pulmonary fibrosis; and reactive lymphoid hyperplasia occurred. The wall thickening and hyperplasia increased further after 26 wk recovery (1).

Carcinogenicity and chronic effects

Increased incidence of pleural sarcomas reported in rats exposed to 40 mg applied directly to the pleural surface by open thoracotomy (2).
Silicon carbide whiskers have been shown to induce mesothelioma after intrapleural injection in rats (3).
No increase in total or cancer mortality, or nonmalignant respiratory disease reported in workers manufacturing abrasives exposed to silicon carbide (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).
Soluble in fused potassium hydroxide and molten iron.

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S32 silicone oil

CAS Registry No. 63148-62-9

Synonyms siloxane; silicone, di-Me; silicone 360; Antifoam FD62; Union Carbide Liquid G; DC 360; dimethylsilicone; dimethylsiloxane

RTECS No. JT 6484500

Uses Joint implants. Skin barrier protectants against water-soluble irritants.

Physical properties

B. Pt. >140°C at 0.02 mmHg **Flash point** 315°C
Solubility Organic solvents: amyl acetate, chlorinated hydrocarbons, diethyl ether, *n*-hexane, petroleum spirit, toluene, xylene. Miscible with carbon tetrachloride, chloroform, ethyl acetate, methyl ethyl ketone

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Two separate three-segment studies using subcutaneous rat, rabbit 20, 200, 1000 mg kg^{-1} showed significant dose-related incidence of *in utero* mortality at 200 and 1000 mg kg^{-1} in rats in one study, but no evidence of foetotoxicity in the second study at the same dose. No evidence of maternal toxicity observed (1).

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S33 silver

Ag

Ag **Mol. Wt.** 107.87 **CAS Registry No.** 7440-22-4

Synonyms argentium; C.I. 77820

EINECS No. 231-131-3 **RTECS No.** VW 3500000

Uses Antibacterial. For coinage. Manufacture of tableware, mirrors, jewellery, ornaments. Electroplating. In food processing.

Occurrence 0.1 ppm of Earth's crust; also found in seawater at 0.01 ppm. Found native or associated with copper, gold and lead.

Physical properties

M. Pt. 960.5°C **B. Pt.** ~2000°C **Specific gravity** 10.49 at 15°C

Occupational exposure

DE-MAK 0.01 mg m^{-3} (inhalable fraction or aerosol)
FR-VME 0.1 mg m^{-3}
JP-OEL 0.01 mg m^{-3}
SE-LEVL 0.1 mg m^{-3}
UK-LTEL 0.1 mg m^{-3}
US-TWA 0.1 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (72 hr) goldfish, carp 0.047, 0.1 mg l^{-1}, respectively (1).

LC_{50} (96 hr) rainbow trout 0.029 mg l^{-1} (2).

LOEC rainbow trout 0.10-0.17 μg l^{-1} (3,4).

The acute toxicity to freshwater fish appears to be due exclusively to [Ag^+]. Other bioavailable forms of silver do not contribute to acute toxicity. The toxicity of Ag^+ is reduced considerably when complexed by chloride, dissolved organic carbon, and sulfide, but the protective effect of calcium is only modest. The toxicity of Ag^+ to fish results from the failure of the organism to maintain constant Na^+ and Cl^- concentrations in the blood plasma (5).

LC_{50} (96 hr) sea-water acclimated rainbow trout 401 μg Ag l^{-1} at 25 ppm salinity. Toxicity increased with increasing salinity, possibly as a result of an incomplete hypoosmoregulatory ability of the rainbow trout (6).

LC_{50} (96 and 168 hr) tidepool sculpin 0.331 mg Ag l^{-1} (96 hr) and 0.119 mg Ag l^{-1} (168 hr) at 25 ppm salinity. The corresponding values at 32 ppm salinity were 0.664 mg Ag l^{-1} (96 hr) and 0.472 mg Ag l^{-1} (168 hr) (7).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 0.6-5.5 μg l^{-1} (8).

EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (9).

Hyalella azteca exposed to laboratory spiked sediments containing 1.27 to 753.3 mg Ag kg^{-1} sediment (as Ag_2S). LC_{50} (10 day) >753.3 mg kg^{-1} (the highest concentration tested). No statistically significant differences in survival rates were seen between *H. azteca* exposed to any of the spiked sediments and controls. There were no concentration-response trends for mean survival. Silver appeared not to be bioavailable under the experimental conditions (10).

Toxicity to other species

LD_{50} (96 hr) *Rana hexadactyla* tadpoles 0.026 mg l^{-1} (11).

Bioaccumulation

Bioconcentration factor in *Euglena* sp. $>10^6$ (12).

Marine mussels accumulated silver linearly over time in soft tissues during 9 days and binding to shell was complete in 1 day; silver content of the mussels was proportional to their surface area (13).

Lumbriculus variegatus exposed to laboratory spiked sediments containing *c.* 444 mg Ag kg^{-1} dry weight for up to 28 days. An accumulation factor for Ag (as Ag_2S) of 0.18 was determined (14).

Mammalian & avian toxicity

Acute data

TC_{Lo} (duration unspecified) inhalation human 1 mg m^{-3} (15).

Metabolism and toxicokinetics

Not absorbed dermally to any great extent in humans (16).

Other effects

Other adverse effects (human)

Reversible neuropathy reported following use in arthoplasty cement (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Silver: maximum admissible concentration 10 μg l^{-1} (18).

Reportable quantity regulated by US Federal Comprehensive Environmental Response, Compensation and Liability Act (19).

Land disposal prohibited by US Federal Resource Conservation and Recovery Act (20).

Other comments

Data used in setting UK occupational exposure limits summarised (21).

Bacterial interactions between bacteria and silver reviewed (22).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (23).

Bioavailability, physiology and toxicity of silver in fish reviewed (5).

Trophic transfer of silver to marine herbivores reviewed (24).

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S34 silver arsenite

Ag_3AsO_3

Ag_3AsO_3 **Mol. Wt.** 446.52 **CAS Registry No.** 7784-08-9

Synonyms arsenious acid, trisilver(1+) salt

EINECS No. 232-048-5 **RTECS No.** CG 3884000

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Ag) (inhalable dust fraction)
FR-VME 0.01 mg m^{-3} (as Ag)
JP-OEL 0.01 mg m^{-3} (as Ag)
SE-LEVL 0.01 mg m^{-3} (as Ag)
UK-LTEL 0.01 mg m^{-3} (as Ag)
US-TWA 0.01 mg m^{-3} (as Ag)

UN No. 1683 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation and if swallowed (R45, R23/25)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity of inorganic arsenic compounds to humans, limited evidence for carcinogenicity of inorganic arsenic compounds in animals, IARC classification group 1 (the evaluation applies to arsenic compounds as a group and not necessarily to all compounds within the group) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Silver: maximum admissible concentration 10 $\mu g\ l^{-1}$. Arsenic: maximum admissible concentration 50 $\mu g\ l^{-1}$ (2).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (3).
Data used in setting UK occupational exposure limits summarised (4).
Soluble in aqueous ammonia.

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S35 silver cyanide

$$AgCN$$

AgCN **Mol. Wt.** 133.89 **CAS Registry No.** 506-64-9

EINECS No. 208-048-6 **RTECS No.** VW 3850000

Uses For silver plating. Formerly used in preparation of dilute hydrocyanic acid.

Physical properties

M. Pt. 320°C (decomp.) **Specific gravity** 3.95
Solubility Water: insoluble

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Ag) (inhalable dust fraction)
JP-OEL 0.01 mg m^{-3} (as Ag)
SE-LEVL 0.1 mg m^{-3} (as Ag)
UK-LTEL 0.01 mg m^{-3} (as Ag)

UN No. 1684 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Contact with acids liberates very toxic gas (R26/27/28, R32)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed – After contact with skin, wash immediately with plenty of water – Do not empty into drains – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7, S28, S29, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 123 mg kg^{-1} (1).

Irritancy

5 mg instilled into rabbit eye caused severe irritation and 500 mg applied to rabbit skin caused mild irritation (duration unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Silver: maximum admissible concentration 10 μg l^{-1}. Cyanide: maximum admissible concentration 50 μg l^{-1} (2).
Land disposal prohibited under US Federal Resource Conservation and Recovery Act (3).
Reportable quantity regulated by US Federal Comprehensive Environmental Response, Compensation and Liability Act (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).

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S36 silver nitrate

$AgNO_3$

$AgNO_3$ **Mol. Wt.** 169.87 **CAS Registry No.** 7761-88-8

Synonyms nitric acid, silver(1+) salt

EINECS No. 231-853-9 **RTECS No.** VW 4725000

Uses Disinfectant. In water analysis. Reagent for primary, secondary and tertiary alcohols. Preparation of aliphatic nitro compounds. In photography. Manufacture of mirrors. Hair dye. Colouring porcelain.

Physical properties

M. Pt. 212°C **B. Pt.** 444°C (decomp.) **Specific gravity** 4.45 at 19°C
Solubility Water: 250 g l^{-1}. Organic solvents: acetone, ethanol

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Ag) (inhalable dust fraction)
FR-VME 0.01 mg m^{-3} (as Ag)
JP-OEL 0.01 mg m^{-3} (as Ag)
SE-LEVL 0.01 mg m^{-3} (as Ag)
UK-LTEL 0.01 mg m^{-3} (as Ag)
US-TWA 0.01 mg m^{-3} (as Ag)

UN No. 1493 **HAZCHEM Code** 2X **Conveyance classification** oxidising 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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow, channel catfish, rainbow trout, bluegill sunfish 7-60 μg l^{-1} (1-3).
A study of the effect of the exposure of freshwater rainbow trout to silver nitrate (2-10 μg l^{-1} for 75 hr) suggests that a disturbance of bronchial ionoregulation, as a result of inhibition of bronchial enzymes involved in ion transport, is the principal mechanism of the physiological toxicity of silver nitrate to freshwater fish (4).

Invertebrate toxicity
LC_{50} (24, 48 hr) *Daphnia magna* 42, 15 μg l^{-1}, respectively (5).
LC_{50} (4 day) *Orconectes immunis* 560 μg l^{-1} (6).
EC_{50} (2, 4 day) *Crangonyx pseudogracilis* 6, 5 μg l^{-1}, respectively (7).
LC_{50} (4 day) *Aplexa hypnorum* 83 μg l^{-1} (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 50 mg kg^{-1} (8).
LD_{Lo} oral dog, rabbit 20, 800 mg kg^{-1}, respectively (9).
LD_{50} intraperitoneal mouse 34,500 μg kg^{-1} (10).
LD_{Lo} intravenous rabbit 8800 μg kg^{-1} (11).
LD_{Lo} intraperitoneal guinea pig 216 mg kg^{-1} (12).
LD_{Lo} subcutaneous guinea pig 62 mg kg^{-1} (13).

Teratogenicity and reproductive effects
50 μg of 10% silver nitrate injected into the vas deferens of rats caused sterility (14).

Irritancy
Transient, minor conjuctivitis is common in infants given silver nitrate eye drops (1% solution); repeated use or high concentrations cause severe eye damage and blindness (15).
1 mg instilled into rabbit eye caused severe irritation (16).

Genotoxicity

SOS chromotest negative (17).
Induced mitotic aneuploidy in *Saccharomyces cerevisiae* D61.M (18).
Escherichia coli WP2s λ Microscreen assay with and without metabolic activation negative (19).

Other effects

Other adverse effects (human)
Symptoms of poisoning include buccal pain, sialorrhoea, diarrhoea, vomiting, coma and convulsions (15).
Absorption of nitrite following reduction of nitrate may cause methaemoglobinaemia; electrolyte disturbances may occur (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Silver: maximum admissible concentration 10 μg l^{-1}. Nitrate: guide level 25 mg l^{-1}; maximum admissible concentration 50 mg l^{-1} (20).

Other comments

In mice treated with a single dermal initiating treatment of 7,12-dimethylbenz[*a*]anthracene, silver nitrate applied dermally 2 × wk^{-1} for 44 wk resulted in tumours in 8/20 mice compared with 5/50 controls (21).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (22).
Data used in setting UK occupational exposure limits summarised (23).

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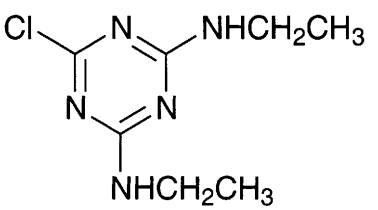
S37 simazine



$C_7H_{12}ClN_5$ **Mol. Wt.** 201.66 **CAS Registry No.** 122-34-9

Synonyms 6-chloro-N^2,N^4-diethyl-1,3,5-triazine-2,4-diamine; 6-chloro-*N*,*N*′-diethyl-1,3,5-triazine-2,4-diamine; 2-chloro-4,6-bis(ethylamino)-*s*-triazine

EINECS No. 204-535-2 **RTECS No.** XY 5250000

Uses Selective systemic herbicide.

Physical properties

M. Pt. 225-227°C **Specific gravity** 1.302 at 20°C **Partition coefficient** log P_{ow} 2.51 (1)
Volatility v.p. 6.075×10^{-9} mmHg at 20°C
Solubility Water: 5 mg l^{-1} at 20°C. Organic solvents: chloroform, diethyl ether, methanol

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 – Wear suitable gloves (S2, S36, S37)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) cichlid, zebra fish, barb, bluegill sunfish, rainbow trout 3.1->100 mg l^{-1} (2,3).
LC_{50} (48 hr) coho salmon, goldfish, carp, 6.6->40 mg l^{-1} (4,5).

Invertebrate toxicity
NOEC (48 hr) *Gammarus fasciatus, Asellus brevicaudus, Palaemonetes kadiakensis, Orconectes nais* 100 mg l^{-1} (6).
LC_{50} (48 hr) *Daphnia magna, Cypridopsis vidua* 1.0, 3.2 mg l^{-1}, respectively (6).
LC_{50} (96 hr) *Gammarus lacustris* 13 mg l^{-1} (6).
EC_{50} *Isochrysis galbana, Phaeodactylum tricornutum* 0.5 mg l^{-1} (7).
EC_{50} (5 min) *Photobacterium phosphoreum* 237 ppm Microtox test (8).

Environmental fate

Anaerobic effects
$t_{1/2}$ 8-12 wk in loamy sand under anaerobic conditions. Degradation products included: 2-chloro-4-ethylamino-6-amino-*s*-triazine, 2-chloro-4,6-diamino-*s*-triazine, 2-hydroxy-4,6-bis(ethylamino)-*s*-triazine and 2-hydroxy-4-ethylamino-6-amino-*s*-triazine (1).

Degradation studies
Biotransformation rate in surface waters 0.005-0.57 day^{-1} ($t_{1/2}$ 1-139 days). In small hydrological systems, such as field ditches and channels, it appears to be transformed rapidly, but it persists for longer in large water bodies such as main discharge channels and lakes (9).
75-100% degradation in soil in 12 months (2).
Loss by volatilisation and photodecomposition is insignificant, but microbial degradation in soil is significant. Low water solubility limits leaching, and several months after application most is found in the top 2 inches of soil (10).
Under aerobic conditions degradation depends largely on soil moisture and temperature. $t_{1/2}$ in sandy loam 36-234 days. Applied to loamy sand and silt loam, $t_{1/2}$ was 16.3 and 25.5 wk, respectively, at 25-30°C. Degradation products included: 2-chloro-4,6-diamino-*s*-triazine, 2-chloro-4-ethylamino-6-amino-*s*-triazine, 2-hydroxy-4,6-bis(ethylamino)-*s*-triazine and 2-hydroxy-4-ethylamino-6-amino-*s*-triazine (1).

Adsorption and retention
Adsorption is correlated with soil organic matter content and cation exchange capacity and clay content. It was slightly mobile in peat and peat moss (k_d >21) and more mobile in clay fractions (k_d 0-12.2) (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 971 mg kg^{-1} (11).
LD_{50} oral hen, pigeon >5000 mg kg^{-1} (10).
LC_{50} (1 hr) inhalation rat 9800 mg m^{-3} (12).
LD_{50} intravenous mouse 100 mg kg^{-1} (13).

Carcinogenicity and chronic effects

No-observed-adverse-effect level in 2-yr feeding trials in rats 100 ppm (10).

Not tumorigenic in an 18-month feeding study in mice at the highest tolerated dose of 215 mg kg^{-1} day^{-1} (14).

Produced injection site sarcomas in rats and mice (1).

Induction of mammary gland tumours has been suggested by an interim report, but further details are not available (15).

Teratogenicity and reproductive effects

No adverse reproductive effects reported in a three-generation study in rats fed 100 ppm in the diet (1).

Administration of 6 mg kg^{-1} for 142 days or 25 mg kg^{-1} for 37-111 days to sheep caused changes in germinal epithelium of testes and disturbed spermatogenesis (1).

Administration by gavage to rabbits at 5, 75 or 200 mg kg^{-1} on days 7-19 of pregnancy caused no malformations, but ≥75 mg kg^{-1} caused maternal and foetal toxicity (1).

Delayed ossification was reported in rats administered 78-2500 mg kg^{-1} day^{-1} by gavage on days 6-15 of pregnancy (1).

Metabolism and toxicokinetics

65-97% eliminated as the deethylated metabolite within 24 hr of an oral dose to mammals (16).

63-74% of a single oral dose of 0.5 mg kg^{-1} was absorbed by rats; urinary metabolites were conjugated mercapturates of hydroxysimazine, 2-hydroxy-4-amino-6-ethylamino-*s*-triazine and 2-hydroxy-4,6-diamino-*s*-triazine (1).

2-Chloro-4,6-diamino-*s*-triazine was the major metabolite in rats given 2 doses of 0.017-167 mg kg^{-1} 24 hr apart; it ranged from 1.6% at the 1.7 mg kg^{-1} dose to 18.2% at the 167 mg kg^{-1} dose, while the mono-*N*-dealkylated metabolite ranged from 0.35% to 2.8% at these doses (1).

Rats receiving 0.5 mg kg^{-1} orally excreted 50.5-62.1% in urine and 13.3-19.1% in faeces; elimination was biphasic and rates were faster in ♀ rats (1).

Irritancy

Non-irritating to eyes and skin of rabbits (16).

80 mg instilled into rabbit eye caused moderate irritation and 500 mg applied to abraded rabbit skin caused mild irritation (17).

Contact dermatitis has been reported in workers manufacturing simazine and propazine (1).

Genotoxicity

Salmonella typhimurium (strain and metabolic activation unspecified) negative (18).

Bacillus subtilis rec assay negative (18).

Did not induce mitotic recombination in *Saccharomyces cerevisiae* (18).

Escherichia coli PQ37 SOS chromotest with or without metabolic activation negative (19).

In tests for unscheduled DNA synthesis in human lung fibroblasts, positive and negative results have been reported (18,20).

Did not induce sister chromatid exchanges in mammalian cells *in vitro* or micronuclei in the mouse bone marrow assay *in vivo* (20).

Drosophila melanogaster sex-linked recessive lethal test positive (21).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (22).

Included in Schedules 5 and 6 (Release into Land/Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).

WHO Toxicity Class Table 5 (24).

EPA Toxicity Class IV (formulation) (3).

ADI 0.005 mg kg^{-1} body weight (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (25).
Environmental fate reviewed (26).
Hazards reviewed (27).
Metabolic pathways reviewed (28).

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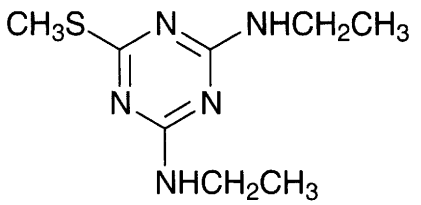
S38 simetryn



$C_8H_{15}N_5S$ **Mol. Wt.** 213.31 **CAS Registry No.** 1014-70-6

Synonyms 2,4-bis(ethylamino)-6-methylthio-1,3,5-triazine; *N,N'*-diethyl-6-(methylthio)-1,3,5-triazine-2,4-diamine; 2,4-bis(ethylamino)-6-(methylthio)-*s*-triazine

EINECS No. 213-801-7 **RTECS No.** XY 4025000

Uses Selective herbicide, used in combination with thiobencarb against broad-leaved weeds in rice.

Physical properties

M. Pt. 82-83°C **Specific gravity** 1.02 **Partition coefficient** log P_{ow} 2.06 (1)
Volatility v.p. 7.1×10^{-7} mmHg at 20°C
Solubility Water: 450 mg l^{-1} at 25°C. Organic solvents: acetone, methanol, *n*-octanol, 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

Invertebrate toxicity
LC_{50} (48 hr) freshwater shrimp, *Moina macrocopa, Daphnia magna* 14.7, 32 and >50 mg l^{-1}, respectively (2).

Bioaccumulation
Bioconcentration factor showed relatively high accumulation in green algae compared with rotifers, daphnids and zebra fish; uptake via food chain amounted to 22-42% of bioconcentration from water; clearance of residues from fish was rapid, $t_{1/2}$ 2.1 days (1).

Environmental fate

Nitrification inhibition
Inhibited Athiorhodaceae and Thiorhodaceae (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1830 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).
WHO Toxicity Class III (7).
EPA Toxicity Class III (formulation) (8).
ADI 0.025 mg kg^{-1} (8).

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S39 sodium

Na

Na **Mol. Wt.** 22.99 **CAS Registry No.** 7440-23-5

Synonyms natrium

EINECS No. 231-132-9 **RTECS No.** VY 0686000

Uses Manufacture of sodium compounds, tetraethyllead. In organic synthesis. For photoelectric cells. In sodium lamps.

Occurrence Principal cation in biosphere; 2.83% of the Earth's crust.

Physical properties

M. Pt. 97.82°C **B. Pt.** 881.4°C **Specific gravity** 0.968 at 20°C **Volatility** v.p. 1.2 mmHg at 40°C

Solubility Water: violently decomposes. Organic solvents: ethanol (decomp.)

Occupational exposure

UN No. 1428 **HAZCHEM Code** 4W **Conveyance classification** substance which in contact with water emits flammable gas

Supply classification highly flammable, corrosive

Risk phrases Reacts violently with water, liberating extremely flammable gases – Causes burns (R14/15, R34)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep contents under oil – Keep container dry – In case of fire, use graphite, soda ash or suitable dry powder – do not use water, carbon dioxide or halogenated extinguishers – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – (S5 not required when safe packaging is used) (S1/2, S5, S8, S43, S45)

Ecotoxicity

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 1480 mg l^{-1} Na_2S (1).

EC_{50} (21 day) *Daphnia magna* 1020 mg l^{-1} Na_2S (1).

LOEC (21 day) *Daphnia magna* 680 mg l^{-1} Na_2S (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 4 g kg^{-1} (form unspecified) (2).

Other effects

Other adverse effects (human)
Extremely caustic to all tissue (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

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S40 sodium acetate

$$CH_3CO_2Na$$

$C_2H_3NaO_2$ **Mol. Wt.** 82.03 **CAS Registry No.** 127-09-3

Synonyms sodium ethanoate

EINECS No. 204-823-8 **RTECS No.** AJ 4300100

Uses The anhydrous form is used in acetylations, the trihydrate is used in photography. Analytical reagent. Mordant in dyeing. Food acidulant. Pharmaceutic aid (in dialysis solutions). For foot and bottle warmers.

Physical properties

M. Pt. 324°C **Specific gravity** 1.528 **Partition coefficient** log P_{ow} –4.22 (1)
Solubility Water: 1.25 g ml^{-1}. Organic solvents: ethanol

Ecotoxicity

Fish toxicity
NOEC (72 hr) fathead minnow >100 ppm (1).
LC_{50} (24 hr) bluegill sunfish 5000 ppm (2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* <5800 ppm (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 3530, 6891 mg kg^{-1}, respectively (3,4).
LD_{50} intravenous rat, mouse 380 mg kg^{-1} (1).

Genotoxicity

Did not induce sister chromatid exchanges in human lymphocytes or chicken embryo cells (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (5).

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S41 sodium amide

$NaNH_2$

H_2NNa **Mol. Wt.** 39.01 **CAS Registry No.** 7782-92-5

Synonyms sodamide

EINECS No. 231-971-0 **RTECS No.** VY 2775000

Uses Dehydrating agent. In production of indigo and hydrazine. Intermediate in sodium cyanide preparation. In ammonolysis reactions, Claisen condensations, alkylation of nitriles and ketones, synthesis of ethynyl compounds and acetylenic carbinols.

Physical properties

M. Pt. 210°C **B. Pt.** 400°C

Occupational exposure

UN No. 1425

Mammalian & avian toxicity

Irritancy

Severe eye and skin irritant (species, dose and duration unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (2).

References

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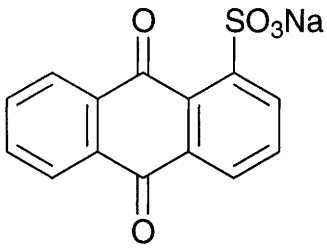
S42 sodium anthraquinone-1-sulfonate



$C_{14}H_7NaO_5S$ **Mol. Wt.** 310.26 **CAS Registry No.** 128-56-3

Synonyms 9,10-dihydro-9,10-dioxo-1-anthracenesulfonic acid, sodium salt; Golden salt

EINECS No. 204-894-5 **RTECS No.** CB 1095540

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, rat, mouse 14, 20, 32 g kg^{-1}, respectively (duration unspecified) (1).

Irritancy

500 mg instilled into rabbit eye caused mild irritation (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (3).

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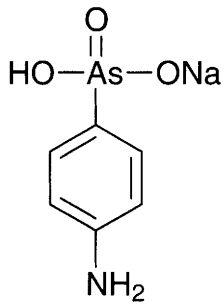
S43 sodium arsanilate



$C_6H_7AsNNaO_3$ **Mol. Wt.** 239.04 **CAS Registry No.** 127-85-5

Synonyms (4-aminophenyl)arsonic acid, sodium salt; arsanilic acid, monosodium salt; sodium-*p*-aminobenzenearsonate; sodium aminophenol arsonate; sodium-*p*-aminophenylarsonate; sodium anilarsonate

EINECS No. 204-869-9 **RTECS No.** CF 9625000

Uses For prophylaxis and treatment of enteric infections in pigs. Growth promoter. Formerly used in treatment of syphilis.

Physical properties

Solubility Water: soluble in 6 parts water. Organic solvents: ethanol

Occupational exposure

UK-LTEL MEL 0.1 mg m^{-3} (as As)

UN No. 2473 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rat, mouse 75, 400 mg kg^{-1}, respectively (1,2).

LD_{Lo} subcutaneous dog, rabbit 5, 200 mg kg^{-1}, respectively (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (4).

Other comments

Poisonous.

References

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S44 sodium arsenate

Na_3AsO_4

$AsNa_3O_4$ **Mol. Wt.** 207.89 **CAS Registry No.** 7631-89-2

Synonyms arsenic acid, sodium salt; sodium *o*-arsenate

EINECS No. 231-547-5 **RTECS No.** CG 1225000

Uses In formulation of wood preservatives. Insecticide in ant killers and animal dips.

Physical properties

M. Pt. 86.6°C (dodecahydrate) **B. Pt.** decomposes at 180°C **Specific gravity** 1.752-1.804 (dodecahydrate)
Solubility Water: 389 g l^{-1} at 15.5°C (dodecahydrate). Organic solvents: ethanol, glycerine

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)

UN No. 1685 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation and if swallowed (R45, R23/25)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity of inorganic arsenic compounds to humans, limited evidence for carcinogenicity of inorganic arsenic compounds to animals, IARC classification group 1 (this evaluation applies to arsenic compounds as a whole and not necessarily to all chemicals within the group) (1,2).
No increased incidence of tumours in rats fed 400 mg As kg^{-1} diet or in dogs receiving 125 mg As kg^{-1} diet for 2 yr (3).
Three papillomas reported in two ♂ mice painted with a 1.58% aqueous solution (4).
Lymphomas reported in mice following 20 subcutaneous injections of 0.5 mg kg^{-1} (5).

Teratogenicity and reproductive effects
Increased foetal resorption and malformations (fused or forked ribs, exencephaly, shortened jaw, open eyes and anophthalmia) reported in mice and rats following intraperitoneal injection of 45 mg kg^{-1} on days 6, 7, 8, 9, 10 or 11 of pregnancy (6).
An oral dose of 10-40 mg kg^{-1} on day 9, 10 or 11 of pregnancy caused resorptions but not malformations in mice (7,8).
Exencephaly and resorptions reported in hamsters following intravenous injection of 20 mg kg^{-1} on day 8 of pregnancy (9).
An oral dose of 120 mg kg^{-1} given to mice on one of gestation days 7-15 caused reduced foetal weight (when given on days 10, 11 or 15), increased prenatal mortality (when given on day 11) and increased incidence of skeletal malformations (when given on day 9) (10).

Genotoxicity

Bacillus subtilis rec assay positive (11).
Escherichia coli SOS chromotest negative (12).
Induced chromosomal aberrations and sister chromatid exchanges in cultured human peripheral lymphocytes (13,14).

Induced sister chromatid exchanges and chromosomal aberrations in Syrian hamster cells and human lymphocytes (15).
Induced chromosomal aberrations in Chinese hamster ovary cells (16).
Drosophila melanogaster wing spot test negative (sodium arsenate is highly toxic to *Drosophila* and hence could only be tested at very low concentrations) (17).

Other effects

Other adverse effects (human)
Sodium arsenate inhibited DNA synthesis and alters metabolism of nucleosides in human lymphocytes *in vitro* (18,19).

Any other adverse effects
♀ Rats were administered sodium arsenate orally in equitoxic doses at 21 and 4 hr before sacrifice. At 60 mg kg^{-1} hepatic haem oxygenase activity was increased fivefold (20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 μg l^{-1} (21).

Other comments

Experiments on B6C3F1 mice maintained for 28 days on a diet deficient, sufficient, or excessive in selenium content and then administered sodium arsenate (5 mg kg^{-1} As) by gavage provided suggestive evidence that selenium status alters arsenate metabolism and disposition (22).
The name sodium arsenate is applied to both the disodium and trisodium salts and some authors do not specify which (2).

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S45 sodium arsenite

$NaAsO_2$

$AsNaO_2$ **Mol. Wt.** 129.91 **CAS Registry No.** 7784-46-5

Synonyms arsenious acid, sodium salt; sodium arsenic oxide; sodium metaarsenite

EINECS No. 232-070-5 **RTECS No.** CG 3675000

Uses In manufacture of arsenical soap. Insecticide. Acaricide.

Physical properties

Specific gravity 1.87 at 25°C

Solubility Water: freely soluble. Organic solvents: ethanol

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)

UN No. 1686 (aqueous solution)

UN No. 2027 (solid) **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification toxic

Risk phrases Toxic by inhalation and if swallowed (R23/25)

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

LD_{50} oral rat 41 mg kg^{-1} (1).

LD_{50} dermal rat 150 mg kg^{-1} (2).

LD_{Lo} intravenous rat 6 mg kg^{-1} (3).

LD_{50} intramuscular mouse 14 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity of inorganic arsenic compounds to humans, limited evidence for carcinogenicity of inorganic arsenic compounds to animals, IARC classification group 1 (this evaluation applies to arsenic compounds as a whole and not necessarily to all chemicals within the group) (5).

Evidence is presented that the human lung cancer observed among arsenic ore smelters and the skin cancer among people exposed therapeutically to Fowler's solution have, as their common origin, the genotoxic arsenite AsO_2^- (6).

No increased incidence of tumours was reported following oral administration of 10 mg l^{-1} to mice or 5 mg l^{-1} to rats in drinking water for life, or in 2-yr feeding trials in dogs and rats receiving up to 125 and 250 mg kg^{-1} *via* diet, respectively. No increased incidence of tumours was seen in mice exposed by inhalation to a 1% (w/w) aqueous solution 20 min day^{-1}, 5 days wk^{-1} for 55 wk (7).

Low micromolar concentrations of sodium arsenite caused increased mRNA transcripts and secretion of keratinocyte growth factors in primary human epidermal keratinocyte cultures. Total cell numbers, as well as c-myc expression and incorporation of [3H]thymidine, both indicators of cell proliferation, were also elevated. As an *in vivo* model, the influence of arsenic on mouse skin tumour development was studied. Following low-dose application of 12-*O*-tetradecanoylphorbol-13-acetate (TPA) to transgenic TG.AC mice (which carry the V-Ha-ras oncogene and can serve as a genetically initiated model for carcinogenesis) a marked increase in the number of

skin papillomas occurred in transgenic mice receiving arsenic in the drinking water, as compared with control drinking water. Papillomas did not develop in arsenic-treated transgenic mice that had not received TPA or in arsenic-treated wild-type FVB/N mice, suggesting that arsenic is neither a tumour initiator nor promoter, but rather an enhancer. It is suggested that arsenic enhances papilloma development via the chronic stimulation of keratinocyte-derived growth factors (8).

Teratogenicity and reproductive effects

Teratogenic in mice and hamsters after oral administration of maternally toxic doses (9,10).

A high rate of resorptions and malformations of the eyes, ribs, tail and brain reported in mice following intraperitoneal injection of 10-12 mg kg^{-1} on days 9-12 of pregnancy (10).

Total resorptions reported in golden hamsters following intraperitoneal injection of 5 mg kg^{-1} on day 9 or 10 of gestation. Treatment on day 11 or 12 reduced foetal weight. Treatment on day 8, 10, 11 or 12 increased prenatal mortality. No malformations were reported (11).

Metabolism and toxicokinetics

Urinary excretion in the first 48 hr was <10% of an intravenous dose in rats and 30% in rabbits. <10% was excreted in faeces. Tissue distribution was highest in the spleen of rats, in the liver, kidneys and lungs of rabbits, and in the liver, kidneys and spleen of mice (12).

16.7% of an intravenous dose to humans was excreted, mainly via urine, in the first 24 hr; highest levels were found in the liver and kidneys (12).

In man the toxicity of inorganic trivalent arsenic is reduced by *in vivo* methylation of the element, leading to the synthesis of monomethylarsenic (MMA) and dimethylarsinic (DMA) acids, which are eliminated in the urine along with unchanged inorganic arsenic (13).

Rabbit renal cortical slices were incubated with 10^{-3} M $NaAsO_2$ and stoichiometric amounts (1-3 times) of glutathione, or with synthetic arsenic-glutathione conjugates (10^{-3} M). Exogenous glutathione had limited if any protective effects against cytotoxicity by $NaAsO_2$ (14).

5-9% of ^{74}As was taken up by humans following inhalation of cigarette smoke containing labelled sodium arsenite; 45% was excreted via urine and 2.5% in faeces after 10 days (15).

Irritancy

Hyperpigmentation and hyperkeratosis have been reported in workers exposed to the dust during pesticide manufacturing (16).

Irritating to the eyes and may cause conjunctivitis (17).

Genotoxicity

Escherichia coli WP100 without metabolic activation positive (18).

Saccharomyces cerevisiae D7 gene conversion at *trp5* negative, reverse mutation weakly positive (19).

Bacillus subtilis rec assay positive (20).

Escherichia coli WP2 tryptophan reversion positive (20).

Induced sister chromatid exchanges in Chinese and Syrian hamster ovary cells *in vitro* (21,22).

In vitro Chinese hamster cell lines CH09, EM-C11, V79, V-H4 and CHE. A high frequency of chromosomal aberrations were observed on the X chromosome of all cell lines. The V79 cell line displayed more aberrations at the Xq21 locus, whereas CH09 displayed the majority of aberrations in the centromeric region (23).

Increased incidence of chromatid breaks in cultured human leucocytes (24).

Other effects

Other adverse effects (human)

Dose-related increases in hyperdiploidy were seen in human lymphocyte cultures treated with 0.001-0.1 μmM sodium arsenite. This effect may occur through a disruption of microtubule function (25).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1}. Arsenic: maximum admissible concentration 50 μg l^{-1} (26).

Other comments

Toxicity reviewed (27).

Very poisonous.

In vitro investigations on Chinese hamster ovary cells suggest that glutathione peroxidase and, to a lesser degree, catalase are involved in defence against arsenite genotoxicity and therefore that increasing the intracellular antioxidant level may have preventative or therapeutive effects in arsenic poisoning (28).

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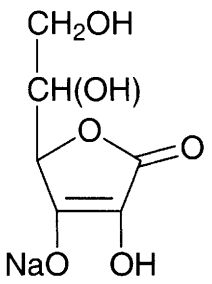
S46 sodium ascorbate



$C_6H_7NaO_6$ **Mol. Wt.** 198.11 **CAS Registry No.** 134-03-2

Synonyms monosodium L-ascorbate; 3-oxo-L-gulofuranolactone sodium enolate

EINECS No. 205-126-1 **RTECS No.** CI 7671000

Uses In vitamin C preparations. Antioxidant in food. Curing meat.

Physical properties

M. Pt. 220°C (decomp.)
Solubility Water: 62 g 100 ml^{-1}

Mammalian & avian toxicity

Metabolism and toxicokinetics

Readily absorbed from the human gastro-intestinal tract and widely distributed in body tissues. Plasma concentrations rise as ingested dose increases, to a plateau of 90-150 mg day^{-1}. Body stores in health are 1.5 g. Concentration in leucocytes and platelets is greater than in erythrocytes and plasma; in deficiency, loss from leucocytes occurs at a slower rate. Reversibly oxidised to dehydroascorbic acid and some is metabolised to ascorbate-2-sulfate and oxalic acid which are then excreted in urine. Intake exceeding body needs (>200 mg day^{-1}) is excreted rapidly unchanged in urine. It crosses the placenta and is present in breast milk (1).

Genotoxicity

Increased incidence of sister chromatid exchanges in Chinese hamster ovary cells and human lymphocytes *in vitro* (2).

DNA synthesis inhibition test in HeLa cells positive (2).

Inhibited mitosis and induced chromosomal aberrations in Chinese hamster ovary cells *in vitro* (3).

Other effects

Other adverse effects (human)

Large doses of ascorbic acid cause diarrhoea, and may cause hyperoxaluria. Prolonged use of large doses may induce tolerance (1).

Any other adverse effects

In rats given sodium ascorbate (dose and route unspecified) for 36 wk, DNA synthesis in bladder epithelium occurred at 2-16 wk and morphological alterations of the urothelial surface at 8-16 wk (4,5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (6).

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S47 sodium azide

NaN_3

N_3Na **Mol. Wt.** 65.01 **CAS Registry No.** 26628-22-8

Synonyms Nemazyd; Smite

EINECS No. 247-852-1 **RTECS No.** VY 8050000

Uses In organic syntheses. Preparation of hydrazoic acid, lead azide, pure sodium. Differential selection of bacteria. Preservative. Propellant for automotive safety bags. Nematicide. Herbicide.

Physical properties

M. Pt. decomposes **Specific gravity** 1.846
Solubility Water: 40.16% at 17°C. Organic solvents: ethanol. (Also soluble in liquid ammonia)

Occupational exposure

DE-MAK 0.2 mg m^{-3}
FR-VLE 0.1 ppm (0.3 mg m^{-3})
UK-STEL 0.3 mg m^{-3} (as NaN_3)
US-STEL ceiling limit 0.29 mg m^{-3} (ceiling limit 0.11 ppm as hydrazoic acid vapour)

UN No. 1687 **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic if swallowed – Contact with acids liberates very toxic gas (R28, R32)
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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S45)

Ecotoxicity

Fish toxicity
5 mg l^{-1} had no effect on trout, bluegill sunfish (24 hr) in lake water (1).

Invertebrate toxicity
Phaeodactylum tricornutum (3-day static bioassay) growth rate decreased by 11% at 6.5×10^{-4} mg l^{-1} (2).

Toxicity to other species
0.65-6500 µg l^{-1} inhibited nitrate reductase in shoots of 6-day-old wheat seedlings (3).

Environmental fate

Nitrification inhibition
23 mg l^{-1} inhibited NH_3 oxidation by activated sludge by 75% (4).

Abiotic removal
Azide will not persist in solution but will shift between the dissolved salt form and hydrazoic acid depending on the pH (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 27 mg kg^{-1} (5,6).
LD_{50} dermal rabbit 20 mg kg^{-1} (5).
LD_{50} intravenous monkey 19 mg kg^{-1} (7).
LD_{Lo} subcutaneous mouse, rat 17, 35 mg kg^{-1}, respectively (8,9).

Sub-acute and sub-chronic data
Gavage rat 0, 1.25, 2.5, 5, 10 or 20 mg kg^{-1} 5 day wk^{-1} for 90 days caused almost total mortality at the highest dose, but no deaths at other doses. Reduced weight gain was seen at 10 mg kg^{-1}. ♀ in all dose groups had slightly increased liver to body weight ratios. Lesions of the brain and lungs were observed in the rats that died. NOEC 5 mg kg^{-1} (10).

Carcinogenicity and chronic effects
National Toxicology Program investigated sodium azide via gavage in rats. No evidence of carcinogenicity reported (11).
Predicted non-carcinogenic in rats (12).

Teratogenicity and reproductive effects
Pregnant Syrian hamsters were administered 3.9 mg kg^{-1} hr^{-1} from subcutaneously implanted osmotic minipumps for days 7-9 of gestation. Most dams exhibited signs of toxicity during this time. Dams were euthanised on day 13 and uteri removed. An increased incidence of resorbed embryos was observed but there was no difference in the incidence of gross malformations compared with controls. No teratogenicity was seen (13).
6.5 µg applied to hatching eggs of hens prior to incubation reduced hatchability by 10% and increased embryo mortality by 10% (14).

Metabolism and toxicokinetics
Rapidly absorbed from the gastro-intestinal tract (species unspecified) (15).
No cumulative tendency indicated by pharmacokinetics and neither sodium azide nor hydrazoic acid were excreted unchanged in the urine of rats (16).

Irritancy
Contact with human eyes or skin caused irritation (1).
Contact with the skin may lead to blistering and symptoms of toxicity (species unspecified) (15).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive, TA98, TA1537 with and without metabolic activation negative (17).
Escherichia coli PQ37 without metabolic activation SOS Chromotest negative (18).
Saccharomyces cerevisiae C658-K42 (metabolic activation unspecified) weakly positive (19).

Other effects

Other adverse effects (human)
A laboratory technician who accidentally ingested 150 mg in aqueous solution suffered headache, nausea, vomiting, diarrhoea, dyspnoea, hypotension and tachycardia (20).
Ingestion of several grams caused collapse and death within 40 minutes with pathological findings of swelling of the brain and lungs and mild fatty degeneration of the liver (21).

Any other adverse effects

Rats, mice, guinea pigs and rabbits administered sodium azide by various routes showed similar symptoms including hypotension, respiratory stimulation and tachycardia. A preliminary stage of excitability, respiratory stimulation and chronic convulsions is caused by some sublethal doses. Severe poisoning causes lesions of the optic nerves and tracts of rats. Lethal doses caused respiratory distress and convulsion, followed by central nervous system depression and death (16,22,23).

Inhibits mitochondrial ATP formation in red abalone (24).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (25).

Included in Schedules 4 and 6 (Release into the Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (26).

Other comments

Human intoxication reviewed (27).

Cytochrome oxidase inhibitor (28).

Reviews on human health effects, epidemiology, workplace experience, experimental toxicology and environmental effects are listed (29).

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S48 sodium bisulfite

$NaHSO_3$

$HNaO_3S$ **Mol. Wt.** 104.06 **CAS Registry No.** 7631-90-5

Synonyms sulfurous acid, monosodium salt; hydrogen sodium sulfite; monosodium sulfite; sodium hydrogen sulfite; sodium acid sulfite

EINECS No. 231-548-0 (aqueous solution) **RTECS No.** VZ 2000000

Uses Wool bleach and disinfectant. In dyeing, papermaking. Stripper in laundering. To remove permanganate stains. Sodium hydrosulfite manufacture. Rubber latex coagulator. Preservative and bleach in food. Pharmaceutic aid.

Physical properties

M. Pt. decomposes on heating **Specific gravity** 1.48
Solubility Water: in 3.5 parts cold water

Occupational exposure

FR-VME 5 mg m^{-3}
UK-LTEL 5 mg m^{-3}
US-TWA 5 mg m^{-3}

UN No. 2693 (aqueous solution) **HAZCHEM Code** 2X (aqueous solution) **Conveyance classification** corrosive substance (aqueous solution)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2000 mg kg^{-1} (1).
LD_{50} intraperitoneal dog, rabbit, rat, mouse 244, 300, 650, 675 mg kg^{-1}, respectively (2).
LD_{50} intravenous rabbit, rat, mouse 65, 115, 130 mg kg^{-1}, respectively (3).

Metabolism and toxicokinetics

Metabolised in rabbits after intravenous injection to sulfate, thiosulfate, *S*-sulfoalbumin, *S*-sulfoglutathione and *S*-sulfocysteine. *S*-sulfocysteine was further metabolised to inorganic sulfate and thiosulfate (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (5).
Escherichia coli WP2s (λ) with and without metabolic activation negative (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (7).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, and workplace experience listed (9).

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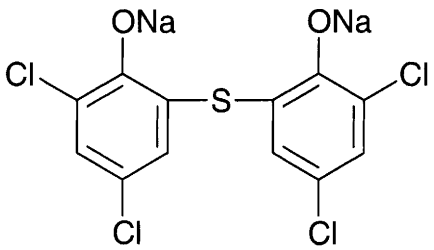
S49 sodium bithionolate



$C_{12}H_4Cl_4Na_2O_2S$ **Mol. Wt.** 400.02 **CAS Registry No.** 6385-58-6

Synonyms 2,2′-thiobis[4,6-dichlorophenol], disodium salt; thiobis[(4,6-dichloro-*o*-phenylene)oxy]disodium; bithionolate sodium; Vancide BN

RTECS No. SN 0700000

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 75 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (2). Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

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S50 sodium borohydride

$NaBH_4$

BH_4Na **Mol. Wt.** 37.83 **CAS Registry No.** 16940-66-2

Synonyms borate(1–), tetrahydro-, sodium; borol; Hidkitex DF; sodium hydroborate; sodium tetrahydroborate; sodium tetrahydridoborate

EINECS No. 241-004-4 **RTECS No.** ED 3325000

Uses Reducing agent. Foaming agent. Used to generate diborane. Scavenger for traces of aldehydes, ketones and peroxides in organic chemicals.

Physical properties

M. Pt. 400°C (decomp.) **Specific gravity** 1.074
Solubility Water: 55% w/w at 25°C

Occupational exposure

UN No. 1426 **Conveyance classification** substance which in contact with water emits flammable gas

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 160 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 18 mg kg^{-1} (2).
LD_{Lo} intraperitoneal mouse, rabbit 18, 60 mg kg^{-1}, respectively (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}. Boron: guide level 1000 mg l^{-1} (3).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

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S51 sodium bromate

$NaBrO_3$

$BrNaO_3$ **Mol. Wt.** 150.89 **CAS Registry No.** 7789-38-0

Synonyms bromic acid, sodium salt; Neutralizer K-126; Neutralizer K-140; Neutralizer K-938

EINECS No. 232-160-4 **RTECS No.** EF 8750000

Uses With sodium bromide to dissolve gold from its ores.

Physical properties

M. Pt. 381°C (decomp.) **Specific gravity** 3.34
Solubility Water: in 2.5 parts water

Occupational exposure

UN No. 1494 **HAZCHEM Code** 1YE **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rabbit 250 mg kg^{-1} (1).
LD_{Lo} subcutaneous guinea pig, dog 100, 120 mg kg^{-1}, respectively (1).
LD_{Lo} intravenous rabbit 360 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 140 mg kg^{-1} (2).

Irritancy
100 µl of 5% (w/v) solution instilled into guinea pig eye (24 hr) caused minimal irritation (3).

Other effects

Any other adverse effects
Sodium bromate administered into the cochlea of guinea pigs by perilymphatic perfusion suppressed cochlear microphonics and the whole nerve action potential of the auditory nerve. K^+ and Cl^- concentrations in the endolymph were decreased and Na^+ concentrations increased. Severe oedema of the stria vasularis and collapse of the Reissner's membrane were histologically evident (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (5).
Included in Schedules 4 and 6 (Release into the Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

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S52 sodium carbonate

$$Na_2CO_3$$

CNa_2O_3 **Mol. Wt.** 105.99 **CAS Registry No.** 497-19-8
Synonyms carbonic acid, disodium salt; bisodium carbonate; soda; soda ash; carbonic acid, sodium salt
EINECS No. 207-838-8 **RTECS No.** VZ 4050000
Uses In manufacture of glass, soap, sodium salts. In washing wool and textiles. Water softener. Bleach for cotton, linen. Analytical reagent. In photography. Pharmaceutic acid. Veterinary emetic, skin cleanser.
Occurrence Occurs as the hydrate thermonatrite, and as the decahydrate natron or natrite.

Physical properties

M. Pt. 851°C (anhydrous) **Specific gravity** 2.53 (anhydrous)
Solubility Water: in 3.5 parts water at 25°C

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) – Do not breathe dust – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S22, S26)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4090 mg kg^{-1} (1).
LC_{50} (2 hr) inhalation guinea pig, mouse, rat 800, 1200, 2300 mg m^{-3}, respectively (2).
LD_{50} intraperitoneal mouse 117 mg kg^{-1} (3).
LD_{50} subcutaneous mouse 2210 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Inhalation ♂ rat (3.5 months) 2% aqueous solution 4 hr day^{-1}, 5 days wk^{-1} resulted in pulmonary alterations including thickening of the intra-alveolar walls, hyperaemia, lymphoid infiltration and pneumocyte desquamation (aerosol concentration = 70 ± 2.9 mg m^{-3}) (5).

Teratogenicity and reproductive effects
Pregnant mice were administered 3.4-340 mg kg^{-1} orally during days 6-15 of gestation. No effects on implantation or survival of dams or foetuses were seen. Soft and skeletal tissue anomalies were noted, but the incidence of these findings did not differ from that of controls. Similar results were found with rats and rabbits administered 245 and 179 mg kg^{-1}, respectively (5).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye (24 hr) caused moderate irritation (1).

Genotoxicity

Escherichia coli PQ35, PQ37 with and without metabolic activation SOS Chromotest negative (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (7).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Considered safe for present use in cosmetics (9).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (10).

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S53 sodium chlorate

$NaClO_3$

$ClNaO_3$ **Mol. Wt.** 106.44 **CAS Registry No.** 7775-09-9

Synonyms chloric acid, sodium salt

EINECS No. 231-887-4 **RTECS No.** FO 0525000

Uses Oxidiser in dye manufacture. In explosives and matches. In dyeing and printing fabrics and tanning and finishing leather. Herbicide. Pharmaceutic aid.

Physical properties

M. Pt. 248°C **Specific gravity** 2.490 at 15°C
Solubility Water: 790 g l^{-1} at 0°C. Organic solvents: ethanol, glycerol

Occupational exposure

UN No. 1495

UN No. 2428 (solution) **HAZCHEM Code** 1YE **HAZCHEM Code** 2S (solution)
Conveyance classification oxidising substance
Supply classification oxidising, harmful
Risk phrases Explosive when mixed with combustible material – Harmful if swallowed (R9, R22)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Keep away from combustible material – If swallowed seek medical advice immediately and show this container or label (S2, S13, S17, S46)

Ecotoxicity

Invertebrate toxicity
EC_{50} (72 hr) *Nitzschia closterium, Dunaliella tertiolecta* under nitrate-limiting conditions (<0.005 mg l^{-1}) typically found in oligotrophic waters 1.9 and 11 mg l^{-1}, respectively. At high nitrate concentrations both algae were insensitive to chlorate with EC_{50} (72 hr) >500 and 1000 mg l^{-1}, respectively (1).
Not toxic to bees (2).

Environmental fate

Degradation studies
Remains in soil for 0.5-5 yr depending on water and organic matter content, fertility, soil type and weather conditions (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1200 mg kg^{-1} (3).
LD_{Lo} oral dog, cat, rabbit 700, 1350, 8000 mg kg^{-1}, respectively (4-6).
LD_{50} intraperitoneal mouse 596 mg kg^{-1} (7).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation and 10 mg instilled into rabbit eye (72 hr) caused mild irritation (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537, TA1538 with and without metabolic activation negative, TA1535 with metabolic activation positive, without metabolic activation negative (9).
Drosophila melanogaster Bax test increased the frequency of sex-linked recessive lethals (9).
In vivo mouse bone marrow micronucleus test negative (9).

Other effects

Other adverse effects (human)

A dose of 5-10 g can be fatal to adults, as can 2 g in small children (2).

Legislation

WHO Toxicity Class III (10).
EPA Toxicity Class III (formulation) (11).
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).

Other comments

Strong oxidising agent (2).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (14).
Decomposes at about 300°C, liberating oxygen.

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S54 sodium chlorite

$NaClO_2$

$ClNaO_2$ **Mol. Wt.** 90.44 **CAS Registry No.** 7758-19-2

Synonyms chlorous acid, sodium salt; Neo Silox D; Textone

EINECS No. 231-836-6 **RTECS No.** VZ 4800000

Uses In preparation of chlorine dioxide. Bleaching agent for textiles, paper pulp. In water purification.

Physical properties

M. Pt. 180-200°C (decomp.)
Solubility Water: 39 g 100 g^{-1} solution at 17°C

Occupational exposure

UN No. 1496 **HAZCHEM Code** 2X **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig, mouse 165, 300, 350 mg kg^{-1}, respectively (1,2).
LD_{50} oral ♂, ♀ rat 158, 177 mg kg^{-1}, respectively. Toxic signs included ataxia, hypnoea, anaemia, haematuria, cyanosis and respiratory paralysis, with congestion of the heart, lung, liver, kidney and gastric mucosa and oedema of the lung observed (3).

Teratogenicity and reproductive effects

♀ Long-Evans rats were administered 0-100 ppm orally for 14 days prior to breeding, during a 10-day breeding period and throughout gestation and lactation. Certain pups were dosed until day 40 post partum. No changes were seen in fertility, length of gestation, litter size and weight abnormalities of the reproductive tract, toxicity or body weight depression of F_0 animals, or post-weaning pup growth and vaginal potency. Significant but inconsistent changes were seen in the T3 and T4 levels in pups (4).

Irritancy

Rabbit dermal patch (dose unspecified) caused oedema of the cutis and subcutis immediately, after removal returned to normal within 24 hr. Instillation into rabbit eye (dose unspecified) caused redness in the conjunctiva and chemotic swelling for 3-8 days (3).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive, TA92, TA94, TA98, TA1535, TA1537 with and without metabolic activation negative (5).
In vitro Chinese hamster lung fibroblast cells without metabolic activation chromosomal aberrations positive (5).
In vivo mouse micronucleus test negative after oral administration, positive after intravenous administration (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (7).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology and workplace experience listed (9).

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S55 sodium chloroacetate

$$ClCH_2CO_2Na$$

$C_2H_2ClNaO_2$ **Mol. Wt.** 116.48 **CAS Registry No.** 3926-62-3

Synonyms chloroacetic acid, sodium salt; SMA; sodium monochloroacetate

EINECS No. 223-498-3 **RTECS No.** AG 1400000

Uses Herbicide.

Physical properties

M. Pt. 199°C (decomp.)

Solubility Water: 850 g l^{-1} at 20°C

Occupational exposure

UN No. 2659 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification toxic

Risk phrases Toxic if swallowed – Irritating to the skin (R25, R38)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S37, S45)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) rainbow trout 900 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig, rabbit, mouse 95, 99, 156, 318 mg kg^{-1}, respectively (2,3).

LD_{50} intravenous mouse 109 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Rats receiving 700 mg kg^{-1} in diet for several months (unspecified) were unaffected (1).

Irritancy

Irritating to rabbit eyes and skin (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} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

Other comments

Toxic to bees (1).
Reviews on human health effects, experimental toxicology, ecotoxicology and physico-chemical properties listed (7).

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S56 sodium chromate

$$Na_2CrO_4$$

$CrNa_2O_4$ **Mol. Wt.** 161.97 **CAS Registry No.** 7775-11-3

Synonyms chromic acid, sodium salt; chromium sodium oxide; disodium chromate; sodium chromate(VI); neutral sodium chromate

EINECS No. 231-889-5 **RTECS No.** GB 2955000

Uses Protection of iron against corrosion and rusting. Used in leather tanning, wood preservation, pigment manufacture and in production of chromium compounds. Used as mordant in dyeing operations.

Physical properties

M. Pt. 792°C **B. Pt.** decomp. **Specific gravity** 2.710-2.736
Solubility Water: 873 g l^{-1} at 30°C. Organic solvents: methanol

Occupational exposure

FR-VME 0.05 mg m^{-3} (as Cr)
JP-OEL 0.05 mg m^{-3} (as Cr)
SE-LEVL 0.02 mg m^{-3} (as Cr)
UK-LTEL MEL 0.05 mg m^{-3} (as Cr)
US-TWA 0.05 mg m^{-3} (as Cr)

Mammalian & avian toxicity

Acute data

LD_{Lo} dermal guinea pig 206 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse, rat 32, 57 mg kg^{-1}, respectively (2,3).

LD_{50} intravenous cat 164 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (hexavalent chromium compounds) (5).

3/50 guinea pigs exposed to mixed chromate dust, sodium chromate, potassium chromate and pulverised residue dust 4-5 hr day^{-1}, 4 days wk^{-1} for life developed pulmonary adenomas (6).

Genotoxicity

Escherichia coli WP2 reverse mutation trp^{-}/trp^{+} without metabolic activation positive (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}. Chromium: maximum admissible concentration 50 μg l^{-1} (8).

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

Chromium-51 (^{51}Cr) is used to label red blood cells to measure cell volume and survival. ^{51}Cr activity in the faeces can indicate gastro-intestinal blood losses (10).

Reviews on human health effects, experimental toxicology and environmental effects listed (11).

Human health effects and experimental toxicology discussed in a review of chromium and its compounds (12).

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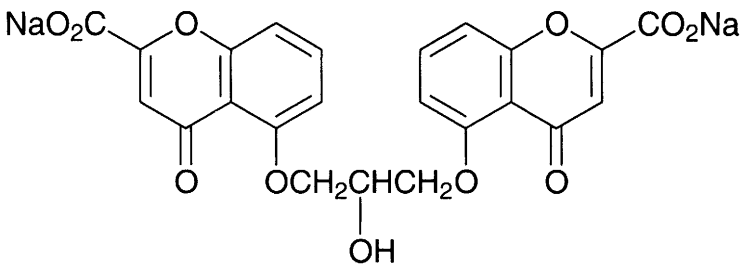
S57 sodium cromoglycate



$C_{23}H_{14}Na_2O_{11}$ **Mol. Wt.** 512.34 **CAS Registry No.** 15826-37-6

Synonyms 5,5′-[(2-hydroxy-1,3-propanediyl)bis(oxy)]bis[4-oxo-4*H*-1-benzopyran-2-carboxylic acid], disodium salt; Aarane; Cromoglycate; Cromolyn sodium; Intal; Lomudal; Nalcrom

EINECS No. 239-926-7 **RTECS No.** DJ 2380000

Uses Prophylactic anti-asthmatic. Anti-allergic.

Physical properties

M. Pt. 241-242°C (decomp.)
Solubility Water: 100 mg ml^{-1} at 20°C

Mammalian & avian toxicity

Acute data
LD_{50} subcutaneous mouse, rat 4400, 6000 mg kg^{-1}, respectively (1).
LD_{50} intraperitoneal mouse 4100 mg kg^{-1} (1).
LD_{50} intravenous rabbit, mouse 2000, 3300 mg kg^{-1}, respectively (1,2).

Other effects

Other adverse effects (human)
A woman with mild, stable, atopic eczema took 200 mg 4 × day^{-1} orally and developed intense pruritis and eczematous rash after 6 days. Withholding the drug resolved the rash, but it became generalised again within 1 wk of restarting treatment (3).

Any other adverse effects
Inhibited the immunological degranulation of rat peritoneal mast cells IC_{30} 4.7 μg ml^{-1} (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (5).

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S58 sodium cyanide

NaCN

CNNa **Mol. Wt.** 49.01 **CAS Registry No.** 143-33-9

Synonyms Cymag; cyanogran

EINECS No. 205-599-4 **RTECS No.** VZ 7525000

Uses In extracting gold and silver from ores. In electroplating baths. Fumigant. In cyanides and hydrocyanic acid manufacture. Case hardening of steel.

Physical properties

M. Pt. 563°C **B. Pt.** 1498°C **Volatility** v.p. 1 mmHg at 817°C
Solubility Water: freely soluble in water. Organic solvents: ethanol

Occupational exposure

DE-MAK 5 mg m^{-3} (as CN) (inhalable dust fraction)
FR-VME 5 mg m^{-3} (as HCN)
SE-CEIL 5 mg m^{-3} (as CN)
UK-LTEL 5 mg m^{-3} (as CN)
US-STEL ceiling limit 5 mg m^{-3} (as CN)

UN No. 1689 **HAZCHEM Code** 2X (solution) **HAZCHEM Code** 4X (solid)
Conveyance classification toxic substance
Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Contact with acids liberates very toxic gas (R26/27/28, R32)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed – After contact with skin, wash immediately with plenty of water – Do not empty into drains – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7, S28, S29, S45)

Ecotoxicity

Invertebrate toxicity
EC_{50} (15 min) *Photobacterium phosphoreum* 2.82 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 6440 μg kg^{-1} (2).
LD_{Lo} oral human 2857 μg kg^{-1} (3).
LD_{50} intraperitoneal rat, mouse 4300, 5881 μg kg^{-1}, respectively (4,5).
LD_{50} subcutaneous mouse 3660 μg kg^{-1} (6).
LD_{50} ocular rabbit 5048 μg kg^{-1} (7).

Sub-acute and sub-chronic data
Short term toxicity studies of oral administration with water to rats and mice scheduled for peer review (8).

Teratogenicity and reproductive effects
Caused degeneration of nerve tissue of chick embryo otocyst *in vitro* (9).
Golden hamsters were infused with 6.18, 6.25, 6.35 mg kg^{-1} hr^{-1} from subcutaneously implanted osmotic minipumps from day 6-9 of gestation. High incidences of malformations and resorptions in the offspring were

observed. Frequent anomalies were neural tube defects, including exencephaly and encephalocoele, with hydropericardium and crooked tail also occurring. Foetal crown-rump length was also decreased compared with controls (10).

Metabolism and toxicokinetics

Rapidly absorbed from the respiratory and gastro-intestinal tracts and through the skin (9).

Irritancy

Caused severe irritation to eyes and skin (species unspecified) (9).

Workers chronically exposed to over 5 mg m^{-3} in the electroplating industry reported nasal irritation, obstruction, bleeding and perforation of the septum in some cases (9).

Sensitisation

1.7 mg kg^{-1} caused allergic dermatitis in rabbits. Skin sensitisation has been reported in gold recovery workers (9).

Genotoxicity

In vitro mouse lymphoma L5178Y tk^+/tk^- with and without metabolic activation negative, DNA strand alkaline unwinding with and without metabolic activation negative (11).

Other effects

Other adverse effects (human)

Cyanide toxicity involves inhibition of respiratory enzymes, hence acute exposure can result in death by asphyxiation. Blood of acutely poisoned victims is a characteristic cherry red colour (9).

Effects of acute poisoning include weakness, headache, dizziness, nausea, anxiety, rapid breathing, convulsions, coma, and in some cases death (9).

Chronic exposure may lead to thyroid diseases (12).

Any other adverse effects

Intravenous infusion to monkeys (dose and duration unspecified) caused tetany, apnoea, and death due to heart failure; brain damage was observed following autopsy (13).

Cats administered 2-2.2 mg kg^{-1} (route unspecified) suffered depression of cerebral tissue respiration and death (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Cyanides: maximum admissible concentration 50 µg l^{-1}. Sodium: guide level 20 mg l^{-1} (15).

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).

Other comments

Reviews on human health effects, experimental toxicology, workplace experience and environmental effects listed (17).

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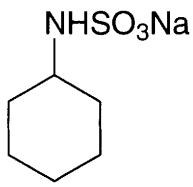
S59 sodium cyclamate



$C_6H_{12}NNaO_3S$ **Mol. Wt.** 201.22 **CAS Registry No.** 139-05-9

Synonyms cyclamate sodium; sodium cyclohexylsulfamate; Assugrin; Sucaryl Sodium; Sucrosa

EINECS No. 205-348-9 **RTECS No.** GV 7350000

Uses Non-nutritive sweetener, about 30 × as sweet as refined cane sugar.

Physical properties

M. Pt. >300°C

Solubility Water: soluble in water. Organic solvents: practically insoluble in benzene, chloroform, ethyl alcohol, ether

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 10-12 g kg^{-1} (1).

LD_{50} oral ♂ and ♀ hamster 9.8, 12.2 g kg^{-1}, respectively (2).

LD_{50} intravenous rat, mouse 3.5, 4 g kg^{-1}, respectively (1)

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (3).

Repeated subcutaneous injections of sodium cyclamate did not elicit sarcomas in rats (4).

A two-generation study of Sprague-Dawley rats receiving a 2% or 5% mixture of sodium cyclamate and sodium saccharin in their feed for life did not result in any carcinogenic effects (5).

A six-generation study with Swiss mice receiving 2% or 5% sodium cyclamate found no evidence of toxic or carcinogenic effects (6).

Teratogenicity and reproductive effects

2.5 g kg^{-1} body weight sodium cyclamate in diet for 28 months caused degeneration and loss of seminiferous epithelium of the testis of ♂ rats (7).

Swiss white mice receiving 2 or 5% sodium cyclamate in the diet over several generations showed no pathological effects and reproductive capacity and perinatal development were unimpaired (6).
More mothers of mentally retarded children had used artificial sweeteners before and during pregnancy than had controls. However, IARC recommend that further epidemiological data are needed before it can be concluded that the use of artificial sweeteners in pregnancy is associated with foetal damage (8).

Metabolism and toxicokinetics

Rats fed cyclamate in their food were found to convert cyclamate into cyclohexylamine (9).
Cyclamate is not metabolised by the liver, spleen or kidney tissue or blood of rats or rabbits. However, cyclamate is converted into cyclohexylamine when incubated anaerobically with the contents of caecum, colon or rectum or with faeces from cyclamate-pretreated rats or rabbits. *Clostridia* in rats and *Enterobacteria* in rabbits converted cyclamate into cyclohexylamine (10).
In several human subjects up to 0.7% of an ingested dose of cyclamate was converted into cyclohexylamine, cyclohexanol, cyclohexanone and conjugated cyclohexanol, which were excreted in the urine (11).

Genotoxicity

Sodium cyclamate is clastogenic but shows no mutagenic activity (12).

Other effects

Other adverse effects (human)

Taking 10 or 18 g day^{-1} sodium cyclamate resulted in 7/8 men developing severe, persistent diarrhoea, but continuous oral administration of 2-5 g day^{-1} for 3 years to patients with liver or kidney disease did not produce obvious adverse clinical effects (13).

Any other adverse effects

Sodium cyclamate has a laxative action in dogs, rats and mice; 1.5 g kg^{-1} body weight in the diet day^{-1} caused diarrhoea in dogs, 5% in the diet caused diarrhoea in rats (14-16).

Legislation

The use of cyclamates as artificial sweeteners in food, soft drinks and sweetening tablets is no longer permitted in Great Britain because of fears over their metabolite cyclohexylamine. The US ban on cyclamates has been reappraised since doubt exists over their carcinogenicity (17).

Other comments

Acceptable daily intake 0-11 mg kg^{-1} body weight (expressed as cyclamic acid) (18).

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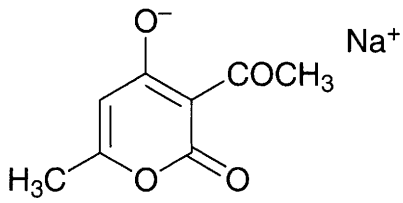
S60 sodium dehydroacetate



$C_8H_7NaO_4$ **Mol. Wt.** 190.13 **CAS Registry No.** 4418-26-2

Synonyms dehydroacetic acid, sodium salt

EINECS No. 224-580-1 **RTECS No.** UP 8225000

Uses Fungicide. Plasticiser. Toothpaste. Pharmaceuticals. Food preservative. Mould inhibitor for strawberries and similar fruits.

Physical properties

Solubility Water: 33% at 25°C. Organic solvents: glycerol, methanol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 500 mg kg^{-1} (1).
LD_{50} oral mouse 1175 mg kg^{-1} (1).
LD_{50} subcutaneous rat 1850 mg kg^{-1} (2).

Irritancy

100 mg instilled into rabbit eye produced mild irritation (3).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative. Chinese hamster chromosomal aberration test showed 23% aberrations in 48 hr with negative polyploidy (4).
Induced micronuclei in mouse bone marrow cells (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

Not recommended as a food preservative because its effective concentration in food may be high enough to be toxic (8).

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S61 sodium dichromate

$Na_2Cr_2O_7$

$Cr_2Na_2O_7$ **Mol. Wt.** 261.97 **CAS Registry No.** 10588-01-9

Synonyms chromic acid ($H_2Cr_2O_7$), disodium salt; chromium sodium oxide; disodium dichromate; dichromic acid ($H_2Cr_2O_7$), disodium salt

EINECS No. 234-190-3 **RTECS No.** HX 7700000

Uses Oxidising agent. Bleach. In manufacture of chromic acid, chromates, corrosion inhibitors, metal treatments. In chrome-tanning of hides. In electric batteries. Defoliant for cotton plants. Topical anti-infective.

Physical properties

M. Pt. 356.7°C (anhydrous) **B. Pt.** 400°C (decomp.) **Specific gravity** 2.348 at 25°C with respect to water at 4°C
Solubility Water: 70.6% at 0°C. Organic solvents: methanol

Occupational exposure

FR-VME 0.05 mg m^{-3} (as Cr)
JP-OEL 0.05 mg m^{-3} (as Cr)
SE-LEVL 0.02 mg m^{-3} (as Cr)
UK-LTEL MEL 0.05 mg m^{-3} (as Cr)
US-TWA 0.05 mg m^{-3} (as Cr)

Supply classification oxidising
Supply classification very toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer by inhalation – May cause heritable genetic damage – Contact with combustible material may cause fire – Harmful in contact with skin – Toxic if swallowed – Very toxic by inhalation – Irritating to respiratory system and skin – Risk of serious damage to eyes – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R49, R46, R8, R21, R25, R26, R37/38, R41, R43, 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 (S53, S45, S60, S61)

Ecotoxicity

Toxicity to other species

LC_{50} (96 hr) *Rana cyanophlyctis* 15 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 50 mg kg^{-1} (2).
LD_{Lo} dermal guinea pig 335 mg kg^{-1} (3).
LD_{Lo} intraperitoneal guinea pig 335 mg kg^{-1} (3).
LD_{Lo} subcutaneous guinea pig, rat 23, 80 mg kg^{-1}, respectively (4,5).
LD_{Lo} intravenous rabbit, mouse 18,400, 26,200 μg kg^{-1}, respectively (6).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (hexavalent chromium compounds) (7).
No tumours were seen at the injection site in Bethesda Black rats given 2 mg in gelatin intramuscularly $month^{-1}$ for 16 month and observed for 2 yr (8).
0/33 rats receiving intramuscular implantations (dose unspecified) had implantation site tumours after 27 months (9).
0/26 rats had tumours at the site of intrapleural implantation after 27 months (dose and tumour type unspecified) (9).
100 μg m^{-3} induced primary tumours in rat respiratory tracts (10).

Teratogenicity and reproductive effects

♂, ♀ rabbits exposed to 0.2-5 mg kg^{-1} for 545 days had morphological changes in the gonads (11).
Exposure of three generations of rats to sodium dichromate aerosols (0.2 mg Cr m^{-3}) for 130 days $generation^{-1}$ had no effect on reproduction and was not teratogenic (12).
No teratogenic effects reported in humans (12).

Metabolism and toxicokinetics

In humans hexavalent chromium is effectively transported through the cell membrane as chromate ion (13).
Chromates(VI) are absorbed from the gastro-intestinal tract at a rate of 2%. 50% of the radioactivity of intraduodenally administered ^{51}Cr(VI) was absorbed and 10% excreted in urine within 24 hr (14).

Irritancy

Irritating to the skin in humans and may lead to ulcers in contact with broken skin. Dermatitis and eczema may also occur (15-17).

Genotoxicity

Salmonella typhimurium his⁻/his⁺ without metabolic activation reverse mutation positive (strain unspecified). Mutagenicity was decreased by addition of metabolic activation or preincubation with human gastric juice (18,19).
Drosophila melanogaster induced somatic mutations in an eye colour test system (somatic UZ test) (dihydrate) (20).
In vitro Chinese hamster ovary cells sister chromatid exchanges positive (metabolic activation unspecified) (21).
In vitro human T-cells were cultured with sodium dichromate which depressed T-cell proliferation at 2.64 g l^{-1} and decreased interleukin 2 production at 2.64 μg l^{-1} (22).

Other effects

Other adverse effects (human)

14/133 workers at a Japanese chromate factory exposed to chromate compounds, including sodium dichromate, reported lung cancer including 10 carcinomas and 4 unspecified cancers (23,24).

Three bronchial carcinomas and one gastro-intestinal cancer were reported among 24 workers at a chromium pigment factory exposed to chromate compounds, including sodium dichromate, for >3 yr (25).
Acute toxic effects include vomiting, diarrhoea, and cardiovascular shock due to blood loss into the gastro-intestinal tract. Necrosis of the liver and kidneys has also been reported (12,26).

Any other adverse effects

20, 40 mg kg^{-1} injected intraperitoneally to rats caused increases in serum lactate, pyruvate, and creatinine concentrations within 15 min. Severe hyperglycaemia, decreased serum total amino acids and cyanosis also occurred (dihydrate) (27).
Application to the conjunctival sacs of rabbits caused morphological changes in the liver and kidneys (28).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chromium: maximum admissible concentration 50 $\mu g\ l^{-1}$. Sodium: guide level 20 mg l^{-1} (29).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (30).

Other comments

Reviews on human health effects, physico-chemical properties, experimental toxicology, ecotoxicology and environmental effects listed (31).
Human health effects and experimental toxicology discussed in a review of chromium and its compounds (32).

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32. *IARC Monograph* 1990, **49**

S62 sodium dichromate dihydrate

$$Na_2Cr_2O_7 \cdot 2H_2O$$

$Cr_2H_4Na_2O_9$ **Mol. Wt.** 298.00 **CAS Registry No.** 7789-12-0

Synonyms chromic acid ($H_2Cr_2O_7$), disodium salt, dihydrate; disodium dichromate dihydrate

RTECS No. HX 7750000

Physical properties

M. Pt. 356.7°C (anhydrous) **B. Pt.** 400°C (decomp.) **Specific gravity** 2.35 at 13°C

Occupational exposure

SE-LEVL 0.02 mg m^{-3} (as Cr)
UK-LTEL MEL 0.05 mg m^{-3} (as Cr)
US-TWA 0.05 mg m^{-3} (as Cr)

UN No. 1479
Supply classification very toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer by inhalation – May cause heritable genetic damage – Harmful in contact with skin – Toxic if swallowed – Very toxic by inhalation – Irritating to respiratory system and skin – Risk of serious damage to eyes – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R49, R46, R21, R25, R26, R37/38, R41, R43, 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 (S53, S45, S60, S61)

Genotoxicity

Drosophila melanogaster induced somatic mutations in an eye colour test system (somatic UZ test) (1).

Other effects

Any other adverse effects
20, 40 mg kg^{-1} injected intraperitoneally to rats caused increases in serum lacatate, pyruvate, and creatinine concentrations within 15 min. Severe hyperglycaemia, decreased serum total amino acids and cyanosis also occurred (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}. Chromium: maximum admissible concentration 50 μg l^{-1} (3).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

Reviews on human health effects, experimental toxicity and environmental effects listed (5).

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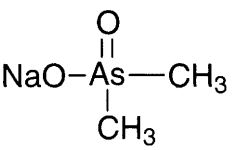
S63 sodium dimethylarsinate



$C_2H_6AsNaO_2$ **Mol. Wt.** 159.98 **CAS Registry No.** 124-65-2

Synonyms sodium cacodylate; arsinic acid, dimethyl-, sodium salt; arsine oxide hydroxydimethyl-, sodium salt; Alkarsodyl; Arsecodile; cacodylic acid sodium salt; Chemaid; sodium dimethylarsonate

EINECS No. 204-708-2 **RTECS No.** CH 7700000

Uses Herbicide. Used in veterinary treatment of eczema and anaemia.

Physical properties

B. Pt. 200°C

Solubility Water: 2 g ml^{-1} at 15-20°C. Organic solvents: ethanol

Occupational exposure

UK-LTEL MEL 0.1 mg m^{-3} (as As)

UN No. 1688 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Environmental fate

Degradation studies

Inactivated in contact with soil (1).

Adsorption and retention

Adsorbed by clay soils (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 4000, 2600 mg kg^{-1}, respectively (3,4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals (arsenic and arsenic compounds) IARC classification group 1 (no specific information given) (5,6).

Irritancy
Non-irritating to rabbit skin and eyes (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 $\mu g\ l^{-1}$. 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).

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S64 sodium dimethyldithiocarbamate

$$(CH_3)_2NCS_2Na$$

$C_3H_6NNaS_2$ **Mol. Wt.** 143.21 **CAS Registry No.** 128-04-1

Synonyms *N,N*-dimethyldithiocarbamic acid, sodium salt; dimethylcarbamodithioic acid, sodium salt; Aceto SDD 40; Alcobam NM; DDC; methyl namate; Na DMDC; MSL; Noeceler S; sodium dimethylaminocarbodithioate

EINECS No. 204-876-7 **RTECS No.** FD 3500000

Uses Disinfectant. Corrosion inhibitor. Coagulant. Vulcanising agent. Chelating agent. Fungicide.

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 2.6 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 0.67 mg l^{-1} (1).
EC_{50} (96 hr) *Chlorella pyrenoidosa* 0.8 mg l^{-1} (1).
EC_{50} (15 min) *Photobacterium phosphoreum* 0.508 ppm, Microtox test (2).

Environmental fate

Nitrification inhibition
75% inhibition of ammonia oxidation by activated sludge at 13.6 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1000, 1500 mg kg^{-1}, respectively (4,5).
LD_{50} intraperitoneal mouse, rat 570, 1000 mg kg^{-1}, respectively (6,7).

Teratogenicity and reproductive effects

Chick embryo, 0.01, 0.10, 1.0 or 10.0 mg egg^{-1} caused paralysis, shortening of the extremities, muscular atrophy, dwarfing and fatality (8).

Metabolism and toxicokinetics

In mammals the major metabolite is the glucuronide which is excreted in the urine and faeces. Other metabolites include carbon disulfide and methyldiethyldithiocarbamate (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538, with and without metabolic activation positive (10).
Escherichia coli WP2 *hcr* with and without metabolic activation positive (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

Other comments

Use, environmental fate, metabolism and mammalian toxicity of dithiocarbamate pesticides reviewed (9).
Photodegradation product of tetramethylthioram disulfide (13).

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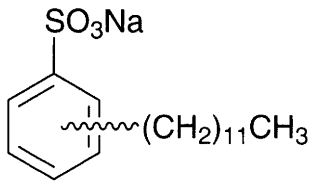
S65 sodium dodecylbenzenesulfonate



$C_{18}H_{29}NaO_3S$ **Mol. Wt.** 348.48 **CAS Registry No.** 25155-30-0

Synonyms benzenesulfonic acid, dodecyl-, sodium salt; Marlon A; Nansa HS80; Neopelex 05; Suponate DS4; sodium laurylbenzenesulfonate; Sulframin 85; Ultrawet 99LS

EINECS No. 246-680-4 **RTECS No.** DB 6825000

Uses Surfactant. Levelling agent for acid dyes or nylon. Wetting agent and detergent for preparations and dyeing assistant for cellulosic fibres.

Physical properties

Specific gravity 1.0 at 20°C (60% slurry) **Partition coefficient** log P_{ow} 0.45

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) catfish 6.97-7.16 mg l^{-1} (calculated), dissolved oxygen content 6.5-8.4 ppm, pH 7.1 ± 0.2, hardness 18 mg l^{-1} at 21 ± 1.8°C (1).

Five crucian carp exposed to 7 mg l^{-1} (total hardness 20-25 ppm $CaCO_3$, pH 6.8-7.2, dissolved oxygen concentration ≥8 ppm, 22-25°C) all died after 5 hr. Examination of the gills showed an increase in the oleic acid content of total fatty acids and decrease in polyunsaturated fatty acids of neutral lipids and lipid complexes. Histopathological examination showed an acute inflammatory reaction in the exposed fish gill (2).

Invertebrate toxicity

EC_{50} *Selenastrum capricornutum* >100-<1000 mg l^{-1} (3).

LC_{50} (48 hr) *Daphnia pulex* 19.87 ppm (4).

LC_{50} (48 hr) *Ceriodaphnia dubia/affinis* 19.87 ppm (4).

Environmental fate

Anaerobic effects

Incubation with diluted anaerobic digesting sludge at 35°C for >60 days inhibited production of methane and carbon dioxide (5).

Degradation studies

Klebsiella sp. identified as showing an excellent sodium dodecylbenzenesulfonate-degrading ability, using it as a sole carbon source (6).

Abiotic removal

Degraded in model wastewater treated with a 500W UV-light lamp (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1260, 2000 mg kg^{-1}, respectively (8,9).

LD_{50} intravenous mouse 105 mg kg^{-1} (9).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation and 250 μg instilled into rabbit eye (24 hr) caused severe irritation (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Surfactants: maximum admissible concentration 200 μg l^{-1}. Sodium: guide level 20 mg l^{-1} (11).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

Other comments

Reviews on human health effects and experimental toxicology listed (13).

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S66 sodium fluoride

NaF

FNa **Mol. Wt.** 41.99 **CAS Registry No.** 7681-49-4

Synonyms sodium monofluoride; Checkmate; Fluoral; Fluorinse; Gell II; Pediaflor

EINECS No. 231-667-8 **RTECS No.** WB 0350000

Uses Insecticide. In vitreous enamel and glass mixes. Steel degassing agent. Electroplating. In fluxes. Fluoridation of drinking water. Wood preservative. Cleaner for fermentation equipment. Dental caries prophylactic. Veterinary anthelmintic, pediculicide, acaricide.

Physical properties

M. Pt. 993°C **B. Pt.** 1700°C **Specific gravity** 2.78 **Volatility** v.p. 1 mmHg at 1077°C
Solubility Water: 43 g l^{-1} at 25°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (inhalable dust fraction)
FR-VME 2.5 mg m^{-3} (as F)

SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)
US-TWA 2.5 mg m^{-3} (as F)

UN No. 1690 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic if swallowed – Contact with acids liberates very toxic gas – Irritating to eyes and skin (R25, R32, R36/38)
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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S36, S45)

Ecotoxicity

Invertebrate toxicity
LC_{50} (96 hr) *Scenedesmus* 43 mg l^{-1} (1).
LC_{50} (48 hr) *Daphnia magna* 340 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit 52, 57, 200 mg kg^{-1}, respectively (3,4,5).
LD_{Lo} dermal mouse 300 mg kg^{-1} (6).
LD_{50} subcutaneous mouse, rat 70, 175 mg kg^{-1}, respectively (7).
LD_{50} intravenous monkey, mouse 26, 50 mg kg^{-1}, respectively (8).
LD_{Lo} intraperitoneal dog, rabbit 50, 250 mg kg^{-1}, respectively (9,10).

Sub-acute and sub-chronic data
Rabbits and rats exposed to 20 or 70 mg kg^{-1} day^{-1} for 5 days had reduced levels of haemoglobin and red blood cells, raised levels of calcium in serum and elevated urine, bone and tooth fluorine concentrations (11).
Rats exposed to 0.03 and 0.1 mg m^{-3} for 5 months had changes in the central nervous system, a cumulative effect in bone and histological changes in the cortex, lungs and liver (12).
Rats fed 10 or 20 mg kg^{-1} day^{-1} for 2-4 months had spongy and paitic cortical bone (13).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (inorganic fluorides) (14).
♂, ♀ weanling Swiss CD1 mice were given 70 μg day^{-1} in drinking water for life. Examination of dead animals showed increased body weight of ♀ and tumours in 22/72 (sex unspecified) compared with 24/71 controls (15).
C3H and DBA ♀ mice aged 4-12 months were given 0.4, 1.0 or 4.0 mg l^{-1} in drinking water for 7-12 months and 20-38 mg kg^{-1} F in diet. Other C3H and DBA mice aged 2-9 months received 1.0 or 10.0 mg l^{-1} in distilled water for 10-17 months. 59% of all experimental deaths were due to mammary gland carcinomas compared with 54% in controls. At 10 mg l^{-1} 63% died of mammary gland carincomas compared with 50% in controls (16).
50 ♀ DBA mice, aged 7-10 wk, fed 900 mg kg^{-1} in diet until aged 97-100 wk, suffered drastic reductions in body weight and 20/40 had mammary gland carcinomas compared with 37/47 controls (17).
Rats fed 4, 10, 25 mg kg^{-1} day^{-1} in diet for 99 wk showed 25% decreased weight gain at 25 mg kg^{-1}, but no increased incidence in preneoplastic or neoplastic lesions compared with controls (18).
The National Toxicology Program studied F344/N rats and $B6C3F_1$ mice given 0, 25, 100, 175 ppm in drinking water for 2 yr. No evidence of carcinogenicity was seen in ♂, ♀ mice or ♀ rats. Equivocal evidence was observed for carcinogenic activity in ♂ rats due to a small number of osteosarcomas in treated animals (19).

Teratogenicity and reproductive effects
Oral administration to pregnant rats resulted in increased rates of foetal resorption, congenital deformities and runt foetuses (20).
Mice fed 500 or 1000 ppm in drinking water had necrosis of the seminiferous tubules (21).
Sprague-Dawley rats were injected in one testis with 50, 175 or 250 ppm of sodium fluoride in saline, and tissues

were examined microscopically 24 hr, 1, 2 and 3 wk after injection. The samples obtained at and distal to the injection site resembled those collected from non-injected controls and testes injected with the vehicle only. Leucocyte infiltration with seminiferous tubule damage was not considered to be treatment related. Spermatogenesis in the rat was not adversely affected by direct, short-term exposure to fluoride at these doses (22).
Reduced urinary testosterone has been reported in workers with chronic fluoride poisoning (23).

Metabolism and toxicokinetics
Rapidly absorbed from the human gut (24).
Fluoride is transported in the blood, distributed throughout soft tissues and excreted mainly via the kidneys. It accumulates in human bones and teeth (24-29).

Irritancy
20 mg instilled into rabbit eye (24 hr) caused moderate irritation (30).
Inhalation of dust may cause respiratory irritation (species unspecified) (31).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (32).
Drosophila melanogaster did not induce sex-linked recessive lethals (33).
In vivo mouse bone marrow cells chromosomal aberrations, sister chromatid exchanges negative (34,35).
In vitro human lymphocyte cells chromosomal aberrations positive (35).

Other effects

Other adverse effects (human)
Ingestion may result in nausea, vomiting, diarrhoea, abdominal pain, muscular weakness, shock, convulsions, spasms, dyspnoea, and may be fatal due to respiratory and cardiac failure (31).
May cause severe corrosive gastroenteritis with gastric haemorrhages. Gastro-intestinal chemical burns, venous plethora, and brain oedema have been reported following acute poisoning (36).

Any other adverse effects
Symptoms of acute intoxication in various laboratory animals included adynamia, weakness, spasms, haemorrhage, respiratory system damage, and damage to liver, kidneys and spleen (37-41).

Legislation

WHO Toxicity Class II (42).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (43).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluorides: maximum admissible concentration 1500 $\mu g\ l^{-1}$ at 8-12°C. Sodium: guide level 20 $mg\ l^{-1}$ (44).

Other comments

Studies on water fluoridation and cancer reviewed (8).
Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicology, exposure levels, and physico-chemical properties listed (45).

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S67 sodium fluoroacetate

FCH_2CO_2Na

$C_2H_2FNaO_2$ **Mol. Wt.** 100.02 **CAS Registry No.** 62-74-8

Synonyms sodium monofluoroacetate

EINECS No. 200-548-2 **RTECS No.** AH 9100000

Uses In baits for rodent control. Used in Australia to control wild rabbits, wild dogs and wild pigs.

Physical properties

M. Pt. 200°C (decomp.)

Occupational exposure

DE-MAK 0.05 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.05 mg m^{-3}
UK-LTEL 0.05 mg m^{-3} **UK-STEL** 0.15 mg m^{-3}
US-TWA 0.05 mg m^{-3}

UN No. 2629 **HAZCHEM Code** 2X **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 away from food, drink and animal feeding stuffs – 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, S13, S22, S36/37, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral starling, redwing blackbird 2.37, 4.22 mg kg^{-1}, respectively (1).
LD_{50} oral dog, rat, mouse 66, 100, 500 µg kg^{-1}, respectively (2,3,4).
LD_{Lo} oral human 714 µg kg^{-1} (5).
LD_{50} intraperitoneal mouse 7 mg kg^{-1} (6).
LD_{50} intravenous dog, monkey 0.06, 5 mg kg^{-1}, respectively (3,7).

Teratogenicity and reproductive effects

♂ Sprague-Dawley rats received 2.2, 6.6 or 20 ppm in drinking water for up to 21 days. Elevated citrate levels, morphological damage, altered appearance and decreased numbers of spermatids and formation of spermatid and spermatocyte giant cells were observed at all doses. At 6.6 and 20 ppm, testicular weight and ATP concentrations decreased and damage progressed to marked seminiferous tubule atrophy. Recovery was complete 7 days after treatment at 2.2 ppm but not after 21 days for higher doses (8).

Metabolism and toxicokinetics

^{19}F NMR indicated defluorination to give fluoride ion in urine after intraperitoneal administration to rats and mice (9).
Urinary metabolites detected using [2-^{13}C]- and [1,2-^{14}C]fluoroacetate included an *S*-(carboxymethyl) conjugate complex in rats and mice and also sulfoxidation products in rats (9).
^{13}C-NMR examination of the bile after treatment with [2-^{13}C]fluoroacetate showed *S*-(carboxymethyl)glutathione and an *O*-conjugate of fluoroacetate (9).

Other effects

Other adverse effects (human)

Lethal dose to man by ingestion 2-10 mg kg^{-1} body weight. Toxic effects include nausea, vomiting, apprehension, muscle twitching, cardiac irregularities, convulsions, respiratory failure, coma and death and may be delayed for several hours after absorption by mouth or inhalation (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}. Fluorides: maximum admissible concentration 1500 µg l^{-1} at 8-12°C. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (11).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).
WHO Toxicity Class Ia (13).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, workplace experience and epidemiology listed (14).
Inhibitor of tricarboxylic acid cycle.

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S68 sodium fluorosilicate

$$Na_2SiF_6$$

F_6Na_2Si **Mol. Wt.** 188.06 **CAS Registry No.** 16893-85-9

Synonyms silicate(2–), hexafluoro-, disodium; disodium hexafluorosilicate; Prodan; silicon sodium fluoride; sodium silicon fluoride

EINECS No. 240-934-8 **RTECS No.** VV 8410000

Uses In china and porcelain enamels. In opal glass manufacture. Insect exterminator and rodent poison. Moth proofing agent. Pediculicide. Drinking water additive.

Physical properties

M. Pt. decomp. **Specific gravity** 2.68
Solubility Water: 6.5 g l^{-1} at 17.5°C. Organic solvents: ethanol

Occupational exposure

SE-LEVL 2 mg m^{-3} (as F)

UN No. 2674 **HAZCHEM Code** 1Z **Conveyance classification** toxic substance
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) – 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, S26, S45)

Ecotoxicity

Invertebrate toxicity

Toxic to microflora at biological wastewater treatment plants (1).

Toxicity to other species

LD_{Lo} subcutaneous frog 448 mg kg^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 125 mg kg^{-1} (3).
LD_{Lo} oral rabbit 125 mg kg^{-1} (4).
LD_{Lo} subcutaneous rat 70 mg kg^{-1} (4).
TD_{Lo} intragastric rat 8 mg kg^{-1} (5).
TC_{Lo} (4 hr) inhalation rat (salt aerosols) 7.4-9.6 mg m^{-3} (5).
Main toxic effects in rat were decreased red blood cell numbers, and decreased activities of cholinesterase and lactate dehydrogenase in blood serum (5).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (inorganic fluorides) (6).

Metabolism and toxicokinetics

Rapidly and extensively absorbed from the human gut (7).

Irritancy

Dermal rabbit (72 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye (72 hr) caused severe irritation (8).
50 mg instilled into rabbit eye caused severe corneal damage after 3 hr (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}. Fluorides: maximum admissible concentration 1500 mg l^{-1} at 8-12°C (9).
Included in Schedules 4 and 6 (Release into the Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

Adverse effects of inorganic fluorides extensively reviewed (11).
Toxic effects similar to sodium fluoride (5).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

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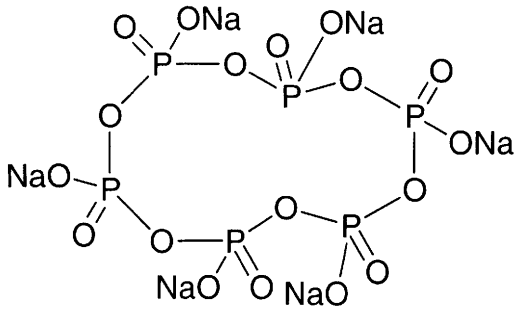
S69 sodium hexametaphosphate



$Na_6O_{18}P_6$ **Mol. Wt.** 611.77 **CAS Registry No.** 10124-56-8

Synonyms metaphosphoric acid ($H_6P_6O_{18}$) hexasodium salt; Calgon; Giltex; hexasodium hexametaphosphate; Micromet; sodium phosphate ($Na_6P_6O_{18}$)

EINECS No. 233-343-1 **RTECS No.** OY 3675000

Physical properties

M. Pt. 883.15°C

Solubility Water: very soluble in cold water

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 7250 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 870 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 1300 mg kg^{-1} (1).

LD_{50} intravenous mouse 62 mg kg^{-1} (1).

LD_{Lo} intravenous rabbit 140 mg kg^{-1} (3).

Teratogenicity and reproductive effects

Oral mouse, rat, hamster, rabbit ~30-110 mg P kg^{-1} day^{-1} on days 6-16, 6-15, 6-10 or 6-18 of gestation, respectively, caused no teratogenic or adverse effects (4).

Irritancy

No serious damage was caused to rabbit eye in transient contact with 0.1 and 5% solutions (5).

Other effects

Any other adverse effects

Repeated patch tests and prolonged soaking of the skin in solutions of up to 25% sodium hexametaphosphate showed no evidence of injurious effects (species unspecified) (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (6).

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

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S70 sodium hydride

NaH

HNa **Mol. Wt.** 24.00 **CAS Registry No.** 7646-69-7

Synonyms sodium monohydride

EINECS No. 231-587-3 **RTECS No.** WB 3910000

Uses In condensation of ketones and aldehydes with acid esters at low temperatures. To reduce oxide scale on metals in solution with molten sodium hydroxide. Reducing agent and reduction catalyst at high temperatures.

Physical properties

M. Pt. 425°C (decomp.) **Specific gravity** 1.396
Solubility Water: reacts explosively with water

Occupational exposure

UN No. 1427 **Conveyance classification** substance which in contact with water emits flammable gas
Supply classification highly flammable
Risk phrases Contact with water liberates extremely flammable gases (R15)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container tightly closed and dry – Avoid contact with skin and eyes – In case of fire, use graphite, soda ash or suitable dry powder – do not use water, carbon dioxide or halogenated extinguishers (S2, S7/8, S24/25, S43)

Mammalian & avian toxicity

Irritancy
Destructive to tissue of respiratory tract, eyes and skin (species unspecified) (1).

Other effects

Other adverse effects (human)
Inhalation may cause coughing, a burning feeling, sore throat, dyspnoea, headache, nausea and vomiting (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (2).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

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S71 sodium hydrogen fluoride

$NaHF_2$

F_2HNa **Mol. Wt.** 61.99 **CAS Registry No.** 1333-83-1

Synonyms sodium hydrogen difluoride; sodium bifluoride

EINECS No. 215-608-3 **RTECS No.** WB 0350010

Uses As a "sour" in laundering.

Physical properties

Specific gravity 2.08 at 25°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
FR-VME 2.5 mg m^{-3} (as F)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)
US-TWA 2.5 mg m^{-3} (as F)

UN No. 2439 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification toxic, corrosive
Risk phrases Toxic if swallowed – Causes burns (R25, R34)
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 gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S26, S37, S45)

Mammalian & avian toxicity

Irritancy
Irritating and may cause burns to eyes and skin. Dust is irritating to the respiratory tract (species unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (2).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

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3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

S72 sodium hydrosulfide

NaSH

HNaS **Mol. Wt.** 56.06 **CAS Registry No.** 16721-80-5

Synonyms sodium bisulfide; sodium hydrogen sulfide; sodium sulfhydrate; hydrogen sodium sulfide; sodium mercaptan

EINECS No. 240-778-0 **RTECS No.** WE 1900000

Physical properties

M. Pt. 350°C **Specific gravity** 1.79

Solubility Water: soluble in water. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2318 (<25% water of cystallisation)

UN No. 2949 (≥25% water of crystallisation) **HAZCHEM Code** 2X **Conveyance classification** spontaneously combustible substance (<25% water of crystallisation) **Conveyance classification** corrosive substance (≥25% water of crystallisation)

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse, rat 18, 30 mg kg^{-1}, respectively (1,2).

LD_{50} subcutaneous mouse 200 mg kg^{-1} (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (4).

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S73 sodium hydroxide

NaOH

HNaO **Mol. Wt.** 40.00 **CAS Registry No.** 1310-73-2

Synonyms caustic soda; soda lye; sodium hydrate

EINECS No. 215-185-5 **RTECS No.** WB 4900000

Uses In manufacture of sodium salts, plastics, soaps, viscose rayon and cellophane. In reclaiming rubber. Pharmaceutic aid.

Physical properties

M. Pt. 318°C **B. Pt.** 1390°C **Specific gravity** 1.12 at 20°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 739°C
Solubility Water: 1 g 0.9 ml^{-1}. Organic solvents: ethanol, glycerol

Occupational exposure

FR-VME 2 mg m^{-3}
JP-OEL ceiling limit 2 mg m^{-3}
SE-CEIL 2 mg m^{-3}
UK-STEL 2 mg m^{-3}
US-STEL ceiling limit 2 mg m^{-3}

UN No. 1823 (solid)

UN No. 1824 (solution) **HAZCHEM Code** 2X (solid) **HAZCHEM Code** 2W (solution >100°C)
HAZCHEM Code 2R (solution) **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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable 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, S37/39, S45)

Ecotoxicity

Invertebrate toxicity
LC_{50} (48 hr) *Crangon crangon* 33-100 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rabbit 500 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 40 mg kg^{-1} (3).

Irritancy
1% solution instilled in monkey eye caused severe irritation (4).
Dermal rabbit (24 hr) 500 mg caused severe irritation (5).
Dermal rabbit (4 hr) 5% solution caused severe necrosis (6).

Genotoxicity

Did not enhance transformation of Syrian hamster embryo cells by a simian adenovirus, SA7 *in vitro* (7).

Other effects

Other adverse effects (human)
Cases of oesophageal cancer 12-42 yr after ingestion of sodium hydroxide may be due to tissue destruction and scar formation in humans (8,9).
Skin biopsies from volunteers after application of 1N sodium hydroxide for 15-180 min showed changes beginning with dissolution of cells in the horny layer and progressing to oedema and total destruction of the epidermis in 60 min (10).
Dissolution of hair, reversible baldness and scalp burns were reported by a worker after a concentrated solution dripped onto his head (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (12).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (13). Hazards reviewed (14,15).

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S74 sodium hypochlorite

NaOCl

ClNaO **Mol. Wt.** 74.44 **CAS Registry No.** 7681-52-9

Synonyms Beachklean; Adeka Hypote; King Chlor; Surchlor; T-Chlor

EINECS No. 231-668-3 **RTECS No.** NH 3486300

Uses Bleach, disinfectant.

Physical properties

M. Pt. 18°C (pentahydrate) **B. Pt.** decomposes
Solubility Water: 293 g l^{-1} at 0°C

Occupational exposure

UN No. 1791 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Contact with acids liberates toxic gas – Causes burns (R31, R34)
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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Do not mix with acids (S1/2, S28, S45, S50)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) rainbow trout 0.07 mg l^{-1} (1).

LC_{50} (96 hr) fathead minnow 5.9 mg l^{-1} (2).

Changes found in percent hatch or time to hatch reported in *Piscicoloa salmotica* exposed to 0.094 mg l^{-1} for 1 day (3).

Invertebrate toxicity

LOEC *Oncorhynchus kisutch* 0.02 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂, ♀ mouse 5.8, 6.8 mg kg^{-1}, respectively (5).

LD_{50} oral rat 8910 mg kg^{-1} (pentahydrate) (6).

Irritancy

100 mg instilled into rabbit eye and 500 mg applied to rabbit skin for 24 hr caused moderate irritation (pentahydrate) (6).

10 mg instilled into rabbit eye caused moderate irritation (7).

Applied to skin of human volunteers for 24 hr, 20 µl of 1% solution caused no irritation but 100 µl caused significant irritation (8).

Persistent and severe corneal and conjunctival injury reported in rabbit eyes (dose and duration unspecified) (5).

Genotoxicity

Salmonella typhimurium TA1535, TA1538 with and without metabolic activation negative (9,10).

Escherichia coli DNA polymerase deficient (pol $A1^{-1}$) positive (10).

Escherichia coli WP2s λ Microscreen assay without metabolic activation positive (11).

Bacillus subtilis rec assay with and without metabolic activation negative (12).

Induced chromosomal aberrations in cultured hamster lung cells with metabolic activation (12).

Induced sister chromatid exchanges but not chromosome breaks in cultured human cells (13).

Did not induce chromosomal aberrations in rat bone marrow cells *in vivo* (12).

Other effects

Other adverse effects (human)

Hypochlorite solutions release hypochlorous acid on contact with gastric juices, and ingestion causes irritation and corrosion of mucous membranes, pain, vomiting, and oedema of the pharynx and larynx; reduced blood pressure, delerium and coma may occur. Inhalation of hypochlorous fumes causes coughing, respiratory tract irritation and pulmonary oedema (14).

Autopsy findings after suicidal ingestion included necrosis and haemorrhage of the upper gastro-intestinal tract, oedema and pulmonary emphysema, and methaemoglobinaemia (15,16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (17).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (18).

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S75 sodium hypochlorite pentahydrate

$NaOCl \cdot 5H_2O$

$ClH_{10}NaO_6$ **Mol. Wt.** 164.52 **CAS Registry No.** 10022-70-5

Synonyms hydrochlorous acid, sodium salt, pentahydrate

RTECS No. NH 3486800

Physical properties

M. Pt. 18°C

Solubility Water: 29.3 g 100 ml^{-1}

Occupational exposure

UN No. 1791 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Supply classification corrosive

Risk phrases Contact with acids liberates toxic gas – Causes burns (R31, R34)

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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Do not mix with acids (S1/2, S28, S45, S50)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 8910 mg kg^{-1} (1).

Irritancy

100 mg instilled into rabbit eyes and 500 mg applied to rabbit skin for 24 hr caused moderate irritation (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (2).

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S76 sodium lauryl sulfate

$$CH_3(CH_2)_{11}NaSO_4$$

$C_{12}H_{25}NaO_4S$ **Mol. Wt.** 288.38 **CAS Registry No.** 151-21-3

Synonyms sodium dodecyl sulfate; sulfuric acid, monododecyl ester, sodium salt; *n*-dodecyl sodium sulfate; Euponol WAQ; Empical LX28; Maprofix WAC; Monogen Y100; Sipon LS; SDS; Stepanol WAC; Sulfopon WA2; Texapon K12

EINECS No. 205-788-1 **RTECS No.** WT 1050000

Uses Surfactant used in cosmetics, shampoos, oral hygiene products, disinfectants and topical pharmaceuticals.

Physical properties

M. Pt. 204-207°C **Specific gravity** 1.1 at 20°C
Solubility Water: miscible

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) trout, zebra fish, flag fish 4.6-8.1 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna, Daphnia pulex* 13 mg l^{-1} (2).
LC_{50} (48 hr) brine shrimp 2.6 mg l^{-1} (3).
EC_{50} (30 min) *Photobacterium phosphoreum* 0.5-1.2 ppm Microtox test (4).
EC_{50} rotifer *Brachionus calyciflorus* 1.4 mg l^{-1} (5).
EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) 27.3 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) 15.9 mg l^{-1} (6).

Environmental fate

Carbonaceous inhibition
IC_{50} sewage bacterial culture 106 mg l^{-1} (exposure not specified) (7).

Degradation studies
Degraded by *Pseudomonas* isolated from sewage sludge (8,9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1300-1860 mg kg^{-1} (10,11).
LD_{50} intraperitoneal rat, mouse 210, 250 mg kg^{-1}, respectively (11-13).
LD_{50} intravenous rat, mouse 120 mg kg^{-1} (14).

Teratogenicity and reproductive effects

Dermal ♀ rats 4 and 6% solution applied on days 6-13 of gestation caused decreased body weight in both dams and offspring and produced teratogenesis (cleft palate) in some young animals. Delayed ossification and development were observed in the embryo (15).

Irritancy

Dermal human (24 hr) 0.25% solution caused irritation with mild erythematous reaction (16).
Dermal rabbit (24 hr) 25-250 mg caused moderate to severe irritation (17-19).
100 mg instilled into rabbit eye for 24 hr caused moderate irritation (20).

Genotoxicity

Aspergillus nidulans induction of mitotic aneuploidy negative (21).
In vitro mouse lymphoma L5178Y tk^+/tk^- without metabolic activation negative (22).

Other effects

Other adverse effects (human)

Caused a concentration-dependent inhibition of E-rosetting formed between human T-lymphocytes and sheep red blood cells *in vitro* (23).
Human gingival S-G cells (24 hr) midpoint (NR_{50}) cytotoxicity value 0.0127% SLS. Vacuolisation was induced at this concentration (24).

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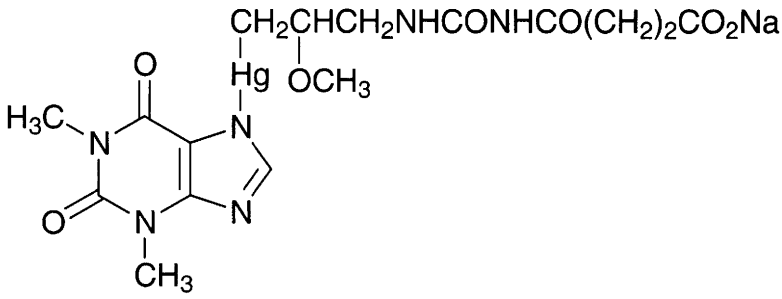
S77 sodium mercuhydrin



$C_{16}H_{21}HgN_6NaO_7$ **Mol. Wt.** 632.96 **CAS Registry No.** 129-99-7

Synonyms Mercuhydrin; Dilurgen; Mercardan; Meralluride

RTECS No. WM 3800000

Uses Diuretic.

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 1070 mg kg^{-1} (1).

LD_{50} intramuscular rat 3160 μg kg^{-1} (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 μg l^{-1} (3).

Included in Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (4). Quality objectives under EC Directives 82/176/EEC and 84/156/EEC 0.3 mg kg^{-1} (wet weight) in a representative sample of fish flesh; 1 μg l^{-1} (annual mean) total mercury in inland surface waters; 0.5 μg l^{-1} (annual mean) dissolved mercury in estuarine waters; 0.3 μg l^{-1} (annual mean) dissolved mercury in marine waters. A 'standstill' provision applies to concentrations in shellfish or sediments. Limit values under EC Directive 84/156/EEC 0.05 mg l^{-1} effluent and 0.1 g l^{-1} vinyl chloride production capacity for chemical industries using mercury catalysts in vinyl chloride production; 0.05 mg l^{-1} effluent and 5 g kg^{-1} mercury processed for chemical industries using mercury catalysts in other processes; 0.05 mg l^{-1} effluent and 0.7 g kg^{-1} mercury processed for manufacture of mercury catalysts used in vinyl chloride production; 0.05 mg l^{-1} effluent and 0.05 g kg^{-1} mercury processed for manufacture of organic and non-organic mercury compounds (other than mercury catalysts for vinyl chloride production); 0.05 mg l^{-1} effluent and 0.03 g kg^{-1} mercury processed for manufacture of primary batteries containing mercury; 0.05 mg l^{-1} effluent for mercury recovery plants and extraction and refining of non-ferrous metals; 0.05 mg l^{-1} effluent for plants treating toxic wastes containing mercury (5).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

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S78 sodium metabisulfite

$$Na_2S_2O_5$$

$Na_2O_5S_2$ **Mol. Wt.** 190.11 **CAS Registry No.** 7681-57-4

Synonyms sodium pyrosulfite; disodium pyrosulfite

EINECS No. 231-673-0 **RTECS No.** UX 8225000

Uses Pharmaceutic aid (antioxidant).

Physical properties

M. Pt. 150°C **Specific gravity** 1.1480

Solubility Water: 540 g l^{-1} at 20°C. Organic solvents: glycerol

Occupational exposure

FR-VME 5 mg m^{-3}

UK-LTEL 5 mg m^{-3}

US-TWA 5 mg m^{-3}

UN No. 2693 (aqueous solution) **HAZCHEM Code** 2X (aqueous solution)

Conveyance classification corrosive substance (aqueous solution)

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat, mouse 115, 192 mg kg^{-1}, respectively (1,2).

Metabolism and toxicokinetics

Oxidised in the human body to sulfate and excreted in urine (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).

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S79 sodium monohydrogen phosphate

Na_2HPO_4

HNa_2O_4P **Mol. Wt.** 141.96 **CAS Registry No.** 7558-79-4

Synonyms sodium phosphate, dibasic; dibasic sodium phosphate; disodium hydrogen phosphate; disodium orthophosphate; disodium phosphate

EINECS No. 231-448-7 **RTECS No.** WC 4500000

Uses Sequestrant, emulsifier and buffer in foods; mordant in dyeing; for weighting silk; in tanning; in manufacture of enamels, ceramics, detergents; fire proofing agent; analytical reagent; in soldering and brazing.

Physical properties

Solubility Water: soluble in 8 parts water

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 17 g kg^{-1} (form unspecified) (1).

LD_{Lo} intramuscular, subcutaneous rat 1000 mg kg^{-1} (form unspecified) (2).

Irritancy

500 mg instilled into rabbit eye or applied to rabbit skin for 24 hr caused mild irritation (1).

Genotoxicity

Escherichia coli PQ37 SOS Chromotest with and without metabolic activation negative (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (4).

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S80 sodium nitrate

$NaNO_3$

$NNaO_3$ **Mol. Wt.** 84.99 **CAS Registry No.** 7631-99-4

Synonyms Chile saltpeter; cubic nitrate; soda niter; nitric acid, sodium salt

EINECS No. 231-554-3 (containing in the dry state >16.3% dry weight nitrogen) **RTECS No.** WC 5600000

Uses In manufacture of nitric acid, sulfuric acid, sodium nitrite, glass, enamels and in matches. Colour fixative in meat. Fertiliser. For preparation of explosives and fireworks.

Occurrence As a mineral in Chile.

Physical properties

M. Pt. 308°C **B. Pt.** 380°C (decomp.) **Specific gravity** 2.26
Solubility Water: 1 g 1.1 ml^{-1}. Organic solvents: ethanol

Occupational exposure

UN No. 1498 **HAZCHEM Code** 1Z **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data
LD_{Lo} oral human 114 mg kg^{-1} (1).
LD_{50} oral rat 3236 mg kg^{-1} (1).
LD_{50} oral rabbit 2680 mg kg^{-1} (2).
LD_{50} intravenous mouse 175 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral F-344 rats (6 wk) 0, 1.25, 2.5, 5.0, 10 or 20%. There was a significant reduction in weight gain in the two high-dose groups and evidence of methaemoglobinaemia at autopsy. The NOEL was 5% (4).
Oral mice (25 wk) 2.5 g kg^{-1} body weight day^{-1} did not affect survival (5).
Oral dog (105 or 125 day) 500 mg kg^{-1} body weight day^{-1}. No adverse effects were reported (6).

Carcinogenicity and chronic effects
Oral ♂ and ♀ rats (2 yr) 0, 0.1, 1.0, 5.0 or 10%. Apart from a slight depression in growth rate at the 5% level and inanition at the highest dose level, there was no evidence of any adverse effects or of any increase in tumour incidence (6).
Oral ♂ and ♀ MRC-derived rats (84 wk) 0 or 0.5% and euthanised 20 wk later. There were statistically significant differences in tumour incidence between the two groups (7).
Oral ♂ and ♀ Sprague-Dawley rats (14 months) 0 or 4000 mg l^{-1}. No difference was observed in the methaemoglobin levels between the two groups (8).
Oral ♂ and ♀ ICR mice 0, 25,000 or 50,000 mg kg^{-1} for their lifespan. No difference in tumour incidence was observed (9).

Teratogenicity and reproductive effects
Oral doses of 1200 mg kg^{-1} day^{-1} for 14 days to ♂ mice caused a reduction (not significant) in fertility and litter size after mating with untreated ♀ (10).
Oral administration of 500 mg kg^{-1} to hamsters on day 11 or 12 of pregnancy did not induce morphological or neoplastic transformation of the cells, micronuclei or chromosomal aberrations in the embryos (11).
Oral sheep 0.3-1.2% on days 21-49 of pregnancy. The doses were sufficient to cause severe methaemoglobinaemia, but no changes in the abortion rates were observed (12).
Oral heifers 445-665 mg from 2 months of pregnancy until parturition, 20-50% methaemoglobinaemia was observed, no effect on the pregnancies (13).

Metabolism and toxicokinetics
When ingested it is readily absorbed from the proximal small intestine and following absorption is rapidly distributed throughout the body in both experimental animals and humans (14).
Oral rats 55% of ^{15}N-labelled compound was excreted unchanged in the urine and 11% was excreted as urea and ammonia in urine and faeces, leaving ~35% unaccounted for (15).
Oral humans 65-70% was excreted in the urine; excretion was maximal at ~5 hr and completed within 18 hr (16).
Excretion has been reported to follow first-order kinetics with an elimination $t_{1/2}$ of ~5 hr (17).

Genotoxicity

Oral doses of 1200 mg kg^{-1} day^{-1} for 14 days caused sex-chromosome univalency and sperm head abnormalities in ♂ mice. It did not induce translocations (10).
Escherichia coli WP2s λ Microscreen assay without metabolic activation positive (18).
Escherichia coli PQ37 SOS Chromotest with or without metabolic activation negative (19).
Salmonella typhimurium, Escherichia coli (metabolic activation unspecified) under aerobic conditions negative; under anaerobic conditions positive (due to reduction of nitrate to nitrite) (20).
In vitro Chinese hamster lung cells chromosomal aberrations positive (21).
In vitro Chinese hamster fibroblast cells chromosomal aberrations positive (22).

Other effects

Other adverse effects (human)

In an area of Australia the death rate from malformations in infants around the time of birth was reported to be significantly higher where the drinking water contained 15 mg l^{-1}, compared with other areas with 2 mg l^{-1} (23).
A study on 12-15 year old girls on an iodine-deficient diet indicated a significant increase in the incidence of goitre in the population exposed to a drinking water nitrate concentration of 22.5 mg l^{-1} compared with the population exposed to 7.5 mg l^{-1} (24).
A study of 1327 ♂ workers producing nitrate-based fertilisers for at least 1 year between 1946-1981 showed no increased risk of developing cancer of the stomach, oesophagus, bladder and lung (25).

Any other adverse effects

Pathological changes in the liver, kidney and spleen have been reported in rats and mice following chronic (25 days-4 months) oral administration (dose unspecified) (26,27).
Oral rats (100 days) 40, 200, 1200 or 4000 mg l^{-1}. Thyroid function was assessed by ^{131}I update, serum iodine level, protein-bound iodine and thyroid weight and histology. Thyroid weight and ^{131}I uptake were slightly affected at all doses and there were associated thyroid histological changes, but there was no dose-related response in the parameters measured (28).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nitrates: guide level 25 mg l^{-1}; maximum admissible concentration 50 mg l^{-1} (as nitrate). Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (29).

Other comments

Risk of nitrate encountered in diet has been assessed (30, 31).

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S81 sodium nitrite

$NaNO_2$

$NNaO_2$ **Mol. Wt.** 69.00 **CAS Registry No.** 7632-00-0

Synonyms nitrous acid, sodium salt; Erinitrit

EINECS No. 231-555-9 **RTECS No.** RA 1225000

Uses In manufacture of diazo dyes, nitroso compounds. In dyeing and printing textiles. Photography. Meat curing. Analytical reagent. Vasodilator and antidote for cyanide poisoning.

Physical properties

M. Pt. 271°C **B. Pt.** decomposes at 320°C **Specific gravity** 2.168
Solubility Water: soluble in 1.5 parts cold water, 0.6 parts boiling water

Occupational exposure

UN No. 1500 **HAZCHEM Code** 1Z **Conveyance classification** oxidising substance
Supply classification oxidising, toxic
Risk phrases Contact with combustible material may cause fire – Toxic if swallowed (R8, R25)
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} (1 day) *Mystus vittatus, Channa punctatus* 33.3, 76.1 mg l^{-1}, respectively (1).
LC_{50} (4 day) *Mystus vittatus, Channa punctatus* 13, 40.6 mg l^{-1}, respectively (1).

Invertebrate toxicity
EC_{100} (14 day) *Chlamydomonas dysosmos, Selenastrum capricornutum, Chlorella emersonii, Scenedesmus obtusiusculus, Monodus subterraneus* and *Tribonema aequale* 4.6, 4.6, 4.3, 4.0, 3.4, 3.4 log mg l^{-1}, respectively (2).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral child 22 mg kg^{-1} (3).
LD_{50} oral rat, mouse 85, 175 mg kg^{-1}, respectively (4,5).
LC_{50} (duration unspecified) rat 5500 μg m^{-3} (6).
LD_{50} intravenous rat 65 mg kg^{-1} (7).
LD_{Lo} subcutaneous rat, mouse 10, 150 mg kg^{-1}, respectively (8,9).
LD_{50} intraperitoneal mouse 158 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Oral rat (200 day) 70 or 340 mg kg^{-1} body weight day^{-1}. Methaemoglobinaemia, raised haematocrit, raised spleen weight in ♀, raised heart weight in ♂ and changes in liver weight in ♀ and kidney weight in both sexes were observed (11).

Carcinogenicity and chronic effects

Currently being tested for carcinogenesis by NTP (12).
Precursor for formation of nitrosamines, many of which are animal carcinogens, although a relationship with human cancer has not been established (13).
Changes in heart and lung pathology and electroencephalogram readings reported in rats fed 2000-3000 mg l^{-1} in drinking water for 2 yr (14).
Methaemoglobinaemia, liver and spleen damage occurred in rats fed 100-3000 mg l^{-1} in drinking water for 2 yr (15).
Increased incidence of liver neoplasms in ♂ rats fed 0.2% diphenhydramine, 0.1% chlorpheniramine or 0.1% *N,N*-dimethyldodecylamine-*N*-oxide with 0.2% sodium nitrite for 106 wk (16).
Increased incidence of squamous papillomas of the forestomach reported in rats receiving 3 g l^{-1} in drinking water for life (total dose 63 g kg^{-1}) (17).
Oral Fischer-344 rats (2 yr) 0, 0.125 or 0.25%. In high-dose ♀, the mean body weight was decreased by more than 10% and there was a significant decrease in tumour incidence compared with controls. The reduced tumour incidence arose from a reduction in monocytic leukaemias which occur with a high incidence in this strain of rat (18).
Oral ICR mice (18 month) 0, 1000, 2500 or 5000 mg l^{-1}. No tumours attributable to treatment were observed (19).

Teratogenicity and reproductive effects

High mortality, poor growth and development reported in pups born to rats fed 660 mg kg^{-1} (total dose) on days 1-22 of pregnancy (14).
Increased foetal methaemoglobin following administration to pregnant rats indicates placental transfer occurs (15).
Oral administration of 120 mg day^{-1} for 14 days caused sperm head abnormalities and reduced fertility in ♂ mice, but no heritable effects occurred in the F_1 generation (20).
Oral Long-Evans rats 0, 0.5, 1, 2 or 3 g l^{-1} throughout gestation and lactation. Erythopoietic development, growth and mortality in the offspring were severely affected. The NOEL was 0.5 g l^{-1}. Cross fostering indicated that treatment during the lactational period was more instrumental in producing lesions than during the gestation period (21).
Oral rats, Syrian hamsters 1000 mg kg^{-1} had no effect on fertility, litter size, post-natal survival, growth rate or lifespan (22).

Metabolism and toxicokinetics

Absorption of nitrite in rats is slower than that of nitrate (23).
In mice intestinal absorption appeared to be faster than in rats (24).
Intravenous mouse, rabbit, rapid equilibration occurs in tissues within 5 min, and within 30 min the levels of free nitrite in body fluid are low (25).
The plasma $t_{1/2}$ in the distribution phase was 48, 12 and 5 min in dogs, sheep and ponies, respectively (26).

Irritancy

500 mg instilled into rabbit eye caused mild irritation (27).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation positive, TA100 with and without metabolic activation weakly positive (28-30).
Salmonella typhimurium TA97, TA98 with and without metabolic activation negative (31).
Bacillus subtilis rec assay positive (32).
Induced chromosomal aberrations and sister chromatid exchanges in hamster lung fibroblasts (32).
Induced micronuclei in bone marrow cells of mice *in vivo* (33).
Escherichia coli WP2s λ Microscreen assay without metabolic activation positive (34).
Escherichia coli PQ37 SOS Chromotest with and without metabolic activation negative (31).
Oral administration of 60-120 mg day^{-1} to ♂ mice for 14 days caused sex chromosome univalency but did not include translocations (35).
125-500 mg kg^{-1} administered orally to hamsters on day 11 or 12 of pregnancy caused mutations, micronuclei and chromosomal aberrations in cultured embryo fibroblasts and morphological/neoplastic cell transformation (20).
Mouse lymphoma cell forward mutation assay positive (36).
Drosophila melanogaster wing spot test positive (37).

Other effects

Other adverse effects (human)
May cause nausea, vomiting, abdominal pain, dizziness, headache, cyanosis, tachypnoea, dyspnoea, vasodilation, hypotension and tachycardia. Overdose may cause cardiovascular collapse, coma, convulsions and death (13).
Cases of methaemoglobinaemia due to consumption of nitrite-contaminated meat have been reported (38).
Most reports of human nitrite poisoning involved children drinking contaminated well water (39), but some resulted from accidental replacement of sodium chloride with sodium nitrite in food (40), or overzealous use of sodium nitrite in meat products (41), some of which were fatal (42,43).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nitrites: maximum admissible concentration 0.1 mg l^{-1} (as nitrite). Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (44).
Reportable quantity regulated under US Federal Comprehensive Environmental Response, Compensation and Liability Act (45).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (46).
Risk of nitrite encountered in diet has been assessed (47).
Decomposes above 320°C.

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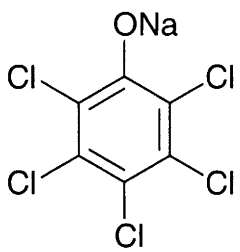
S82 sodium pentachlorophenolate



C_6Cl_5NaO **Mol. Wt.** 288.32 **CAS Registry No.** 131-52-2

Synonyms pentachlorophenate sodium; pentachlorophenol, sodium salt; pentachlorophenoxy sodium; sodium pentachlorophenol; sodium pentachlorophenoxide

EINECS No. 205-025-2 **RTECS No.** SM 6490000

Uses Herbicide.

Occupational exposure

FR-VME 0.5 mg m^{-3}
SE-LEVL 0.5 mg m^{-3} (after conversion to pure pentachlorophenol)
SE-STEL 1.5 mg m^{-3} (after conversion to pure pentachlorophenol)

UN No. 2567 **HAZCHEM Code** 2X **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, respiratory system and skin – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R26, R36/37/38, R40, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – 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) – Not recommended for interior use on large surface areas – 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, S28, S36/37, S45, S52, S60, S61)

Ecotoxicity

Fish toxicity
Behavioural changes reported in *Channa orientalis* at >0.3 ppm (1).
LC_{50} (8 day) fathead minnow larvae 322 μg l^{-1} (2).

Invertebrate toxicity
LC_{50} (96 hr) *Indoplanorbis exustus* 0.184 mg l^{-1} (3).
LC_{50} (48 hr) *Daphnia pulex*, *Daphnia magna* 10.2, 10.8 mg l^{-1}, respectively (4).

Bioaccumulation
Bioconcentration factor in earthworm *Allolobophora caliginosa* from aqueous solutions of 1 and 10 μg ml^{-1} over 24 hr 2.5. Bioconcentration factor from soil at 2.2 and 11.2 mg g^{-1} was 8 and 3, respectively. Bioconcentration ability of *Lumbricus terrestris* >3 × *A. caliginosa* (5).

Environmental fate

Adsorption and retention
Microbial biomass was unaffected 12 wk after soil application (concentration unspecified) (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit 126, 197, 328 mg kg^{-1}, respectively (7-9).
LC_{50} (2 hr) inhalation mouse, guinea pig 240, 341 mg m^{-3}, respectively (8).
LD_{Lo} dermal rabbit 250 mg kg^{-1} (10).
LD_{50} dermal mouse 124 mg kg^{-1} (8).
LD_{Lo} intravenous, intraperitoneal, subcutaneous rabbit 22, 50, 108 mg kg^{-1}, respectively (10,11).

Teratogenicity and reproductive effects
Reproductive and teratogenic effects reported in rats fed 360 mg kg^{-1} (total dose) on days 8-19 of pregnancy (7).

Genotoxicity

Salmonella typhimurium TA1535, TA1537, TA1538 (metabolic activation unspecified) negative (12).
Escherichia coli WP2 negative (12).
Bacillus subtilis rec assay positive (12).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (13).

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S83 sodium perchlorate

$NaClO_4$

$ClNaO_4$ **Mol. Wt.** 122.44 **CAS Registry No.** 7601-89-0

Synonyms perchloric acid, sodium salt; Irenat

EINECS No. 231-511-9 **RTECS No.** SC 9800000

Uses In explosives. Thyroid inhibitor.

Physical properties

M. Pt. 482°C (decomp.) **Specific gravity** 2.02

Solubility Water: very soluble in water. Organic solvents: ethanol

Occupational exposure

UN No. 1502 **HAZCHEM Code** 2W **Conveyance classification** oxidising substance

Supply classification oxidising, harmful

Risk phrases Explosive when mixed with combustible material – Harmful if swallowed (R9, R22)

Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Do not breathe dust – Take off immediately all contaminated clothing (S2, S13, S22, S27)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2100 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 551 mg kg^{-1} (2).

Sub-acute and sub-chronic data

An increase in blood urea, organ aldolase, lactate dehydrogenase and arginase, and decreases in blood glucose and glucose 6-phosphatase activity occurred in rats fed 500 mg kg^{-1} day^{-1} for 45 days (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (5).

References

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S84 sodium persulfate

$$Na_2S_2O_8$$

$Na_2O_8S_2$ **Mol. Wt.** 238.11 **CAS Registry No.** 7775-27-1

Synonyms disodium peroxodisulfate; disodium peroxydisulfuric acid; sodium peroxydisulfate

EINECS No. 231-892-1 **RTECS No.** SE 0525000

Uses Disinfectant. Bleaching agent. Polymerisation catalyst. Oxidising agent.

Physical properties

M. Pt. decomposes on heating **Specific gravity** 2.400
Solubility Water: 550 g l^{-1} at 20°C

Occupational exposure

UK-LTEL 1 mg m^{-3} (as S_2O_8)
US-TWA 0.1 mg m^{-3}

UN No. 1505 **HAZCHEM Code** 2W **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 226 mg kg^{-1} (1).
LD_{Lo} intravenous rabbit 178 mg kg^{-1} (2).

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

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

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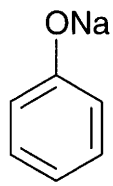
S85 sodium phenolate



C_6H_5NaO **Mol. Wt.** 116.09 **CAS Registry No.** 139-02-6

Synonyms sodium phenoxide; sodium phenate; sodium carbolate; phenol sodium

EINECS No. 205-347-3 **RTECS No.** SM 8780000

Physical properties

M. Pt. 384°C

Solubility Water: soluble. Organic solvents: ethanol

Ecotoxicity

Invertebrate toxicity

LD_{Lo} subcutaneous frog 350 mg kg^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} subcutaneous mouse 350 mg kg^{-1} (1).

Teratogenicity and reproductive effects

Results from *Hydra attennata* and postimplantation rat embryo cultures suggest it is not a potent teratogen (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (3).

References

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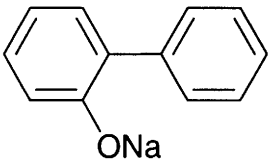
S86 sodium *o*-phenylphenolate



$C_{12}H_9NaO$ **Mol. Wt.** 192.19 **CAS Registry No.** 132-27-4

Synonyms 2-biphenylol, sodium salt; sodium *o*-phenylphenate; sodium *o*-phenylphenoxide; *o*-phenylphenol, sodium salt; 2-phenylphenol, sodium salt

EINECS No. 205-055-6 **RTECS No.** DV 7700000

Physical properties

M. Pt. 78°C

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to the skin – Risk of serious damage to eyes (R22, R38, R41)
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 (S2, S22, S26)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 678, 656 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).
Oral administration increased incidence of bladder carcinomas in rats, and haemangiosarcomas and hepatocellular carcinomas in ♂ mice (3).
Given in the diet it enhanced the incidence of bladder cancer induced by orally administered *N*-nitroso-*N*-(4-hydroxybutyl)-*N*-butylamine in rats (4).
Significantly increased incidence of bladder carcinoma reported in ♂ rats administered 2% in the diet for 104 wk (5).
Dermal application of 5 mg $mouse^{-1}$ 2 × wk^{-1} for 47 wk after applications of 10 μg DMBA as an initiator 2 × wk^{-1} for 5 wk resulted in significantly increased incidence of skin tumours over mice treated with DMBA alone.
Sodium *o*-phenylphenolate appeared to act as an ulcerogenic agent, inducing epidermal proliferation and acting as a promoter but not initiator or complete carcinogen in the two-stage mouse skin carcinogenic process (6).

Irritancy
Dermal rabbit (24 hr) 50 mg caused severe irritation (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (8).

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S87 sodium phosphide

Na_3P

Na_3P **Mol. Wt.** 99.94 **CAS Registry No.** 12058-85-4

Synonyms trisodiophosphine

EINECS No. 235-031-0 **RTECS No.** WD 6475000

Physical properties

M. Pt. decomp.

Occupational exposure

UN No. 1432 **Conveyance classification** substance which in contact with water emits flammable gas, toxic

Mammalian & avian toxicity

Acute data

LC_{Lo} inhalation (1 hr) rat 580 ppm (1).

LC_{Lo} inhalation (2 hr) cat, guinea pig 173, 288 ppm, respectively (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (2).

References

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S88 sodium pyrophosphate

$Na_4P_2O_7$

$Na_4O_7P_2$ **Mol. Wt.** 265.90 **CAS Registry No.** 7722-88-5

Synonyms TSPP; pyro; tetrasodium diphosphate; pyrophosphate; tetrasodium pyrophosphate

EINECS No. 231-767-1 **RTECS No.** UX 7350000

Uses Sequestering agent used in cheese emulsification, water treatment, in cleaning agents and in toothpastes.

Physical properties

M. Pt. 988°C **Specific gravity** 2.534

Solubility Water: 6.7 g 100 ml^{-1} at 25°C

Occupational exposure

FR-VME 5 mg m^{-3}

UK-LTEL 5 mg m^{-3}

US-TWA 5 mg m^{-3} (anhydride and decahydrate)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4 g kg^{-1} (1).

LD_{Lo} oral mouse 40 mg kg^{-1} (2).

LD_{50} intraperitoneal rat 59 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 380 mg kg^{-1} (4).

LD_{50} intravenous rabbit 50 mg kg^{-1} (2).

Genotoxicity

In vitro Paramecium sp. negative (5).

Other comments

The compound appears to potentiate the action of fluoride in toothpastes in the remineralisation of teeth (6). Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

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S89 sodium selenate

Na_2SeO_4

Na_2O_4Se **Mol. Wt.** 188.94 **CAS Registry No.** 13410-01-0

Synonyms disodium selenate; selenic acid, disodium salt

EINECS No. 236-501-8 **RTECS No.** VS 6650000

Uses Superseded insecticide.

Physical properties

Specific gravity 3.098

Solubility Water: 840 g l^{-1} at 35°C

Occupational exposure

JP-OEL 0.1 mg m^{-3} (as Se)

SE-LEVL 0.1 mg m^{-3} (as Se)

UK-LTEL 0.1 mg m^{-3} (as Se)

US-TWA 0.2 mg m^{-3} (as Se)

UN No. 2630 **Conveyance classification** toxic substance

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)

Ecotoxicity

Invertebrate toxicity

LC_{50} (1 day) *Daphnia magna* 1.51 mg l^{-1} (1).

LC_{50} (4 day) *Daphnia magna* 0.58 mg l^{-1} (1).

LC_{50} (48 hr) adult, juvenile *Daphnia magna* 0.75, 0.55 ppm, respectively (1).

Subchronic exposure caused supression of growth over instars 1-5 and reduced egg production in instar 9 when adults were exposed from instar 6 onwards (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit 1600, 2250 μg kg^{-1}, respectively (2).

LD_{Lo} intravenous rabbit, rat 3600, 4786 μg kg^{-1}, respectively (3).

LD_{Lo} intraperitoneal rat 8970 μg kg^{-1} (4).

LD_{Lo} subcutaneous rat 11.4 mg kg^{-1} (5).

Sub-acute and sub-chronic data

♂ weanling rats were fed diets containing 2.5, 5.0, 10.0 μg Se g^{-1} as sodium selenate for 6 wk. Rats fed 2.5 μg g^{-1} showed no evidence of depressed growth and survived the experimental treatment period, whereas rats fed 10 μg g^{-1} showed severe growth depression and died within 29 days (6).

Chronic toxic hepatitis was the predominant lesion seen in rats fed a commercial diet supplemented with sodium selenate at 8 mg Se kg^{-1} (duration unspecified) (7).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (8).
Available animal data are insufficient to allow an evaluation of the carcinogenicity of selenium compounds (9).
Oral mice 0 or 3 mg Se l^{-1} in drinking water as sodium selenate. Tumours were found in 15% of mice and all tumours were malignant (7).

Teratogenicity and reproductive effects

Gavage mouse (8-12 day gestation) Chernoff/Kavlock developmental toxicity screen positive (10).
The developmental toxicity of the compound was evaluated using the frog embryo teratogenesis assay: *Xenopus*. Small cell *Xenopus laevis* blastulae were exposed to sodium selenate for 96 hr. The compound was considered to have moderate teratogenic potential (11).
Oral ♂, ♀ Wistar rats (8 month) 0 or 7.5 mg Se l^{-1} in drinking water as sodium selenate. Mating of normal ♂ with treated ♀ was unsuccessful, whereas mating of treated ♂ with normal ♀ resulted in normal reproduction and survival (7).

Metabolism and toxicokinetics

Gastro-intestinal absorption is rapid with excretion via urine, faeces, sweat and breath. The major urinary metabolite is the trimethylselenium ion and the liver and kidney are the principal sites of deposition (species unspecified) (12).

Genotoxicity

Salmonella typhimurium TA1535 positive, TA100 negative (metabolic activation unspecified) (13).
Salmonella typhimurium TA98, TA1537 with metabolic activation negative, TA100 positive (14).
Escherichia coli WP2s(λ) Microscreen assay without metabolic activation positive (15).
Bacillus subtilis rec assay, showed slight DNA-modifying activity (14).
In vitro Chinese hamster V79 cells with or without metabolic activation negative (16).
Sodium selenate fed by gavage to ♂ Swiss albino mice induced chromosome breaks and spindle disturbances in bone marrow cells. The effects were directly proportional to the dose of chemical administered. Sodium selenite induced a slightly higher frequency of chromosomal aberrations than sodium selenate (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1}. Sodium: guide level 20 mg l^{-1}, maximum admissible concentration 150 mg l^{-1} (18).

Other comments

Data used in setting UK occupational exposure limits summarised (19).

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S90 sodium selenite

Na_2SeO_3

Na_2O_3Se **Mol. Wt.** 172.94 **CAS Registry No.** 10102-18-8

Synonyms selenious acid, disodium salt; disodium selenite; disodium selenium trioxide; sodium selenium oxide

EINECS No. 233-267-9 **RTECS No.** VS 7350000

Uses Removing green colour from glass during manufacture. Reagent for detecting alkaloids.

Physical properties

M. Pt. 710°C (decomp.) **B. Pt.** (decomp.) **Specific gravity** 3.1
Solubility Water: 85 g 100 g^{-1} at 20°C

Occupational exposure

JP-OEL 0.1 mg m^{-3} (as Se)
SE-LEVL 0.1 mg m^{-3} (as Se)
UK-LTEL 0.1 mg m^{-3} (as Se)
US-TWA 0.2 mg m^{-3} (as Se)

UN No. 2630 **Conveyance classification** toxic substance
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)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 8.1 mg l^{-1} (1).
LC_{50} (4 day) rainbow trout 1.8 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (1 day) *Daphnia magna* 1.65 mg l^{-1} (3).
LC_{50} (4 day) *Daphnia magna* 0.44 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 7 mg kg^{-1} (4,5).
LD_{50} intraperitoneal rat 3 mg kg^{-1} (6).

LD_{50} intravenous mouse 5 mg kg^{-1} (7).
LD_{Lo} subcutaneous dog 4 mg kg^{-1} (8).
LD_{50} intracervical mouse 300 μg kg^{-1} (7).

Sub-acute and sub-chronic data

Oral rats (6 wk) 0, 1.6, 3.2, 4.8, 6.4, 8.0, 9.6 or 11.2 mg Se kg^{-1} as sodium selenite. Liver cirrhosis, splenomegaly, and significant growth depression were seen in rats fed ≥6.4 mg kg^{-1}. At ≥8.0 mg kg^{-1} additional effects such as pancreatic enlargement, anaemia and death were observed (9).
12/12 rats given drinking water containing 9 mg Se l^{-1} as sodium selenite died within 6 wk (9).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (10).
Available animal data are insufficient to allow an evaluation of the carcinogenicity of selenium compounds (11).
Oral ♀ mice (50 wk) 0, 1, 4 or 8 mg Se l^{-1} in drinking water as sodium selenite. No signs of neoplasia were seen (9).
Oral mice 0 or 3 mg Se l^{-1} in drinking water as sodium selenite for their lifespan. Tumours were found in 15% of mice and all tumours were malignant (9).

Teratogenicity and reproductive effects

Mallard ducks were fed a diet containing 1, 5, 10 or 25 ppm of Se as sodium selenite. 25 ppm caused a 40-44% decrease in the number of eggs that hatched compared with controls, as well as a 19% decrease in mean embryonic weight at day 18 of incubation and a 6% decrease in crown-rump length. An increase in the incidence of oedema and stunted embryonic growth was also observed (12).
Mallard ducks were fed a diet containing 1, 5, 10, 25 or 100 ppm of Se as sodium selenite. The 3 lower doses had no effect on the weight or survival of adults or on reproductive success; 25 and 100 ppm caused weight loss in adults. ♀ fed 25 ppm took longer to begin laying eggs than in other dosage groups and the survival of the ducklings was reduced. 11/12 adults died when fed 100 ppm; 1 ♂ fed 25 ppm died. 10 and 25 ppm caused mainly embryotoxic effects rather than teratogenic effects (13).
Oral Duroc gilts 10 mg Se kg^{-1} in their diet as sodium selenite. 5/10 conceived with the first service, 2/10 with the second and 3/10 failed to conceive after 3 services; all controls but one conceived with the first service. The treated animals produced fewer litters and fewer live pigs than the controls (9).

Metabolism and toxicokinetics

In mice, the compound is mainly metabolised to trimethylselenium ions and excreted in the urine. 6 hr after a single dose, 1.9% of total Se was found in faeces and 78.9% was found in urine (both as trimethylselenium); 1.6% in expired air as dimethyl selenide (14).
Following oral or intravenous administration to rabbits, steady-state blood Se(IV) concentrations were reached 35 days after treatment with 2 mg kg^{-1} wk^{-1}, 45 days after treatment with 2 mg kg^{-1} every 2 wk, and 30 days after treatment with 1.5 mg kg^{-1} for 10 days (15).
Readily absorbed from the intestinal tract with the highest levels of Se being found in the liver and kidney. Excretion is mainly by the urinary route (species unspecified) (9).

Genotoxicity

Salmonella typhimurium TA98, TA1537 without metabolic activation negative, TA100 positive (16).
Escherichia coli WP2s(λ) Microscreen assay without metabolic activation equivocal (17).
Bacillus subtilis rec assay, showed slight DNA-modifying activity (16).
In vitro Chinese hamster V79 cells with metabolic activation positive (18).
Sodium selenite fed by gavage to ♂ Swiss albino mice induced chromosome breaks and spindle disturbances in bone marrow cells. The effects were directly proportional to the dose of chemical administered. Sodium selenite induced a slightly higher frequency of chromosomal aberrations than sodium selenate (19).

Other effects

Other adverse effects (human)

The mitotic index and cell count of human hepatoma cells exposed to the compound *in vitro* decreased as the concentration of Se increased. At 1 μg ml^{-1}, mitotic activity of the cells was partially arrested. The cell count of

human embryonic liver cells treated continuously with 1 μg ml^{-1} decreased only by day 7 of treatment. In mixed cultures of the 2 cell types treated with 3 and 5 μg ml^{-1} for 24 hr, hepatoma cells showed vacuolated cytoplasms, distorted nuclei, condensed chromatin and pyknosis; the embryonic liver cells retained a normal morphology (20).

Any other adverse effects

Found to stimulate light sensitivity in rabbits (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Selenium: maximum admissible concentration 10 μg l^{-1}. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (20).

Other comments

Oral ♂ Wistar albino rats (2 months old) were exposed during 30 days to 200 ppm Cd (as $CdCl_2$), 0.1 ppm Se (as Na-selenite), or to the same dosages of Cd + Se, simultaneously. The results indicated that Se only partially improved the antioxidant defence system that is insufficient to prevent Cd-induced nephrotoxicity (21).

Data used in setting UK occupational exposure limits summarised (22).

Rat epithelia exposed to 5-methylcholanthrene showed hyperplasia, squamous metaplasia and atypical hyperplasia. However, these effects were prevented when sodium selenite was present, suggesting Se may be an antagonist against chemical carcinogens or act as an antioxidant to protect cells from oxidation damage (23).

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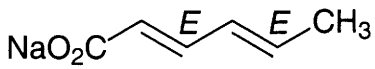
S91 sodium sorbate



$C_6H_7NaO_2$ **Mol. Wt.** 134.11 **CAS Registry No.** 7757-81-5

Synonyms sorbic acid, sodium salt; sodium *E,E*-2,4-hexadienoate; 2,4-hexadienoic acid, sodium salt, *E,E*-

EINECS No. 231-819-3 **RTECS No.** WG 2220000

Uses Food preservative.

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 7160 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 2500 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (3).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges, HGPRT assay negative (3).

In vivo Chinese hamster, mice bone marrow cells chromosomal aberrations, induction of micronuclei, sister chromatid exchanges negative with use of freshly prepared aqueous solutions; stored solutions showed weak clastogenic activity by increased chromosomal aberrations and elevated numbers of micronuclei at doses of 200 mg kg^{-1} (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (4).

ADI 25 mg kg^{-1} body weight (5).

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S92 sodium sulfate

Na_2SO_4

Na_2O_4S **Mol. Wt.** 142.04 **CAS Registry No.** 7757-82-6

Synonyms sodium sulfate (anhydrous); disodium monosulfate; disodium sulfate; Kemsol; Salt cake

EINECS No. 231-820-9 **RTECS No.** WE 1650000

Uses In manufacture of glass and paper pulp. In dyeing and printing textiles. Cathartic.
Occurrence Occurs in nature as the minerals mirabilite and thenardite (1).

Physical properties

M. Pt. 884°C **Specific gravity** 2.633 at 15°C
Solubility Water: 280 g l^{-1}. Organic solvents: glycerol

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 5990 mg kg^{-1} (2).
LD_{Lo} intravenous mouse 1220 mg kg^{-1} (3).
LD_{50} intravenous rabbit 1220 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Inhalation rat (3 month) 1 mg m^{-3} resulted in an increase in blood coagulation time and in relative number of neutrophils in blood, and a decrease in cholinesterase activity in blood and liver, in testes and liver weight and in relative number of lymphocytes in blood. Inhalation of 0.1 mg m^{-3} had no effect on the animals (5).

Carcinogenicity and chronic effects
Subcutaneous mouse 50 μg g^{-1} administered as 26 wkly injections did not induce tumours (target organ skin) (6).

Teratogenicity and reproductive effects
Gavage mouse (8-12 day gestation) Chernoff/Kavlock developmental toxicity screen positive; the compound caused a slight but significant increase in neonatal body weight on day 1 (7).

Genotoxicity

Escherichia coli WP2s(λ) Microscreen assay without metabolic activation negative (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1}. Sulfates: guide level 25 mg l^{-1}; maximum admissible concentration 250 mg l^{-1} (9).

Other comments

Reviews on health effects, experimental toxicology, ecotoxicology listed (10).

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S93 sodium sulfide

Na_2S

Na_2S **Mol. Wt.** 78.05 **CAS Registry No.** 1313-82-2

Synonyms disodium monosulfide; disodium sulfide; sodium monosulfide

EINECS No. 215-211-5 **RTECS No.** WE 1905000

Uses In dehairing hides and wool pulling; desulfurising viscose rayon; manufacture of rubber, sulfur dyes; in ore flotation, metal refining, engraving, cotton printing; as chemical intermediate, as laboratory reagent; in paper-pulping process.

Physical properties

M. Pt. 950°C; 1180°C *in vacuo* **Specific gravity** 1.860
Solubility Water: 186 g l^{-1} at 20°C. Organic solvents: ethanol

Occupational exposure

UN No. 1385 (anhydrous)

UN No. 1849 (hydrated) **HAZCHEM Code** 2X **Conveyance classification** spontaneously combustible substance (anhydrous) **Conveyance classification** corrosive substance (hydrated)
Supply classification corrosive
Risk phrases Contact with acids liberates toxic gas – Causes burns (R31, 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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Ecotoxicity

Invertebrate toxicity
EC_{50} (15 min) *Photobacterium phosphoreum* 4.29 ppm Microtox test (1).

Environmental fate

Nitrification inhibition
Inhibition of nitrification in Agar test, limit concentration 35 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 205-208 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 147 mg kg^{-1} (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, workplace experience, ecotoxicology listed (5).

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S94 sodium sulfite

$$Na_2SO_3$$

Na_2O_3S **Mol. Wt.** 126.04 **CAS Registry No.** 7757-83-7

Synonyms sulfurous acid, disodium salt; disodium sulfite

EINECS No. 231-821-4 **RTECS No.** WE 2150000

Uses In photographic developers. Bleaching wool, straw, silk. Generating sodium dioxide as reducer in manufacturing dyes. Used to remove traces of chlorine in bleached textiles and paper.

Physical properties

Specific gravity 2.633

Solubility Water: soluble in 3.2 parts water. Organic solvents: glycerol

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rabbit 2825 mg kg^{-1} (1).

LD_{50} intravenous rabbit, rat, mouse 65, 115, 130 mg kg^{-1}, respectively (2).

LD_{Lo} subcutaneous dog, cat 1300 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Inhalation rat (3 month) 1 mg m^{-3} resulted in an increase in blood coagulation time and in relative number of neurophils in blood, and a decrease in cholinesterase activity in blood and liver, in testes and liver weights and in the relative number of lymphocytes in blood. Inhalation of 0.1 mg m^{-3} had no effect on the animals (4).

Teratogenicity and reproductive effects

Pregnant rats were fed diets containing 0.32-5% on days 8-20 of pregnancy. A significant reduction in foetal body weight was seen at all doses except for a dose of 2.5%, but no significant differences in the number of live foetuses and intra-uterine death or sex ratio of foetuses were seen between treated animals and controls. No foetal external, skeletal or internal malformations were observed, but some skeletal and internal variations were seen in

treated animals, although the incidences were not significantly different from controls. Survival rate of offspring by wk 4 and their body weight gain at wk 3 were not affected by the treatment. Maternal toxicity was observed at the 5% dose level, indicated by decreased body weight gain and decreased food consumption, but no clinical signs of toxicity were seen (5).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6).
In vitro Chinese hamster fibroblasts chromosomal aberrations negative (6).
Mutagenic as tested by the *Tradescantia* micronucleus technique (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (8).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology listed (9).

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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

S95 sodium tellurite

$$Na_2TeO_3$$

Na_2O_3Te **Mol. Wt.** 221.58 **CAS Registry No.** 10102-20-2

Synonyms telluric acid, disodium salt; sodium tellurium oxide; sodium tellurite(IV)

EINECS No. 233-268-4 **RTECS No.** WY 2450000

Physical properties

M. Pt. 710-760°C
Solubility Water: soluble in water

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

Acute data
LD_{50} oral rabbit 54 mg kg^{-1} (1).
LD_{50} oral mouse, rat 20, 83 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal rat 2.4 mg kg^{-1} (2).
LD_{Lo} oral human 30 mg kg^{-1} (3).

Genotoxicity

Salmonella typhimurium TA98 positive, TA100, TA1535, TA1537, TA1538 negative (metabolic activation unspecified) (4).
Bacillus subtilis H17, M45 *rec* assay strongly positive (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (5).

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S96 sodium tetraborate

$$Na_2B_4O_7$$

$B_4Na_2O_7$ **Mol. Wt.** 201.22 **CAS Registry No.** 1330-43-4

Synonyms borax; disodium tetraborate; boron sodium oxide; boric acid, disodium salt; borax glass; fused borax; FR 28

EINECS No. 215-540-4 **RTECS No.** VZ 2275000

Uses In soaps and detergents. In fire-retardant paints. In fertilisers.

Physical properties

M. Pt. 75°C **B. Pt.** 320°C **Specific gravity** 2.367
Solubility Water: 20.1 g l^{-1} at 20°C

Occupational exposure

FR-VME 1 mg m^{-3}
UK-LTEL 1 mg m^{-3}
US-TWA 1 mg m^{-3} (anhydrous); 5 mg m^{-3} (decahydrate); 1 mg m^{-3} (pentahydrate)

Mammalian & avian toxicity

Sub-acute and sub-chronic data
In 90-day feeding trials 525 ppm was tolerated by rats, but 1750 and 5250 ppm were toxic (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials 350 ppm was tolerated by rats and dogs (1).

Teratogenicity and reproductive effects
350 ppm had no effect on the fertility, lactation, litter size, weight or appearance in a three-generation feeding study of rats (1).

Metabolism and toxicokinetics
Absorbed from the gastro-intestinal tract and excreted in the urine with $t_{1/2}$ 24 hr. Concentrates in the brain, liver, adipose tissue and cerebrospinal fluid shortly after absorption (species unspecified) (2).

Irritancy
Non-irritating to human skin (3).

Other effects

Other adverse effects (human)
Chronic exposure leads to accumulation in bone. High doses may produce kidney damage, shock and atrophy of cells in the central nervous system. Excessive doses to man have caused headaches, peeling of the skin, severe gastro-intestinal disturbances and erythematous rash. Fatal doses are ~5-6 g for children and 10-25 g for adults (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1}. Boron: guide level 1000 μg l^{-1} (4).

References

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3. Kato, L. et al *Can. Med. Assoc. J.* 1955, **73**, 31.
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

S97 sodium trichloroacetate

CCl_3CO_2Na

$C_2Cl_3NaO_2$ **Mol. Wt.** 185.37 **CAS Registry No.** 650-51-1

Synonyms TCA-sodium; Antiperz; acetic acid, trichlorosodium salt; trichloroacetic acid, sodium salt; Varitox

EINECS No. 211-479-2 **RTECS No.** AJ 9100000

Uses Selective systemic herbicide.

Physical properties

M. Pt. 165-200°C (decomp.) **Volatility** v.p. $<7.5 \times 10^{-7}$ mmHg

Solubility Water: 1.2 kg l^{-1} at 25°C. Organic solvents: acetone, benzene, diethyl ether, heptane, 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) – Avoid contact with the skin – Avoid contact with the eyes (S2, S24, S25)

Ecotoxicity

Fish toxicity

Threshold value for toxic effect to perch ~1000 mg l^{-1} (duration unspecified) (1).

LC_{50} (96 hr) common carp 2500 mg l^{-1} (2).

LC_{50} (96 hr) minnow 2000 mg l^{-1} (3).

Invertebrate toxicity

LC_{50} (96 hr) mosquito 5500 mg l^{-1} (2).

LC_{50} (96 hr) *Daphnia magna* 3100 mg l^{-1} (2).

LC_{50} (48 hr) *Daphnia magna* 2000 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken 4280 mg kg^{-1} (1).

LD_{50} oral rat, mouse 3200-5600 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat >365 mg l^{-1} (1).

LD_{50} percutaneous rat >2000 mg kg^{-1} (1).

Genotoxicity

Incubation of human peripheral lymphocytes with 10 μg ml^{-1} for 54 hr increased the frequency of aberrant metaphases from 2.5 to 7.0%. The herbicide also induced aberrations in germinating onions and *Crepis tectorum* at 1000-10,000 μg ml^{-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).

EPA Toxicity Class III (formulation) (7).

Other comments

Not toxic to bees (1).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

References

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6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, 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

S98 sodium triphosphate

$$Na_5P_3O_{10}$$

$Na_5O_{10}P_3$ **Mol. Wt.** 367.86 **CAS Registry No.** 7758-29-4

Synonyms sodium tripolyphosphate; sodium phosphate ($Na_5P_3O_{10}$); Thermphos

EINECS No. 231-838-7 **RTECS No.** YK 4570000

Uses In water softening. A preservative, sequestrant and texturiser in food. Emulsifier and dispersing agent.

Physical properties

Solubility Water: 145 g l^{-1} at 25°C

Environmental fate

Degradation studies

Surface soil treated with 500 μg g^{-1} at 25°C for 7 days. The amount of orthophosphate produced was correlated with soil pH and negatively correlated with dithionite-extractable Al^{3+} and Fe^{3+} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 3100, 3900 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal rat, mouse 525, 700 mg kg^{-1}, respectively (3,4).
LD_{50} subcutaneous guinea pig, mouse 750, 900 mg kg^{-1}, respectively (5,6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1}; maximum admissible concentration 150 mg l^{-1} (7).

Other comments

Reviews on health effects, experimental toxicology, ecotoxicology listed (8).
Moderately irritating to skin and mucous membrane. Ingestion can cause violent purging (9).

References

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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. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

S99 sodium tungstate

Na_2WO_4

Na_2O_4W **Mol. Wt.** 293.83 **CAS Registry No.** 13472-45-2

Synonyms sodium tungstate(VI)

EINECS No. 236-743-4 **RTECS No.** YO 7875000

Uses For fireproofing and waterproofing fabrics. In X-ray barrier inks and as a laboratory reagent.

Physical properties

M. Pt. 698°C **Specific gravity** 4.179

Occupational exposure

SE-LEVL 1 mg m^{-3} (as W)
UK-LTEL 1 mg m^{-3} (as W) **UK-STEL** 3 mg m^{-3} (as W)
US-TWA 1 mg m^{-3} (as W) **US-STEL** 3 mg m^{-3} (as W)

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, guinea pig, rat 875, 1150, 1190 mg kg^{-1}, respectively (1).
LD_{50} subcutaneous rat 240 mg kg^{-1} (2).
Intrathecal inoculation of tungstate into laboratory animals causes pigmentation and interstitial cell proliferation near particles and may cause bronchiolitis (species unspecified) (3).

Sub-acute and sub-chronic data

Rabbits can tolerate 12 mg day^{-1} in diet for 6 wk, but a diet of 0.5% tungsten as tungstate causes stunted growth (4,5).

Metabolism and toxicokinetics

In ruminants the compound is thought to be capable of rapid absorption from the gastro-intestinal tract, although in sheep there is interference by rumen bacteria. Tungstate is eliminated mainly in urine with 2% of an injected dose and 25% of an oral dose being eliminated in faeces. It can cross the placental barrier. There is significant retention of tungstate in bones, but little in liver or kidney (4-7).

Genotoxicity

Salmonella typhimurium TA1535 SOS chromotest negative (8).

Other effects

Any other adverse effects

Tungstate inhibits xanthine oxidase activity in lactating cows and goats (9).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

The toxicology of tungsten compounds has been reviewed (5).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (11).

References

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8. Nakamura, S. et al *Sangyo Igaku* 1989, **31**(6), 430-431 (Japan.) (*Chem. Abstr.* **112**, 153457k).
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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

S100 sodium valproate

$$(CH_3CH_2CH_2)_2CHCO_2Na$$

$C_8H_{15}NaO_2$ **Mol. Wt.** 166.20 **CAS Registry No.** 1069-66-5

Synonyms sodium 2-propylpentanoate; Convulex; Epilim; Orfiril; sodium dipropylacetate

EINECS No. 213-961-8 **RTECS No.** YV 7876000

Uses Anticonvulsant, antiepileptic agent.

Physical properties

Solubility Water: 200 g l^{-1}. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 670 mg kg^{-1} (1).
LD_{50} oral mouse 1020 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse, rat 470, 970 mg kg^{-1}, respectively (2).
LD_{50} subcutaneous mouse, rat 860, 1029 mg kg^{-1}, respectively (2,3).
LD_{50} intravenous rat, mouse 509, 750 mg kg^{-1}, respectively (4,5).

Teratogenicity and reproductive effects

Oral Dutch belted rabbits given 350 mg on days 6-18 of gestation. Post-implantation loss and the incidence of malformed vertebrae and ribs, rudimentary or absent pollices, and extra vertebrae and ribs were observed (6).
Intraperitoneal CD-1 ♀ mouse, 340 mg kg^{-1} on day 8 of gestation. A 30% incidence of neural tube defects in the cranial region of the embryos, a reduction in head size indicating a drug-induced microcephaly. Increased cellular-blebbing was apparent at the ependymal surface and large protrusions of cells were seen invading the neural tube lumen. The lumen was distorted in shape and frequently contained blood cells. Irregularities and gaps were observed in the underlying basal lamina (7).
Oral CD-1 mouse 225, 338 or 563 mg kg^{-1} on days 8-16 of gestation. The length and width of fore- and hind-limbs were affected, as was long bone ossification (8).

Other comments

Toxicity reviewed (9).

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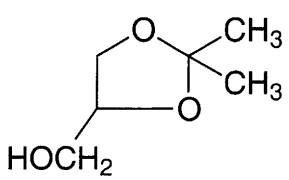
S101 solketal



$C_6H_{12}O_3$ **Mol. Wt.** 132.16 **CAS Registry No.** 100-79-8

Synonyms isopropylidene glycerol; 2,2-dimethyl-1,3-dioxolane-4-methanol; acetone glycerin ketal; Dioxolan; glycerol acetonide; glycerol dimethylketal; 1,2-isopropylideneglycerol; 2,3-isopropylideneglycerol; acetone ketal of glycerine

EINECS No. 202-888-7 **RTECS No.** JI 0400000

Uses Versatile solvent and plasticiser. Pharmaceutical aid.

Physical properties

M. Pt. –26.4°C **B. Pt.** 82°C at 10 mmHg **Flash point** 80°C **Specific gravity** 1.065 at 20°C
Volatility v.den. 2.6

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 7 g kg^{-1} (1).
LD_{50} interperitoneal rat 3 g kg^{-1} (1).

Legislation

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

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
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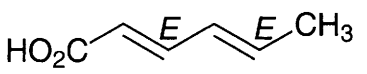
S102 sorbic acid



$C_6H_8O_2$ **Mol. Wt.** 112.13 **CAS Registry No.** 110-44-1
Synonyms (*E,E*)-2,4-hexadienoic acid; *trans,trans*-sorbic acid; 2-propenylacrylic acid; Sorbistat
EINECS No. 203-768-7 **RTECS No.** WG 2100000
Uses Mould and yeast inhibitor. Preservative.
Occurrence As parasorbic acid in berries of Mountain Ash *Sorbus aucuparia*.

Physical properties

M. Pt. 134.5°C **B. Pt.** 228°C (decomp.) **Flash point** 127°C **Specific gravity** 1.204 at 19°C with respect to water at 4°C **Volatility** v.p. 50 mmHg at 143°C ; v.den. 3.87
Solubility Water: 0.25% in water at 30°C. Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} fathead minnow, rainbow trout, bluegill sunfish 315, 310, 330 mg l^{-1}, respectively (predicted values) (1).

Environmental fate

Degradation studies
Confirmed to be biodegradable (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 3200, 7360 mg kg^{-1}, respectively (3,4).
LD_{50} intraperitoneal mouse 2820 mg kg^{-1} (5).
LD_{50} subcutaneous mouse 2820 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Oral rat (90-120 days) 8-10% in diet resulted in reduced weight gain and increased liver weight. There was no evidence of any gross abnormalities or of histological changes in the tissues (6).

No differences were seen between dogs fed a diet containing 4% sorbic acid in cheddar cheese and controls given unadulterated cheese (6)

Carcinogenicity and chronic effects

Oral rat ≤10% in diet or 0.1% in drinking water. No increase in tumour incidence was observed (6).

Teratogenicity and reproductive effects

In vitro Hydra assay, embryo minimal effect ratio equals 3, indicating some possible developmental selectivity (7).

No adverse effects on reproduction or post-natal development were seen in a four-generation study in mice receiving 40 g kg^{-1} of sorbic acid and 2 g kg^{-1} of nisin (6).

No effect was seen on the reproductive performance of rats given diet containing 10% sorbic acid for 60 days prior to mating and throughout gestation and lactation. The F_1 generation were weaned on the diet for 70 days and then mated; no difference was observed between the reproductive performance of these animals and that of controls. Some ♂ showed a small reduction in weight gain (6).

Metabolism and toxicokinetics

The compound is readily absorbed and metabolised. Following administration of [1-^{14}C]sorbic acid to rats, 85% of the radioactivity occurred as CO_2 in expired air. ~2% appeared in urine as [^{14}C]urea and [^{14}C]carbonate and the remainder was found in the tissues (6).

Irritancy

Dermal rabbit 1 mg caused severe irritation (8).

Dermal man (1 hr) 150 mg caused severe irritation (9).

Associated with a non-immunological contact urticaria (6).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (10).

In vitro Chinese hamster fibroblasts chromosomal aberrations negative (10).

In vitro mammalian cells unscheduled DNA synthesis negative (6).

In vivo mice micronucleus test, sister chromatid exchanges negative (6).

In vivo in rats and *in vitro* with and without metabolic activation DNA binding studies negative (6).

Other effects

Other adverse effects (human)

Subjects who are especially sensitive to lactic acid have also been found to be unusually sensitive to sorbic acid developing more erythema in response to 0.5% sorbic acid and more oedema in response to 1% sorbic acid (6).

Legislation

ADI 25 mg kg^{-1} body weight (6).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology, environmental effects and exposure levels listed (11,12).

References

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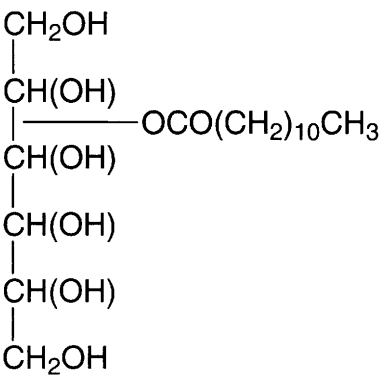
S103 sorbitan monolaurate



$C_{18}H_{36}O_7$ **Mol. Wt.** 364.48 **CAS Registry No.** 1338-39-2

Synonyms Span 20; sorbitan monododecanoate; Glycomul LC; Nonion LP 20R; Sorgen 90; Value SP 20

EINECS No. 215-663-3 **RTECS No.** WG 2920000

Uses Surfactant.

Physical properties

Flash point >110°C **Specific gravity** 1.032

Solubility Organic solvents: liquid paraffin, miscible with ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 33,600 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral rat (13 wk) 0, 2.5, 5 or 10% in feed. At 5 or 10%, rats had reduced haemoglobin concentrations and packed cell volumes but other haematological parameters and serum enzyme levels were normal. Dose-related reductions in the rate of body weight gain were associated with reduced intakes of the diet. Variations in organ weight were mainly associated with the lower body weights. Those related to treatment were increases in relative liver and small intestine weights in animals fed 5% and 5 or 10% diets, respectively, and increases in kidney weight at all dose levels. Periportal fat-containing vacuoles were seen in the livers of the rats fed the 10% diet, but the increased kidney weights were not accompanied by histological changes or impairment of renal function. A no-untoward-effect level could not be established due to this kidney enlargement (2).

References

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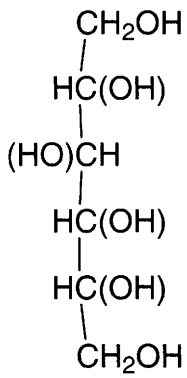
2. Cater, B. R. et al *Food Cosmet. Toxicol.* 1978, **16**(6), 519-526

S104 D-sorbitol



$C_6H_{14}O_6$ **Mol. Wt.** 182.17 **CAS Registry No.** 50-70-4

Synonyms D-glucitol; Sorbex; Karion; Sorbol; Neosorb; Sionite; Siosan

EINECS No. 200-061-5 **RTECS No.** LZ 4290000

Uses Pharmaceutic aid. In manufacture of sorbose, ascorbic acid, propylene glycol, plasticisers and resins. Humectant. Used in writing inks and antifreeze.

Physical properties

M. Pt. 110-112°C (anhydrous) **B. Pt.** 200°C at 0.001 mmHg **Specific gravity** 1.489 at 20°C with respect to water at 4°C **Volatility** v.p. 23.5 mmHg at 25°C ; v.den. liquid density 1.472 g cm^{-3} at 9.5°C
Solubility Water: freely soluble in water. Organic solvents: acetic acid, acetone, butanol, methanol, phenol, pyridine

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 15,900, 17,800 mg kg^{-1}, respectively (1,2).
LD_{50} intravenous rat, mouse 7100, 9480 mg kg^{-1}, respectively (1,2).
LD_{Lo} intraperitoneal mouse 15 g kg^{-1} (3).

Metabolism and toxicokinetics

In humans it is poorly absorbed from the gastro-intestinal tract following oral or rectal administration. Metabolised in the liver to fructose, although some sorbitol may be converted directly into glucose by aldose reductase (4).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (5).
In vitro Chinese hamster fibroblasts chromosomal aberrations negative (5).
In vitro Chinese hamster ovary cells chromosomal aberrations positive (6).

Other effects

Other adverse effects (human)

Large doses administered orally may cause flatulence, abdominal pain and diarrhoea. Lactic acidosis and hyperuricaemia can follow intravenous infusions; some fatalities have occurred (4).

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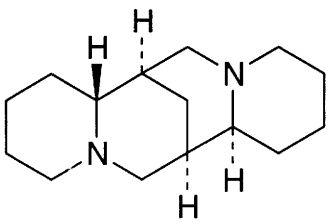
S105 sparteine



$C_{15}H_{26}N_2$ **Mol. Wt.** 234.38 **CAS Registry No.** 90-39-1

Synonyms [7*S*-(7α,7*a*α,14α,14*a*α)]-dodecahydro-7,14-methano-2*H*,6*H*-dipyrido[1,2-α:1′,2′-*e*][1,5]diazocine; lupinidine; 6β,7α,9α,11α-pachycarpine

EINECS No. 201-988-8 **RTECS No.** WG 5950000

Uses Oxytocic.

Occurrence In yellow and black lupin beans *Lupinus luteus*.

Physical properties

B. Pt. 173°C at 8 mmHg **Flash point** >110°C **Specific gravity** 1.020 at 20°C with respect to water at 4°C

Solubility Water: 1 g in 325 ml of water. Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Toxicity to other species

Concentration producing complete narcosis in *Rana temporaria* 83.3 (observed) and 492 (predicted) mg l^{-1} (1).

LD_{Lo} intramuscular, subcutaneous frog 1665, 3330 mg kg^{-1}, respectively (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 220 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 36 mg kg^{-1} (3).

LD_{Lo} intravenous guinea pig, rabbit 27, 30 mg kg^{-1}, respectively (2,3).

LD_{Lo} subcutaneous pigeon, rabbit 86, 100 mg kg^{-1}, respectively (3).

Metabolism and toxicokinetics

In vivo ♂ rats metabolised sparteine to lupanine, but *in vitro* metabolic conversion in the presence of rat liver homogenate did not produce detectable lupanine. In the presence of inducers of microsomal enzymes, levels of lupanine in the rat urine did not increase, but they did decrease in the presence of inhibitors. Thus, the bioconversion of sparteine to lupanine appears to be mediated by microsomal enzymes and may proceed via an aldehyde intermediate (4).

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S106 spermidine

$$H_2N(CH_2)_4NH(CH_2)_3NH_2$$

$C_7H_{19}N_3$ **Mol. Wt.** 145.25 **CAS Registry No.** 124-20-9

Synonyms 1,4-butanediamine, *N*-(3-aminopropyl)-; 1,5,10-triazadecane

EINECS No. 204-689-0 **RTECS No.** EJ 7000000

Physical properties

B. Pt. 128-130°C at 14 mmHg **Flash point** >110°C **Specific gravity** 0.925

Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 78 mg kg^{-1} (1).

Acute oral toxicity Wistar rats 600 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Wistar rat no-observed-adverse-effect level (6 wk) 1000 ppm in diet (83 mg kg^{-1} day^{-1}). At 10,000 ppm decreased body weights associated with diminished food intake and decreased plasma creatinine, calcium, and inorganic phosphate levels were seen (2).

Carcinogenicity and chronic effects

Predicted to be noncarcinogenic by a CASE study (3).

Genotoxicity

A CASE study based on qualitative structural features predicted the compound to show marginal mutagenicity (4).

Other effects

Any other adverse effects

Treatment of yolk-sac membranes of 4-day-old chick embryos with spermidine resulted in angiogenesis in the membranes (5).

Other comments

Metabolism and metabolic functions reviewed (6,7).
Detected in amniotic fluid, peripheral blood and urine of pregnant women, and in the umbilical cord blood collected at birth. The amniotic and urinary concentrations were not affected by gestational age, but the maternal blood concentration increased with gestational age (8).

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S107 spermine

$$H_2N(CH_2)_3NH(CH_2)_4NH(CH_2)_3NH_2$$

$C_{10}H_{26}N_4$ **Mol. Wt.** 202.34 **CAS Registry No.** 71-44-3

Synonyms 1,5,10,14-tetraazadecane; *N,N'*-bis(3-aminopropyl)-1,4-butanediamine; Neuridine; Musculamine; Gerontine

EINECS No. 200-754-2 **RTECS No.** EJ 7175000

Occurrence Occurs in animal tissues.

Physical properties

M. Pt. 28-30°C **B. Pt.** 141-142°C at 0.5 mmHg **Flash point** >110°C
Solubility Organic solvents: chloroform

Occupational exposure

UN No. 1760

Mammalian & avian toxicity

Acute data

Acute oral toxicity Wistar rats 600 mg kg^{-1} (1).
LD_{50} intravenous rat 65 mg kg^{-1} (2).
LD_{Lo} intraperitoneal mouse 8 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Wistar rats (6 wk) 5000 ppm in diet caused emaciation, aggressiveness, convulsions, and paralysis of the hind legs. Growth, food intake, and water intake were considerably decreased. Slight anaemia (♂s) and changes in plasma clinical chemistry occurred. The relative weights of the thyroid, adrenals, spleen, and heart were increased and that of the liver decreased. There was impaired kidney function, together with renal histopathological changes and changes in plasma electrolytes and urea. Histopathological examinations also revealed decreased glycogen content in the liver, reduction of spermatogenesis, severe depletion of splenic white pulp, acute involution of the thymus, and moderate myocardial degeneration of the heart. The no-observed-adverse-effect level was 200 ppm (19 mg kg^{-1} day^{-1}) (1).

Other effects

Any other adverse effects

Treatment of yolk-sac membranes of 4-day-old chick embryos with spermine resulted in angiogenesis in the membranes. The angiogenesis was inhibited by tissue inhibitors of metalloproteinases (4).

Spermine produced a dose-dependent inhibition of BHK-21/C13 cell growth. The cell growth was monitored using cell number, protein content and [^{3}H]thymidine incorporation into DNA; the compound caused significant reductions in all three measurements. A rapid loss of reduced glutathione (GSH) also occurred. The effect on both cell growth and GSH was reversible following removal of spermine from the extracellular medium (5).

Other comments

Metabolism and metabolic functions reviewed (6,7).

Detected in amniotic fluid, peripheral blood and urine of pregnant women and in the umbilical cord blood collected at birth. The amniotic and urinary concentrations were not affected by gestational age but the maternal blood concentration increased with gestational age (8).

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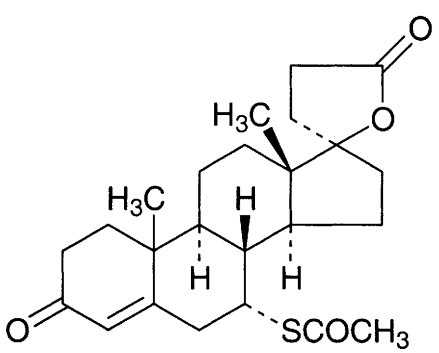
S108 spironolactone



$C_{24}H_{32}O_4S$ **Mol. Wt.** 416.58 **CAS Registry No.** 52-01-7

Synonyms 7α-acetylthio-3-oxo-17α-pregn-4-ene-21,17β-carbolactone; spiro[17*H*-cyclopento[*a*]phenanthrene-17,2′(5′*H*)furan], pregn-4-ene-21-carboxylic acid derivative; pregn-4-ene-21-carboxylic acid, 7-(acetylthio)-17-hydroxy-3-oxo,γ-lactone, (7α,17α)

EINECS No. 200-133-6 **RTECS No.** TU 4725000

Uses Diuretic. Aldosterone antagonist.

Physical properties

M. Pt. 134-135°C resolidifies; 201-202°C (decomp.)
Solubility Organic solvents: acetone, benzene, chloroform, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal rat, mouse, rabbit 790, 360, 870 mg kg^{-1}, respectively (1).
LD_{50} intragastric rat, mouse, rabbit >1000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (2).
Oral ♂, ♀ rats (78 wk) 0, 50, 150 or 500 mg kg^{-1} day^{-1}. Thyroid tumours were seen in 0/59, 4/33, 15/31 and 18/28 ♂ rats, respectively; in ♀ the incidences were 1/62, 1/31, 12/34 and 13/34, respectively. Testicular tumours occurred in 0/72, 0/36, 5/36 and 12/36 ♂, respectively (1).
Oral rat (104 wk) 0, 10, 30 or 100 mg kg^{-1} day^{-1}. No increase in the incidence of thyroid and testicular tumours was seen (1).

Teratogenicity and reproductive effects
Intraperitoneal rats (8-14 day of pregnancy) and mice (7-13 day of pregnancy) ≤80 mg kg^{-1} of potassium canrenoate (a metabolite of spironolactone in humans). No defects were produced in offspring, but some resorptions occurred in mice administered 80 mg kg^{-1} (3).

Metabolism and toxicokinetics
Rapidly absorbed in humans, dogs, rats and monkeys after oral administration, then extensively metabolised. In humans, ~90% of a radio-labelled oral dose of 500 mg was recovered in urine (53%) and faeces (36%) in 6 days. In rats, dogs and monkeys the total recovery in urine and faeces following an intravenous dose of 5 mg kg^{-1} was 97, 88 and 101%, respectively. The major metabolite is canrenone, which is biologically active (3).
Food was found to increase the absorption of spironolactone and to possibly decrease its first-pass metabolism (4).
The compound and its metabolites may cross the placenta; its metabolite canrenone is excreted in breast milk. The extent of absorption from the gastro-intestinal tract depends on the particle size and formulation administered; modern formulations provide a bioavailability of ~90% (5).

Other effects

Other adverse effects (human)
Side-effects in humans include gynaecomastia and impotence. Treatment can increase the dialysable fraction of testosterone in serum by 20% (3).
5 ♀ developed breast cancer following administration of a drug containing spironolactone and hydrochlorothiazide for 4-24 months (6).
Side-effects include headaches, drowsiness, gastro-intestinal disturbances, ataxia, mental confusion and skin rashes. Gynaecomastia, hirsutism, deepening of the voice, impotence and menstrual irregularities have also been reported. Breast enlargement has also been seen (5).

Any other adverse effects
The testicular toxicity of the compound was evaluated using a miniaturised primary culture of immature pig Leydig cells. Spironolactone was found to block testosterone secretion and increase progesterone concentration without inducing cell mortality (7).
Treatment of 24-day-old rats resulted in hypertrophy of the liver cells, whereas treatment of 48-day-old rats resulted in both hypertrophy and hyperplasia of the hepatocytes (8).

Other comments

Not known to occur in nature (3).
Metabolism and biopharmacokinetics in humans reviewed (9).
Metabolism in humans and laboratory animals reviewed (10).

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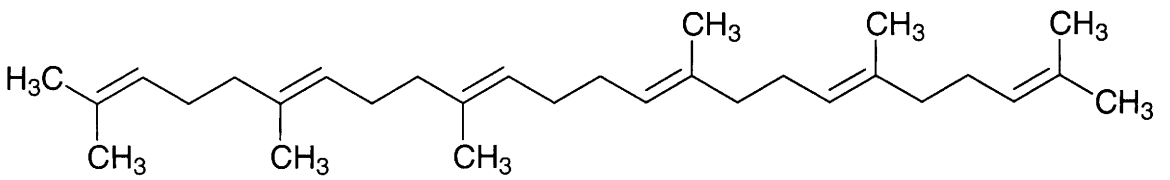
S109 squalene



$C_{30}H_{50} **Mol. Wt.** 410.73 **CAS Registry No.** 111-02-4

Synonyms 2,6,10,14,18,22-tetracosahexaene, 2,6,10,15,19,23-hexamethyl-, (*all-E*)-; spinacene; *E,E,E,E*-squalene; *trans*-squalene

EINECS No. 203-826-1 **RTECS No.** XB 6010000

Uses Bactericide. Intermediate in the manufacture of pharmaceuticals, rubber chemicals and colouring materials.
Occurrence Found in human sebum and shark liver oil (1).

Physical properties

M. Pt. -75°C **B. Pt.** 285°C at 25 mmHg **Flash point** >110°C **Specific gravity** 0.858-0.860
Solubility Organic solvents: acetone, carbon tetrachloride, diethyl ether

Environmental fate

Degradation studies

Biodegradation was assessed in batch bioassays inoculated with anaerobic granular sludge at 30°C and the assays were supplied with 35-200 mg l^{-1} of squalene to prevent methanogenic inhibition. No indication of methanogenic degradation was obtained (2).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Oral ♂, ♀ dogs, respectively, (13 wk) 400 or 1200 mg kg^{-1} day^{-1} resulted in accumulation of squalene in the liver at ~3% or ~6% of the daily dose. However, no toxic signs were observed in serum biochemical tests and hepatic functional tests (3).

Metabolism and toxicokinetics

Following a single oral dose of 1200 mg kg^{-1} to dogs, 83% was excreted in the faeces during the first 2 days. On day 3 the absorbed compound was mostly distributed in the hair and skin; these concentrations decreased on day 6. This suggests the compound is largely not absorbed from the gastro-intestinal tract; some is absorbed and excreted through the hair (4).

Other comments

Properties, metabolism and uses reviewed (3).

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S110 starch

$(C_6H_{10}O_5)_n$ **CAS Registry No.** 9005-25-8

Synonyms Amicol; Emjel 200; Farinex; rice starch; corn starch, W-Gum; Snowflake 30091

EINECS No. 232-679-6 **RTECS No.** GM 0900000

Uses Soluble starch is used for the determination of diastalic powder of malt. Indicator in iodometric analysis.
Occurrence Occurs as discrete granules in the mature grain of corn and wheat, in tubers of potato and in rice.

Occupational exposure

UK-LTEL 10 mg m^{-3} (total inhalable dust); 4 mg m^{-3} (respirable dust)
US-TWA 10 mg m^{-3}

Environmental fate

Degradation studies

In four strains of *Pseudomonas* sp. growth was observed in a synthetic medium with soluble starch as a sole carbon source (1).

Two strains of *Blastocladia ramosa* and one strain of *B. pringsheimii* were able to utilise starch under strict and anaerobic conditions (2).

ThOD 1.18 g O_2 g^{-1} (3).

Other effects

Any other adverse effects

Oral rats single 5 mg doses of 7,12-dimethylbenz[*a*]anthracene, and fed punria Chow diet for 1 wk. After 1 wk this diet was replaced by a 68% by weight diet of sugar or starch (wheat, rice or potato) and 5% fat. Wheat starch was also fed at 49% in a diet containing 20% fat. Rats fed sugar diets developed more mammary tumours than those fed starch diets, of both low and high levels of dietary fat. These results are consistent with epidemiological data showing that age-adjusted breast cancer mortality in humans is positively correlated with sugar intake and negatively correlated with intake of complex carbohydrates (4).

Other comments

The effects of ozone and soil water availability on the portioning and translocation of carbon assimilates were studied in Douglas fir (*Pseudotsuga menziesii*) seedlings exposed to 0 and 106 μg m^{-3} or 0 and 514 μg m^{-3} ozone for 8 hr day^{-1} for 9 days. The dynamics of carbon from assimilated $^{14}CO_2$ were followed. No interactions between ozone and soil water content were observed. Total starch content in needles was reduced by low soil water content, but was unaffected by ozone. Translocation of carbon to the root-soil compartment was additively affected by ozone and low soil water content (2).

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S111 stearamine

$$CH_3(CH_2)_{16}CH_2NH_2$$

$C_{18}H_{39}N$ **Mol. Wt.** 269.51 **CAS Registry No.** 124-30-1

Synonyms octadecylamine; 1-octadecanamine; Adogeren 142; Alamine 7; 1-aminooctadecane; Crodamine 1.18D; Farmin 80; stearylamine

EINECS No. 204-695-3 **RTECS No.** RG 4150000

Uses Organic synthesis. Corrosion inhibitor. Flotation agent. Surfactant. Lubricant oil additive. Preparation of pharmaceutical liposomes.

Physical properties

M. Pt. 55-57°C **B. Pt.** 348°C **Flash point** >110°C **Specific gravity** 0.8618 at 20°C with respect to water at 4°C
Volatility v.den. 9.29
Solubility Water: <1 g l^{-1} at 22°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
Predicted LC_{50} (96 hr) fathead minnow 0.2 μg l^{-1} (QSAR modelling system) (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 2400, 3000 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal mouse 250 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral rat, 3000 ppm diet for 89-209 days caused anorexia, weight loss and some histological changes in mesenteric lymph nodes, gastrointestinal mucosa and the liver (4).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (5).

Sensitisation
Reported to be a primary skin sensitiser (species unspecified) (4).

Genotoxicity

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

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 (7).

Any other adverse effects

Dermal application to rats and guinea pigs induced oedema, hyperaemia and necrosis. Chronic exposure caused damage to the liver, kidney, central nervous system and haemopoietic organs. Body growth and diuresis were impaired. Delayed allergy was also induced (8).

Other comments

Identified as a poor substrate for the rat liver monoamine oxidase (*in vitro*) (5).

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S112 stearic acid

$$CH_3(CH_2)_{16}CO_2H$$

$C_{18}H_{36}O_2$ **Mol. Wt.** 284.48 **CAS Registry No.** 57-11-4

Synonyms octadecanoic acid; 1-heptadecanecarboxylic acid; Neo-Fat 18; Stearex Beads; stearophanic acid; Vanicol

EINECS No. 200-313-4 **RTECS No.** WI 2800000

Uses For coating pills, for suppositories and ointments. In the manufacture of stearates of metals, candles, insulators. In cosmetics.

Occurrence As glyceride in animal fats and vegetable oils. Primary component of the aerosol emissions from meat-cooking (that contributes ≤21% of the primary fine carbon particle emissions in the Los Angeles area) (1). In airborne particulates (2).

Physical properties

M. Pt. 69-70°C **B. Pt.** 383°C **Flash point** 196°C (closed cup) **Specific gravity** 0.847 at 70°C

Volatility v.p. 1 mmHg at 173.7°C ; v.den. 9.80

Solubility Organic solvents: acetone, amyl acetate, benzene, carbon disulfide, carbon tetrachloride, chloroform, ethanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} guppy 14 mg l^{-1} (form unspecified) (3).

Invertebrate toxicity
Delayed the starter acidification activity of dairy starter cultures (4).

Bioaccumulation
Incorporated in animal fat (5).

Environmental fate

Nitrification inhibition
Non-inhibitory of NH_3 oxidation by *Nitrosomonas* sp. at 100 mg l^{-1} (6).

Anaerobic effects
An inhibitory effect on methanogenic bacteria in an up-flow anaerobic sludge bed reactor (7).

Degradation studies
Fermented by an anaerobic obligately syntrophic fatty acid degrading acetogenic bacterium (probably *Syntrophomonas* sp.) in co-culture with a H_2-utilising methanogen to methanol, propionic acid and acetic acid. Calcium chloride was an essential component to the medium for growth (8).
BOD_5 1.44 mg O_2 l^{-1} (9).
BOD_5, 4% ThOD; COD, 30% ThOD (10).
Wastewater treatment methods (bench-scale activated sludge, fill and draw operations) after: 6 hr, 0.2% ThOD; 12 hr, 0.6% ThOD; 24 hr, 1.3% ThOD (11).
$t_{1/2}$: silt loam, 2.0-39 days; loam, 4.1 days; sandy loam, 3.5 days; and compost, 0.7 day (12).

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse, rat 23, 21.5 mg kg^{-1}, respectively (13).
In dogs, 10 mg kg^{-1} administered intravenously had no haemodynamic effect (14).

Metabolism and toxicokinetics
Incorporated into plasma lipids and body store of fat in humans, following dietary intake (15).

Irritancy
Non-irritant and safe in present practice of use and concentration in cosmetics, based on animal and human data (16).

Other comments

In domestic sewage effluent, 0.05 mg l^{-1} (17).
Autoignition temperature 395°C.

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S113 stearyl alcohol

$$CH_3(CH_2)_{16}CH_2OH$$

$C_{18}H_{38}O$ **Mol. Wt.** 270.50 **CAS Registry No.** 112-92-5

Synonyms 1-octadecanol; octadecan-1-ol; octadecyl alcohol; stenol; Alfol 18 NF; Adol 61 NF; Hyfatol 18-95

EINECS No. 204-017-6 **RTECS No.** RG 2010000

Uses Used in cosmetics at concentrations of <0.1 to >50% (1).
Plastics processing lubricant.

Physical properties

M. Pt. 60-61°C (99% pure) **B. Pt.** 336°C; 170-171°C at 2 mmHg (99% pure) **Flash point** 170°C
Specific gravity 0.8124 at 59°C **Partition coefficient** log P_{ow} 8.22 (calc.) **Volatility** v.p. 1 mmHg at 150.3°C
Solubility Water: 3 mg l^{-1} at 34°C. Organic solvents: acetone, alcohol, benzene, chloroform, ether

Ecotoxicity

Invertebrate toxicity
A 21-day test in daphnids indicated that stearyl alcohol may be toxic at a range of between 1 and 3 mg ml^{-1} (2).

Environmental fate

Degradation studies
Microorganisms isolated from cosmetic products and some species of *Penicillium*, *Candida*, and *Pseudomonas* easily utilised stearyl alcohol as sole source of carbon (3).
Wastewater treatment: bench-scale activated sludge, fill and draw operations, after 6 hr 0.3% of ThOD, after 12 hr 0.5% of ThOD, after 24 hr 0.3% of ThoD (4).

Adsorption and retention
Binds firmly to sediments (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 20 g kg^{-1} (5).
LD_{50} implant mouse 1000 mg kg^{-1} (neoplastic effects) (6).

Irritancy
Produced minimal eye irritation in rabbits and minimal to mild cutaneous irritation (1).

Sensitisation
No evidence of contact sensitisation or blackhead development. Clinical patch testing indicated a very low order of skin irritation potential and sensitisation. No evidence of photosensitisation (1).

Genotoxicity

Non-mutagenic in the Ames test and mouse bone marrow micronucleus test (7).
Non-mutagenic in *Escherichia coli* strain WP2 (8).
Non-mutagenic in *Salmonella typhimurium* histidine autotrophs his TA98, his TA100, his TA1535, his TA1537, his TA1538 (9).

Other comments

Metabolism of stearyl alcohol in rats described (1).
Free fatty acids occur as lipid components of *Escherichia coli* K-12. In aerobically grown cells the major alcohols were identified as 1-tetradecanol (18%), 1-hexadecanol (28%), 1-octadecanol (14%), and 2-pentadecanol (27%) (10).

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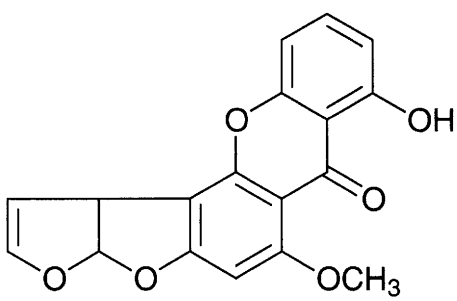
S114 sterigmatocystin



$C_{18}H_{12}O_6$ **Mol. Wt.** 324.29 **CAS Registry No.** 10048-13-2

Synonyms 3a,12c-dihydro-8-hydroxy-6-methyl-7*H*-furo[3′,2′:4,5]furo[2,3-*c*]xanthen-7-one

Occurrence Produced by *Aspergillus versicolor, A. nidulans, A. aurantio-brunneus, A. quadrilineatus,* and *A. ustus* (1).

Physical properties

M. Pt. 246°C (decomp.)

Solubility Organic solvents: sparingly soluble in most organic solvents; readily soluble in chloroform, dimethyl sulfoxide, pyridine

Occupational exposure

UN No. 2811

Ecotoxicity

Fish toxicity

Rainbow trout embryos (14-day-old) 0.5 ppm for 1 hr resulted in a 13% incidence of hepatocellular carcinomas in survivors after 1 yr (2).

Mammalian & avian toxicity

Acute data

Chicks (1-day-old) administered 100 μg died on day 2, whereas chicks administered ≤ 10 μg survived (3).
LD_{50} intraperitoneal chicks 10.0-14.0 mg kg^{-1}. Most deaths occurred between 9 and 21 hr following injection. Autopsies showed haemorrhage, foci of degeneration, and necrosis with fibroblastic proliferation in sinusoids of the liver and tubular degeneration and necrosis of the kidneys (4).
LD_{50} oral rat, ♂ 166, ♀ 120 mg kg^{-1} body weight (5).
LD_{50} intraperitoneal ♂ rat 60-65 mg kg^{-1} body weight (5).
LD_{50} intraperitoneal vervet monkey 32 mg kg^{-1} body weight (6).

Sub-acute and sub-chronic data

Chicks (1-day-old) administered ≤500 μg as a single dose or on different days showed suppressed growth and signs of toxicity in the liver, kidney, heart and brain (3).
Intraperitoneal weanling rats (55 day) 0.5 mg kg^{-1} on alternate days. Blood glycogen synthetase, lactate dehydrogenase and hexokinase activities decreased and glycogen phosphorylase activity increased. Also, alanine transaminase, aspartate transaminase and γ-glutamyl transferase activities in the blood increased and γ-glutamyl transferase activity in the liver increased. Liver glycogen levels decreased and blood sugar levels increased. Neoplastic changes occurred in the liver (7).
Chicks were administered 5 successive intraabdominal injections on days 11, 13, 15, 17 and 19 after birth. 0.5 mg and 0.7 mg per injection caused reduced growth and a decrease in the relative size of the bursa of Fabricius. Elevated serum aspartate aminotransferase activity and numbers of circulating granulocytes were seen, but depressed concentrations of total serum proteins, albumin, potassium, and total numbers of circulating white blood cells and agranulocytes. Liver and kidneys showed degenerative changes and the higher dose caused peritonitis (8).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (9).
Oral mice (58 wk) 5 mg sterigmatocystin or 5 mg *Aspergillus versicolor* culture kg^{-1} diet for 2-wk periods, alternating with 2-wk periods of control diet. Of the animals that survived 30 or more wk, 21/25 treated with pure sterigmatocystin, 33/55 treated with *Aspergillus versicolor*, and 4/37 controls developed pulmonary adenomas. Pulmonary adenocarcinomas occurred in 9/25 and 3/55 treated mice, but not in controls (10).
Oral Wistar rats (52 wk) 0.15-2.25 mg day^{-1} in diet (or via gavage). Of the animals that survived 42 or more wk, 39/50 developed hepatocellular carcinomas within 123 wk. No liver tumours were seen in controls (6).
Dermal ♂ Wistar rats (70 wk) 1 mg sterigmatocystin 2 × wk^{-1}. A significant number of animals developed skin papillomas and carcinomas and hepatocellular carcinomas. No liver or skin tumours occurred in controls (11).
Subcutaneous rats (65 wk) 0.5 mg 2 × wk^{-1} for 24 wk. Local sarcomas were seen in 3/6 rats by 65 wk. No malignant tumours occurred in 6 control rats (12).

Metabolism and toxicokinetics

Twelve hours after a single intraperitoneal injection of 6.4 mg ^{14}C-labelled sterigmatocystin to rats, 5.6% of the activity had appeared in the urine, 67% in the faeces and gastro-intestinal tract and 11% in the liver (13).
Following administration of [^{3}H]sterigmatocystin to rats the highest concentration of radioactivity in the serum occurred after 3 hr. Half-lives of distribution and excretion were 0.51 hr and 43.9 hr, respectively. 56.5% of the

radioactivity administered had been excreted in the faeces and 20.1% in the urine after 48 hr. Radioactivity was found mainly in the liver, stomach, kidney, duodenum and lung and, to a lesser extent, in fat, muscle, testis, rectum and bone. The authors propose that the major route of excretion may be via the bile (14).

Genotoxicity

Saccharomyces cerevisiae expressing cytochrome P450 CYP2B1 showed a dose-dependent increase in mutation frequency up to 4-fold when exposed to sterigmatocystin. No increase was seen in control cells. The authors propose that CYP2B1 converts sterigmatocystin into its mutagenic, epoxide form (15).
Intraperitoneal rats 0.1 mM kg^{-1} showed an increased incidence of chromosome aberrations (chromatid breaks and gaps) in bone marrow cells which peaked at 12 hr after injection and decreased gradually to the original level after 96 hr (16).

Other comments

Carcinogenic risk to man evaluated (9).

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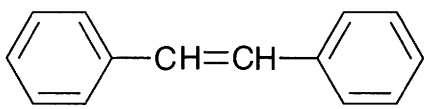
S115 stilbene



$C_{14}H_{12}$ **Mol. Wt.** 180.25 **CAS Registry No.** 588-59-0

Synonyms 1,1'-(1,2-ethenediyl)bisbenzene; bibenzal; bibenzylidene; 1,2-diphenylethene; 1,2-diphenylethylene

EINECS No. 209-621-3 **RTECS No.** WJ 4925000

Uses Nutritional aid in agriculture. Chemical intermediate, particularly in dyes manufacture.

Physical properties

M. Pt. 124°C (*trans*); solidifies –5°C (*cis*) **B. Pt.** 306-307°C at 760 mmHg (*trans*); 135°C at 10 mmHg (*cis*)
Specific gravity 0.9707

Ecotoxicity

Fish toxicity

No adverse effects seen with threespine stickleback, steelhead trout and sockeye salmon kept in 10 mg l^{-1} for 24 hr. Water characteristics: total hardness, 61-120 mg l^{-1}; methyl orange alkalinity, 151-183 mg l^{-1}; total dissolved solids, 160-175 mg l^{-1}; pH 7.1 (form unspecified) (1).

No adverse effects seen with brook trout, bluegill sunfish and goldfish exposed to 5 ppm for 24 hr (2).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 1150 mg kg^{-1} (3).

LD_{50} intravenous mouse 34 mg kg^{-1} (3).

Metabolism and toxicokinetics

Metabolised by several species (no further details given) (4).

Covalently bound to rat liver microsomal protein (5).

Rabbit liver microsomes cleave the ethylenic linkage to produce benzoic acid (6).

Other comments

No human hazard predicted (4).

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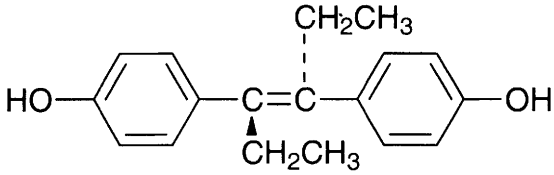
S116 stilbestrol



$C_{18}H_{20}O_2$ **Mol. Wt.** 268.36 **CAS Registry No.** 56-53-1

Synonyms (*E*)-4,4′-(1,2-diethyl-1,2-ethenediyl)bisphenol; α,α′-diethyl-4,4′-stilbenediol; *trans*-diethylstilbestrol; Agostilben; Bio-DES; Cyren; Di-estryl; 4,4′-dihydroxydiethylstilbene; DES; Oestromenin

EINECS No. 200-278-5 **RTECS No.** WJ 5600000

Uses In replacement therapy for oestrogen deficiency. Control of menstrual disorders. Post-coital contraceptive. Antineoplastic agent.

Physical properties

M. Pt. 169-172°C

Solubility Water: practically insoluble. Organic solvents: acetone, chloroform, diethyl ether, dioxane, ethyl acetate, ethanol, methanol, arachis oil, olive oil

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat, mouse 34, 67 mg kg^{-1}, respectively (1,2).

LD_{50} intravenous mouse 630 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (4).

Subcutaneous hamster, implantation of a single pellet of 15 mg induced hepatocellular carcinomas (5).

Oral mouse (26 wk) 320 or 640 ppb diet. Mammary adenocarcinomas developed in 96% of treated animals (6).

Oral ♀ mouse (2 yr) 0, 10, 100 or 500 μg kg^{-1} diet. Adenocarcinomas of the cervix, mammary gland and uterus, carcinomas of the vagina, and osteosarcomas of the cranium and sternum were observed (7).

Subcutaneous mouse (12 month) single injection of 10 or 100 mg kg^{-1} induced an increased incidence of ovarian cystadenomas in ♀ mice given the high dose (8).

Subcutaneous mouse (16 month) implantation of 0.2-3.0 mg induced scrotal hernias, interstitial-cell tumours of the testes, mammary tumours and lymphoid tumours (9).

Prenatal exposure of mouse (12 month); offspring of mothers given single intraperitoneal injections of 10 mg kg^{-1} suffered an increased incidence of papillary adenomas of the lung and tumours of the ovary (8).

Mice exposed prenatally to diethylstilbestrol can transmit a carcinogenic influence to the next generation (DES-lineage mice) when mated to control mice. The persistence of this effect was studied one generation further (DES-lineage-2 mice) by mating DES-lineage ♀ mice to ♂ controls. The frequency of tumours in DES-lineage-2 mice was not significantly lower than in DES-lineage mice from a previous experiment (10).

Subcutaneous mouse (13 month) 5 μg day^{-1} for the first 5 days after birth, extensive adenosis was observed, comprising most of the squamous metaplasia (11).

Intravaginal mouse, 1-4 μg 3 × wk^{-1} in implanted pellets for up to 37 wk caused an increased incidence of epidermoid carcinomas of the vagina and/or cervix (12).

Subcutaneous ♂ rat (14 month) single injection of 20 mg induced tumours and hyperplasia of the pituitary (13).

Subcutaneous ♂ hamster (9 month) 0.6 mg 3 × wk^{-1} resulted in renal carcinomas in all surviving animals. Hyperplastic and neoplastic changes were also observed in the pituitaries (14).

Prenatal exposure of hamster, progeny of both sexes of mothers given 1 or 2 intragastric doses of 20 or 40 mg kg^{-1}

on days 14 and 18 of gestation developed a high incidence of metaplastic, dysplastic and neoplastic lesions in various segments of the genital tract (15).
Induced tumours in uterus, cervix and mammary gland of test animals; induced tumours in vagina and uterus of humans (16).

Teratogenicity and reproductive effects

Subcutaneous rat 0.015-0.6 mg kg^{-1} on days 13, 16, 18 and 20 of gestation and/or 0.2-10 mg kg^{-1} for 3 wk *post partum*. In ♀ offspring hypospadia and urethrovaginal cloaca formation were seen. In ♂ offspring hypospadia, phallic hypoplasia, inhibition of the growth and descent of testes, as well as abnormalities of Wolffian derivatives were observed (17).
Oral rhesus monkey 1 mg day^{-1} on day 21 of gestation to delivery, resulted in vaginal ridging and/or cervical hooding in offspring. In some cases vaginal adenosis was also observed. No vaginal or cervical adenocarcinomas had been observed by year 6 of observation (18).
Teratogenic effects have been observed in the daughters of women exposed to diethylstilbestrol during pregnancy. These include transverse fibrous cervical and vaginal septa, vaginal adenosis and cervical ectropion. Non-malignant structural changes have also been reported in the reproductive tract of ♂ children (19).

Metabolism and toxicokinetics

Following injection into hamsters, DNA adducts were formed in the kidney, liver and testes. Adduct concentrations were 4-6 × higher in ♀ than in ♂ hamsters. Diethylstilbestrol-4,4'-quinone was identified as the major reactive intermediate metabolite responsible for the genotoxic activity of diethylstilbestrol (20).
~ 40% of ^{14}C-diethylstilbestrol injected into human volunteers was recovered from the urine within 24 hr, glucuronides representing 90% of the radioactivity; of the glucuronide conjugates, 70% were derived from diethylstilbestrol, 10% from dienoestrol and 20% from ω-hydroxydienoestrol (21).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with and without metabolic activation negative (22).
Saccharomyces cerevisiae gene conversion, with and without metabolic activation negative (23).
Drosophila melanogaster somatic mutation assay positive (24).
In vitro L5178Y mouse lymphoma forward mutation assay negative (25).
In vitro human and rat lymphocytes DNA fragmentation and DNA repair assays positive (26).
In vivo mouse micronucleus assay negative (27).

Other effects

Other adverse effects (human)

Exposed women (4 studies) have shown an increased risk of breast cancer. In each study it was indicated that there may be a latent period of 15-20 yr. These studies also suggested a link with the occurrence of cancer of the ovary, colon and rectum (28-31).
Some data indicate a greater frequency of abnormalities of the reproductive tract of prenatally exposed men and a number of unusual tumours have also been reported in women exposed to diethylstilbestrol *in utero* (4,32).
A case of a Leydig-cell tumour has been reported in a man treated with 1 mg day^{-1} for 2.5 yr (33).
Cases of a hepatic angiosarcoma, a hepatoma and 3 renal carcinomas have been reported in exposed men (19).

Other comments

Residues have been isolated from beef and sheep livers and some water supplies (19).
Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity, teratogenicity, mutagenicity and metabolism of diethylstilbestrol reviewed (19).
Inhibits ATPase (34).
Veterinary growth promoter; this use has been banned in some countries (35).
Oestrogenic activity is reviewed (36).

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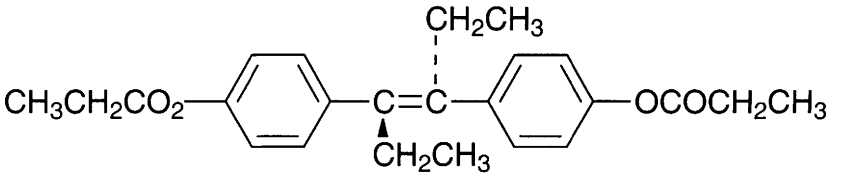
S117 stilbestrol dipropionate



$C_{24}H_{28}O_4$ **Mol. Wt.** 380.48 **CAS Registry No.** 130-80-3

Synonyms diethylstilbestrol dipropionate; phenol, 4,4'-(1,2-diethyl-1,2-ethenediyl)bis-, dipropanoate, (*E*)-; 4,4'-stilbenediol, α,α'-diethyl-, dipropionate, (*E*)-; Clinestrol; Estilbin; Orestol

EINECS No. 204-995-4 **RTECS No.** LP 6330000

Uses Oestrogenic hormone formerly used in human and veterinary medicine. No longer permitted as an anabolic steroid and growth promoter.

Physical properties

M. Pt. 104-108°C

Solubility Organic solvents: acetone, chloroform, vegetable oils

Ecotoxicity

Toxicity to other species

When 40-200 μg l^{-1} diethylstilbestrol dipropionate was injected subcutaneously into frogs, neoplasms of the haematopoietic tissue and liver were observed (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (2).

Diethylstilbestrol has been tested extensively for carcinogenicity by oral and other routes, and consistently produced positive results (3).

Diethylstilbestrol dipropionate administered to rats 20 mg rat^{-1} subcutaneously by single injection induced tumorous enlargement of pituitaries at 406 days and pituitary hyperplasia (4).

Teratogenicity and reproductive effects

Intraperitoneal mice (day-17 of gestation) 100 mg kg^{-1} induced abortion (5).

Prenatal exposure to diethylstilbestrol in mice is associated with poor semen quality, prostatic disease, cryptorchidism and testicular neoplasia (6).

Metabolism and toxicokinetics

The compound is readily absorbed from the gastro-intestinal tract and slowly inactivated (species unspecified) (7).

Some of the compound is converted directly into a glucuronide which is secreted into bile and hydrolysed by intestinal bacteria to yield free diethylstilbestrol which is then reabsorbed (3).

Species variations in metabolism have been noted, with cattle and mice eliminating most metabolites in faeces, whereas in humans, metabolites are found in urine and faeces (7-9).

The liver is the principal site of metabolism, with oxidative metabolism being enhanced by phenobarbitone pretreatment (10,11).

Genotoxicity

Saccharomyces cerevisiae induction of mitotic chromosome loss negative (12).
In vivo mice bone marrow sister chromatid exchanges negative; induced increase in aneuploidy and polyploidy but did not induce micronuclei (5).

Other effects

Other adverse effects (human)
Stilbestrol has been associated with production of renal and liver carcinomas in men and increased incidence of breast cancer in women (7).
Induction of adenocarcinomas and vaginal carcinomas in ♀ offspring of women treated with stilbestrol during pregnancy has been well documented and non-malignant structural changes in ♂ children have also been reported (3,7).

Other comments

Extensive studies of teratogenicity, carcinogenicity and genotoxicity have been undertaken with diethylstilbestrol (3,13).
Metabolism differs between species and has been studied extensively (3).
Review entitled 'Are estrogens carcinogenic during development of the testes?' (6).

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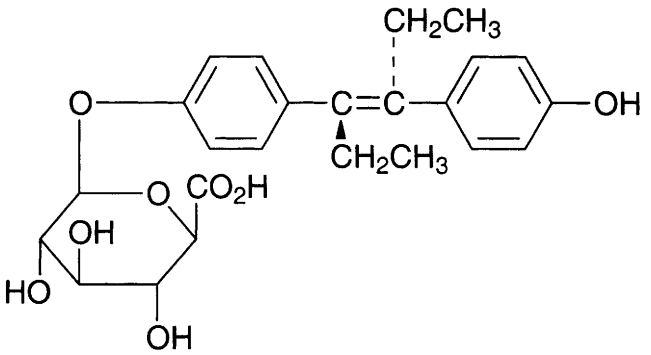
S118 stilbestrol monoglucuronide



$C_{24}H_{28}O_8$ **Mol. Wt.** 444.48 **CAS Registry No.** 2408-40-4

Synonyms diethylstilbestrol monoglucuronide; β-D-glucopyranosiduronic acid, 4-[1-ethyl-2-(4-hydroxyphenyl)-1-butenyl]phenyl, (*E*)-; β-D-glucopyranosiduronic acid, *p*-(α,β-diethyl-*p*-hydroxystyryl)phenyl, (*E*)-

EINECS No. 219-310-4

Mammalian & avian toxicity

Teratogenicity and reproductive effects

After administration of stilbestrol to pregnant mice, the glucuronide is present in both maternal and foetal liver (1).

Metabolism and toxicokinetics

Following administration of diethylstilbestrol to humans, 25% of dose can be eliminated in urine as glucuronide. Additional glucuronide can be extracted from faeces (2).

Some of the glucuronide secreted into the gastro-intestinal tract in bile is hydrolysed by bacteria and the free diethylstilbestrol reabsorbed (3).

In mice and cattle, after administration of diethylstilbestrol, the glucuronide is largely eliminated in faeces (4-5).

Other comments

Metabolite of diethylstilbestrol salts, excreted in bile of humans and animals treated with diethylstilbestrol preparations and related compounds (6,7).

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S119 Stoddard solvent

CAS Registry No. 8052-41-3

Synonyms naphtha safety solvent; varnoline; white spirit

EINECS No. 232-489-3 **RTECS No.** WJ 8925000

Uses Solvent as diluent for paint coatings, printing ink, rubber and cements. As dry-cleaning solvent. Degreasing agent. Solvent for herbicides and pesticides in aerosols.

Physical properties

B. Pt. 200-300°C **Flash point** 37.8-148.9°C **Specific gravity** 0.768-0.820 at 15.6°C
Solubility Organic solvents: miscible with absolute ethanol, benzene, diethyl ether, chloroform, carbon tetrachloride, carbon disulfide

Occupational exposure

SE-LEVL ~50 ppm (300 mg m^{-3}) **SE-STEL** ~100 ppm (600 mg m^{-3})
US-TWA 100 ppm (525 mg m^{-3})

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)

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 0.15 ml for animals weighing 30 g (1).
Inhalation rat (8 hr) no deaths occurred at saturated vapour (2).
No ill-effects concentration (8 hr) inhalation rat, dog 2.4, 2.9 mg l^{-1}, respectively (2).

Sub-acute and sub-chronic data
During a 66-day inhalation period at 0.48-1.9 mg l^{-1} no statistically significant indications of toxicity stress were observed in dogs (2).

Teratogenicity and reproductive effects
Not regarded as teratogenic, hazardous in pregnancy, embryotoxic or capable of causing infertility in men (3).

Irritancy
Non-irritating to the human eye (4).
Defatting, scaling and drying of human skin occurs on direct contact (5).
Human volunteers exposed by inhalation to 0.14 mg l^{-1} showed no irritation. 1/6 had slight and transitory eye irritation at 0.85 mg l^{-1}. At 2.7 mg l^{-1} all 6 experienced eye irritation; three had tears. Slight dizziness was reported in 2 volunteers. All effects had disappeared within 15 min of the end of the exposure (2).

Sensitisation
Dermatitis may develop in humans (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1530, TA1535, TA1537, TA1538 with and without metabolic activation negative (1).
In vitro human lymphocytes sister chromatid exchange negative (1).
In vivo mouse bone marrow cells micronucleus test negative (1).

Other effects

Other adverse effects (human)

Abuse of solvent naphthas in 'glue sniffing' and deaths have occurred when used as medicinal rubbing solutions (3).

Increasing exposure to vapours leads to headaches, dizziness, drunkenness and convulsions. At very high concentrations unconsciousness and death have occurred (2,6).

Permeates the skin causing systemic disease. Frequent cleaning of hands has led to liver and bone marrow damage (7,8).

Not particularly toxic by ingestion; caused gastro-intestinal disturbance (3).

Vomiting followed by aspiration of the liquid to the lungs may result in oedema and chemical pneumonitis (9).

In humans, inhalation is the primary route of exposure. Symptoms of toxicity include central nervous system effects ranging from dizziness and headache to impaired performance of neuropsychological tests. In severe cases, chronic toxic encephalopathy has been diagnosed. The main findings from clinical studies of exposed workers include decreased erythrocyte, leucocyte, and platelet counts, and increased mean corpuscular volume (10).

Any other adverse effects

Inhalation rat (7 hr) at saturated vapour showed no increase in erythrocyte fragility (2).

Other comments

Most manufactured white spirit is eventually released to the environment, where it largely partitions to the atmosphere and undergoes photodegradation. Exposure in the general environment is likely to be low, given the volatility of the lower molecular weight alkane and aromatic components of white spirit and sorption to soil and sediment of the higher molecular weight alkanes and cycloalkanes (10).

Reviews on experimental toxicology, human health effects, environmental effects, ecotoxicology, exposure levels and workplace experience listed (11).

Environmental health criteria reviewed (10).

Consists of 30-50% paraffins (mainly nonanes and decanes), 30-45% naphthenes and 10-20% aromatics (mainly mesitylene).

Autoignition temperature 200-260°C

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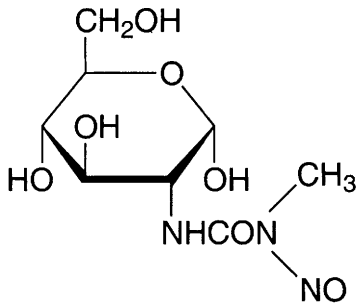
S120 streptozocin



$C_8H_{15}N_3O_7$ **Mol. Wt.** 265.22 **CAS Registry No.** 18883-66-4

Synonyms streptozotocin; 2-deoxy-2-[[(methylnitrosoamino)carbonyl]amino]-D-glucose; D-glucopyranose, 2-deoxy-2-(3-methyl-3-nitrosoureido)-; STRZ

EINECS No. 242-646-8 **RTECS No.** LZ 5775000

Uses Antibiotic, anticancer drug. To produce experimental diabetes in laboratory animals.
Occurrence Produced by *Streptomyces achromogenes*.

Physical properties

M. Pt. 115°C (decomp.)
Solubility Water: soluble in water. Organic solvents: lower alcohols, ketones

Environmental fate

Abiotic removal
In aqueous solution maximum stability is at pH 4. Rapid decomposition occurs at other pH values. Decomposition to diazomethane occurs at alkaline pH (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 264 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 335 mg kg^{-1} (3).
LD_{50} intraperitoneal ♀ mouse 360 mg kg^{-1} (4).
LD_{50} intravenous ♂ dog, ♀ mouse 50, 275 mg kg^{-1}, respectively (4).

Sub-acute and sub-chronic data
Single intraperitoneal injection of 50 mg kg^{-1} to rat. Blood glucose levels were significantly increased at 1, 3 and 6 months after the dose. At 1 month increased nuclear heterochromatin and contraction of nucleoli had occurred in the pancreatic exocrine cell. Other effects included atrophy of Golgi apparatus, lamellated granular cytoplasmic reticulum and damaged pancreatic exocrine cell, giving rise to residual bodies and fatty droplets and showing an intracellular crystalline structure. Pancreatic endocrine A cells increased in number while the B cells were damaged to necrosis and reduced in number. The rats suffered severe diabetes and ultrastructural alterations of the pancreatic exocrine and endocrine cells (5).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (6).
May reasonably be anticipated to be a carcinogen (7).
A single intravenous injection to Holtzman rats of 50 mg kg^{-1} body weight led to 5 ♂ and 1 ♀, out of 27 animals, developing kidney tumours (8).

13 hamsters, from a group of 35, developed liver tumours. The parenchyma (hepatomas) and biliary epithelium were mainly affected, but within the liver 3 sarcomas were seen (details unspecified) (9).

Teratogenicity and reproductive effects

Wistar rats were given the compound on days 16-20 of gestation (route unspecified). Severe lesions in the maternal thymus and increased ATP and AMP hydrolysis in the thymus cortex were seen. The maternal and foetal liver, kidneys, lung and spleen were unaffected (10).

Metabolism and toxicokinetics

Parenteral administration leads to concentration in the liver and kidney of mice, dogs, cats, rats and monkeys. In the dog, retention within the liver lasts for many hours after it can no longer be detected in the blood. Absorption from the gastro-intestinal tract is high in mice, slight in monkeys and zero in dogs (11).

Genotoxicity

Salmonella typhimurium TA97, TA100 without metabolic activation positive (12).
Escherichia coli PQ37 SOS Chromotest without metabolic activation positive (12).
In vivo mouse bone marrow and thymus DNA synthesis briefly inhibited (13).

Other effects

Other adverse effects (human)

Nephrotoxicity, including fatal irreversible renal failure, severe nausea, altered liver function with occasional severe hepatotoxicity and vomiting reported. Other effects include myelosuppression, diabetogenesis, and hypoglycaemia (14).
Febrile reaction recorded, in which the patient developed confusion, somnolence, hypotension and a rise in rectal temperature to 41.4°C (15).

Any other adverse effects

Transient selective reduction of circulating lymphocytes and cortical thymocytes in mice following single subdiabetogenic dose (13).
Intraperitoneal Wistar rats 65 mg kg^{-1} had a direct toxic effect to the renal proximal convoluted tubules and induced diabetic glomerulonephropathy (16).
In vitro monolayer cultures of rat pancreatic β-cells showed reduced NAD concentration, insulin secretion and an 80% decrease of intracellular ATP level 12 hr after 1 hr exposure. Oxygen consumption of rat liver mitochondria decreased in a time dose-dependent manner and hydroxyl radical generation was increased. A significant reduction was seen in mitochondrial ATP production (17).
Induced cataracts in rat lens with a reduction in water-soluble protein and aldose reductase activity. Levels of glucose, sorbitol and fructose increased, as did the activities of phosphofructokinase, glutathione reductase and glucose 6-phosphate dehydrogenase (18).

Legislation

Land disposal regulated under the US Federal Resource Conservation and Recovery Act (19).

Other comments

Antibiotic action against *Streptococcus mutans* studied (20).
Genetic effects studied in cancer patients and their nurses (one of a suite of drugs given) (21).
Toxic effects reviewed (22).
Induction of diabetes in rats and mice reviewed (23).

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S121 strontium

Sr

Sr **Mol. Wt.** 87.62 **CAS Registry No.** 7440-24-6

EINECS No. 231-133-4 **RTECS No.** WK 7849000

Uses In fireworks and flares. On tracer bullets.

Occurrence Occurs as the sulfate (celestine) or the carbonate (strontianite). Small amounts associated with barium, or calcium minerals. Forms 0.02-0.03% of the Earth's crust. Detected in human tissues.

Physical properties

M. Pt. 757-769°C **B. Pt.** 1366-1384°C **Specific gravity** 2.6 at 20°C **Volatility** v.p. 10 mmHg at 898°C
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal (species unspecified) 90-250 mg kg^{-1} (form unspecified) (1).

Metabolism and toxicokinetics

Migration from maternal to foetal bones occurs (species unspecified) (2).
Excretion and retention vary depending on the route of administration (3).
Absorbed from the human gastro-intestinal tract in limited amounts (4).
Excreted in human breast milk (2).
The average whole-body content of a 70 kg man is 320 mg (5,6).
99% of human body load is stored in bone (7).
Following oral doses of 5-250 mg in adults and children retention was 16.3-22.7% in 2 wk and 10-12% in a month (8).
Renal plasma clearance 7.4-12.7 l day^{-1} in humans (9).

Irritancy
Causes irritation to eyes and prolonged skin contact may cause severe irritation or burns in humans (1). Moderately irritating to the respiratory tract of humans on inhalation (10).

Other effects

Other adverse effects (human)
Ingestion causes gastro-intestinal disorders, painful contractions in limbs and, rarely, myocardial involvement. Epidemiological studies have suggested a correlation between exposure in drinking water and protection from cardiovascular mortality (4).

Any other adverse effects
Death occurs within 1 hr of injection in animal studies (species unspecified) and follows respiratory failure (1).

Legislation

Included in Schedules 4 and 6 (Release into the Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Toxicity reviewed (12).
Soluble in acid and liquid ammonia.

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S122 strontium chromate

$SrCrO_4$

CrO_4Sr **Mol. Wt.** 203.61 **CAS Registry No.** 7789-06-2

Synonyms chromic acid (H_2CrO_4), strontium salt (1:1); C.I. Pigment Yellow 32; deep lemon yellow; strontium yellow

EINECS No. 232-142-6 **RTECS No.** GB 3240000

Uses In pyrotechnics. Corrosion inhibitor in metal protective coatings. Yellow pigment in polyvinyl chloride resins. In electroplating to control sulfate concentration of solution.

Physical properties

M. Pt. decomp. **Specific gravity** 3.895 at 5°C
Solubility Water: 1.2 g l^{-1} at 15°C

Occupational exposure

FR-VME 0.05 mg m^{-3} (as Cr)
SE-LEVL 0.02 mg m^{-3} (as Cr)
UK-LTEL MEL 0.05 mg m^{-3} (as Cr)
US-TWA 0.05 mg m^{-3} (as Cr)
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer – Harmful if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R22, R50/53)
Safety phrases 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 – Avoid exposure – obtain special instruction before use – Restricted to professional users (S45, S60, S61, S53)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3118 mg kg^{-1} (1).
LD_{50} intratracheal rat 16,600 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (applied to hexavalent chromium compounds as a group) (2).
Intramuscular implantation (dose unspecified) in rats led to tumours (unspecified) after 27 months in 15/33 treated animals. No tumours were seen in the controls. Intrapleural implantation caused implantation-site tumours in 17/28 rats at 27 months (tumour type and dose unspecified). Controls showed no tumours (3).
Implantation of 0.25 g (embedded in 0.5 g cholesterol pellets) in the lower left bronchus of rats caused inflammation in most animals by the end of the 2-yr study. 105 bronchial carcinomas were seen in the 200 animals used. No cancers occurred in the controls (4).

Teratogenicity and reproductive effects
Hexavalent chromium (as chromium trioxide) is teratogenic in hamsters (5).

Irritancy
A respiratory and eye irritant; inhalation may cause lung damage in humans. May cause eye damage (6).

Sensitisation
Skin irritant in man causing dermatitis and skin ulcers. Occupationally exposed workers have exhibited skin and nasal lesions (7).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive, with metabolic activation negative. Addition of nitrilotriacetic acid, a chelating agent, gave positive results with and without metabolic activation (8).
In vitro Syrian hamster embryo cells showed dose-response relation in induction of morphological transformation. The transformation frequency was a function of the chromium concentration per cell; strontium played no part in the transforming activity (9).

Other effects

Any other adverse effects
Dystrophy of the kidneys and paresis of the digestive system followed oral administration to rats (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chromium: maximum admissible concentration 50 μg l^{-1} (11).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).
WHO provisional guideline value for chromium in drinking water 0.05 mg l^{-1} (13).

Other comments

Carcinogenicity reviewed (14).
Reviews on experimental toxicology, human health effects, physico-chemical properties and epidemiology listed (15).
Human health effects and experimental toxicology discussed in a review of chromium and its compounds (16).
Soluble in hydrochloric, nitric and acetic acids and in ammonium salts.

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S123 strontium nitrate

$$Sr(NO_3)_2$$

N_2O_6Sr **Mol. Wt.** 211.63 **CAS Registry No.** 10042-76-9

Synonyms nitric acid, strontium salt; strontium dinitrate

EINECS No. 233-131-9 **RTECS No.** WK 9800000

Uses Pyrotechnics (red fire), flares and matches, marine signals.

Physical properties

M. Pt. 570°C **Specific gravity** 2.99 at 25°C
Solubility Water: 709 g l^{-1} at 18°C

Occupational exposure

UN No. 1507 **HAZCHEM Code** 1Z **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1826, 2750 mg kg^{-1}, respectively (1).
LD_{50} intraperitoneal rat 540 mg kg^{-1} (2).
Threshold of acute inhalation toxicity in rats and mice is 74 mg m^{-3} (1).

Sub-acute and sub-chronic data

Rats exposed by inhalation to 45 mg m^{-3} for 30 days at 4 hr day^{-1} showed decreased weight gain and morphological changes in the heart, liver, lungs, kidneys and spleen (3).
Doses of 50 mg kg^{-1} diet to rats had no effect on food intake, weight gain, calcium and phosphorus composition of the skeleton or total bone ash (4).

Irritancy

Irritant of mucous membranes and skin of rabbit (dose and duration unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nitrates: guide level 25 mg l^{-1}; maximum admissible concentration 50 mg l^{-1} (5).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

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S124 strontium phosphide

SrP

PSr **Mol. Wt.** 118.59 **CAS Registry No.** 12504-13-1

Occupational exposure

UN No. 2013 **Conveyance classification** substance which in contact with water emits flammable gas, toxic

Mammalian & avian toxicity

Acute data

LC_{Lo} (2 hr) inhalation cat, guinea pig 173, 288 ppm, respectively (1).
LC_{Lo} (1 hr) inhalation rat 580 ppm (1).

Legislation

Included in Schedules 4 and 6 (Release into the Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

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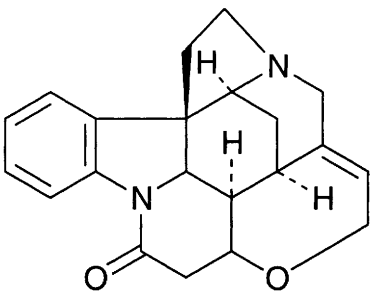
S125 strychnine



$C_{21}H_{22}N_2O_2$ **Mol. Wt.** 334.42 **CAS Registry No.** 57-24-9

Synonyms strychindin-10-one; strychinin

EINECS No. 200-319-7 **RTECS No.** WL 2275000

Uses Rodent poison baits. Has been used as a veterinary tonic and stimulant.

Occurrence From seeds of *Strychnos nux-vomica* and other *Strychnos* (Loganiaceae) species.

Physical properties

M. Pt. 268-290°C (depending on speed of heating) **B. Pt.** 270°C at 5 mmHg

Specific gravity 1.36 at 20°C with respect to water at 4°C

Solubility Water: 143 mg l^{-1}. Organic solvents: amyl alcohol, benzene, chloroform, ethanol, glycerol, methanol, toluene

Occupational exposure

DE-MAK 0.15 mg m^{-3} (inhalable fraction or aerosol)

FR-VME 0.15 mg m^{-3}

UK-LTEL 0.15 mg m^{-3} **UK-STEL** 0.45 mg m^{-3}

US-TWA 0.15 mg m^{-3}

UN No. 1692 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

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)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegilll sunfish, Mississippi silverside 0.87, 0.95 mg l^{-1}, respectively (1).

Spinally transected rainbow trout exposed to acutely lethal dose exhibited an increased cough frequency and decreased ventilation frequency and volume. Oxygen consumption was not significantly affected, but arterial oxygen, pH and carbon dioxide declined. Haematocrit and Hb levels remained constant or tended to increase (2).

Environmental fate

Nitrification inhibition

The hydrochloride caused 75% inhibition of NH_3 oxidation by activated sludge at 175 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral dog, mouse, rat 500, 2000, 2350 μg kg^{-1}, respectively (4,5).
LD_{50} intravenous rat 582-960 μg kg^{-1} (6,7).
LD_{50} subcutaneous mouse, rat 474, 1200 μg kg^{-1}, respectively (8,9).
Lethal dose for rat, man 1-30, 30-60 mg kg^{-1}, respectively (10).

Genotoxicity

Drosophila melanogaster white-ivory test reversions negative (11).

Other effects

Other adverse effects (human)

Stimulates the central nervous system. Early symptoms of poisoning occurring within 15 to 30 min include tremors, slight twitching and stiffness of face and legs. Painful convulsions develop. All sensation is heightened. Few patients survive more than 5 episodes of convulsions, with respiratory arrest causing death. Death has occurred with 16 mg dose. Lactic acidosis, renal failure, hyperthermia and rhabdomyolysis occur as secondary effects arising from the severe spasms (12).

Any other adverse effects

Injection to cat brain caused convulsant effects in a laminar-specific manner (13).
No effect on rats attempting to solve a stressful task in either terms of probability or rapidity (14).
Intravenous administration to rats inhibited bethanechol-stimulated acid secretion in the stomach and was associated with convulsions. Inhibition did not occur in *d*-tubocurarine-paralysed animals (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).
Regulated under US Federal Comprehensive Environmental Response, Compensation and Liability Act and the Federal Occupational Safety and Health Act (18,19).
WHO Toxicity Class Ib (20).

Other comments

Squalane administered orally accelerated the faecal excretion of strychnine in mice (21).
Mechanisms and products of strychnine degradation in soil reviewed (22).
Strychnine (1mM) protects rabbit renal proximal tubule suspensions from a variety of diverse nephrotoxicants. It does not need to be present at the time of toxic insult, cytoprotection is reversible, and the compound acts in the late phase of necrotic cell injury (23).
Hazards reviewed (24).
Reviews on experimental toxicology, human health effects and physico-chemical properties listed (25).

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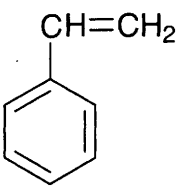
S126 styrene



C_8H_8 **Mol. Wt.** 104.15 **CAS Registry No.** 100-42-5

Synonyms ethenylbenzene; cinnamene; phenethylene; phenylethene; styrol; styrolene; vinylbenzene; vinylbenzol

EINECS No. 202-851-5 **RTECS No.** WL 3675000

Uses In the manufacture of plastics (particularly polymerisation to polystyrene), resins, synthetic rubber and insulators. Solvent.

Occurrence Occurs in sap of styraceous trees, in bituminous-coal and shale-oil.

Physical properties

M. Pt. –30.6°C **B. Pt.** 145-146°C **Flash point** 31°C (closed cup) **Specific gravity** 0.9059 at 20°C
Partition coefficient log P_{ow} 2.95-3.05 **Volatility** v.p. 6.6 mmHg at 25°C (extrapolated) ; v.den. 3.6
Solubility Water: 300 mg l^{-1} at 20°C. Organic solvents: acetone, carbon disulfide, diethyl ether, ethanol, methanol

Occupational exposure

DE-MAK 20 ppm (86 mg m^{-3})
FR-VME 50 ppm (215 mg m^{-3})

JP-OEL 50 ppm (210 mg m^{-3})
SE-LEVL 20 ppm (90 mg m^{-3}) **SE-STEL** 50 ppm (200 mg m^{-3})
UK-LTEL MEL 100 ppm (430 mg m^{-3}) **UK-STEL** MEL 250 ppm (1080 mg m^{-3})
US-TWA 20 ppm (85 mg m^{-3}) **US-STEL** 40 ppm (170 mg m^{-3})

UN No. 2055 (monomer, inhibited) **HAZCHEM Code** 3Y (monomer, inhibited)
Conveyance classification flammable liquid (monomer, inhibited)
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation – Irritating to eyes and skin (R10, R20, R36/38)
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) sheepshead minnow, bluegill sunfish 9.1, 25 mg l^{-1}, respectively (1,2).
LC_{50} (24 hr) goldfish 26 mg l^{-1} (3).
LC_{50} (96 hr) fathead minnow 10 mg l^{-1} (4).
No-observed-effect level, fathead minnow 4.0 mg l^{-1} (4).

Invertebrate toxicity
LC_{50} (96 hr) *Hyalella azteca* 9.5 mg l^{-1}, no-observed-effect level 4.1 mg l^{-1} (4).
Cell multiplication inhibition test *Pseudomonas putida, Scenedesmus quadricauda* and *Entosiphon sulcatum* 72, >200 and >256 mg l^{-1}, respectively (5).
Cell multiplication inhibition test *Uronema parduczi Chatton-Lwoff* 185 mg l^{-1} (6).
LOEC (reproduction) *Microcystis aeruginosa* 67 mg l^{-1} (7).
LC_{50} (48 hr) *Daphnia magna* 23 mg l^{-1} (8).
EC_{50} (48 hr) *Daphnia magna* 4.7 mg l^{-1} (4).
No-observed-effect level *Daphnia magna* 1.9 mg l^{-1} (4).
LC_{50} (24 hr) *Artemia salina* 68 mg l^{-1} (2).
EC_{50} (5 min) *Photobacterium phosphoreum* 5.47 ppm Microtox test (9).
EC_{50} (96 hr) *Selenastrum capricornutum* 0.72 mg l^{-1}, no-observed-effect level 0.063 mg l^{-1} (4).

Bioaccumulation
Bioaccumulation factor for goldfish, 13.5 (10).

Environmental fate

Anaerobic effects
Degraded by methanogenic microbes, including *Enterobacter* and *Clostridium* sp., isolated from anaerobic sewage sludges, to CO_2. Intermediate products were benzoic acid and phenol. No methane production was seen during incubation for 8 months. Degradation was initiated through an oxidation-reduction reaction with the most likely mechanism being the addition of water across the double bond in the alkenyl side-chain (11).

Degradation studies
BOD_5 2.45 mg O_2 l^{-1} adapted sludge; BOD_5, 65% biological oxidation (fresh dilution water), 8% biological oxidation (salt dilution water); COD, 2.88 mg O_2 l^{-1}; and ThOD, 3.07 mg O_2 l^{-1} (12).
In sandy loam and landfill soil degradation reached 87-95% over 16 wk (13).
In subsurface aquifers a degradation rate of 2.3-12% wk^{-1} has been observed (14).
Degraded by mixed propane-utilising bacteria, isolated from soil and lakes, to form styrene oxide (15).
Inoculation of microorganisms from an industrial wastewater lagoon to soils and groundwater at the site of a spill led to 90% degradation within the first 10 wk of operation and reduction from >100 ppm to <100 ppb over the 24-wk period of the study (16).

Abiotic removal
Activated carbon wastewater treatment; adsorbability, 0.028 g g^{-1} C; 88% reduction, influent 180 mg l^{-1}, effluent 18 mg l^{-1} (17).

Volatilisation $t_{1/2}$ from river of 1 m depth, current speed of 1 m sec^{-1} and wind velocity of 3 m sec^{-1} was ~3 hr. Hydrolysis not expected to be significant (18).
Atmospheric $t_{1/2}$ (estimated) 2.5-9 hr (18,19,20).

Adsorption and retention
Low to moderate soil mobility dependent on soil conditions. Has leached in to ground water. Persistence of 2 hr in soil following leakage from drums (14).
K_{oc} values of 270-550 suggest moderate to low soil mobility (21-23).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 316, 5000 mg kg^{-1}, respectively (24,25).
TC_{Lo} inhalation human 600 ppm (duration unspecified) (26).
LC_{50} (4 hr) inhalation mouse, rat 9.5, 24 g m^{-3}, respectively (27,28).
LD_{50} intraperitoneal mouse, rat 660, 898 mg kg^{-1}, respectively (29,30).
LD_{50} intravenous mouse 90 mg kg^{-1} (29).

Sub-acute and sub-chronic data
Rats exposed to 650 or 1300 ppm for 6 months in inhalation study showed no signs of toxicity, only irritation to eyes and nose (31).
Accumulated in brain and perinephric fat of rats exposed by inhalation to 1.3 mg l^{-1} for 2-11 wk for 6 hr day^{-1} wk^{-1}. Lysosomal acid proteinase activity in brain increased from the 9th wk (32).
Inhalation rat 6 hr day^{-1}, 5 days wk^{-1}, for 2 wk or intraperitoneally (3 days) 40 or 400 mg kg^{-1}. Electron microscopy showed diffuse cell damage involving the tracheal, bronchiolar, and alveolar epithelium. In the tracheal epithelium ciliated cells showed vacuolation, detachment of cilia, compound cilia, and blebbing of the apical cytoplasm. Secretory cells showed a reduction in granules; dense bodies and fibrillary inclusions were seen in intermediate and basal cells. Alterations of cytoplasmic components in type II pneumocytes and bronchiolar cells as well as thickness of the alveolar wall was seen. These abnormalities were accompanied by depletion of glutathione in lung tissue (33).
Groups of CD rats (10 ♂s/10 ♀s) were exposed to 0-1500 ppm styrene for 6 hr day^{-1}, 5 days wk^{-1} for 13 wk. High-dose ♂s had reduced body weight and both sexes exposed to ≥1000 ppm styrene showed increased water consumption. Histopathological changes were confined to the nasal passages. Groups of ♂ and ♀ CD-1 and B6C3F1 mice were similarly exposed to 0-500 ppm styrene for 2 wk, and a further group of CD-1 mice was exposed to 0-200 ppm for 13 wk. Liver and lung toxicity was observed, with ♀s more susceptible than ♂s. There were some deaths in ♀ mice at 200 ppm and liver pathology at 150 and 200 ppm. Changes were observed in the lungs of mice exposed to 100-200 ppm styrene and in the nasal passages of all treatment groups. A no-observed-adverse-effect level (NOAEL) was not identified for nasal tract effects in mice; it was 200 ppm in CD rats. For other effects NOAEL was 500 ppm in rats and 50 ppm in mice (34).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (35).
In a cohort study of 15,826 occupationally exposed workers no increase in mortality was observed. There was no increased mortality from haematopoietic and lymphatic cancers overall or from any specific haematological malignancies. In particular, there was no increase in mortality from non-Hodgkin's lymphoma, multiple myeloma, Hodgkin's disease or leukaemia. There was no relation between exposure and any of these haematological malignancies (36).
US National Toxicology Program tested rats and mice via gavage. Negative for rats and ♀ mice, equivocal for ♂ mice (37).
Pregnant mice were given a single dose of 1350 mg kg^{-1} body weight in olive oil by gavage. Neonatal mortality of the offspring was 43%, compared with 2% in olive-oil treated controls. The progeny were then given the same dose weekly for 16 wk. The mothers showed no raised incidence of tumours compared with the olive oil controls. The offspring showed lung tumours, adenomas and adenocarcinomas; 20/23 ♂ and 32/32 ♀ compared with 8/19

and 14/21 in olive oil controls and 34/53 and 25/47 in untreated controls. No differences in cancer incidence at other sites in the body were found (38).
In another study following rats from weaning to 120 wk of age with 500 mg kg^{-1} body weight wk^{-1} by gavage, total tumour incidence was not statistically different from controls (38).

Teratogenicity and reproductive effects

In a study of 511 occupationally exposed women and their children there was no evidence of an association with birth defects, in fact the rates were lower than expected (39).
In occupationally exposed workers, menstrual and ovulatory disorders reported (40).
Rats exposed during pregnancy by inhalation to 1.5-5 mg m^{-3} 4 hr day^{-1} showed embryotoxic effects and a decreased number of newborns (41).
Gavage rat (60 days) 200 or 400 mg kg^{-1} day^{-1}. At the higher dose some marker enzymes for testicular function were altered and spermatozoa number was decreased. Seminiferous tubules degenerated and the lumen lacked sperm (42).
Oral rat 250 or 400 mg kg^{-1} day^{-1} from gestation day 6 to 15 led to decreased maternal weight, decreased foetal weight and increased foetal resorptions at the high dose. Neither dose gave teratogenic effects (43).
Offspring of pregnant rats exposed to 500 ppm exhibited behavioural development retardation and low learning abilities (44).

Metabolism and toxicokinetics

The hepatotoxic and pneumotoxic effects of styrene in mice are associated with its metabolism to styrene oxide (45).
Following multiple inhalation exposure of mice and rats to styrene (200 ppm, 6 hr day^{-1}, 1-5 days) an induction of styrene metabolism occurs, resulting in an increased uptake and(or) clearance for styrene (46).
Detected (levels unspecified) in 8/8 human breast milk samples (47).
Detected at 8-350 ppb in human adipose tissue; 100% of samples tested positive (48).
Metabolised in humans and other mammals in the liver, kidney, lung, skin, and intestine to styrene 7,8-epoxide, which is present in the *R* and *S* enantiomeric forms, and is considered to be directly responsible for the most toxic effects of styrene. The major urinary metabolites derived from the biotransformation of styrene oxide in man are mandelic acid and phenylglyoxylic acid. In rats an alternative pathway has been demonstrated, which involves the conjugation of styrene oxide to glutathione, leading to the excretion of two specific mercapturic acids, *N*-acetyl-*S*-(1-phenyl-2-hydroxyethyl)-cysteine and *N*-acetyl-*S*-(2-phenyl-2-hydroxyethyl)-cysteine (49).
It is a lipophilic molecule that is easily absorbed and crosses the placental barrier. Levels in human foetal and umbilical blood are proportional to those in maternal blood (50).
Following injection to pregnant mice the greatest concentrations of volatile compound were found in the maternal lung, kidney, adipose tissue and brain. The liver, lung, gall bladder, kidney and intestine were sites having a concentration of non-volatile metabolites. Foetal levels were lower than those of the mother. Concentrations of unmetabolised compound and metabolites in the amniotic fluid and placenta were ca. twice foetal levels (51).

Irritancy

500 mg applied to rabbit skin caused well defined erythema and slight oedema (duration unspecified) (52).
Liquid reported to cause conjunctivitis in man (53).
Up to 5 min skin contact in humans should cause no irritation, but over 1 hr irritation, swelling and blistering can occur (54).
Repeated skin contact in humans can result in defatting of the skin, with skin cracking, dermatitis and secondary infection (54).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 without metabolic activation negative (55-57).
Salmonella typhimurium TA100, TA1535 with metabolic activation positive, without negative (58).
Saccharomyces cerevisiae gene conversion homozygosis and reverse mutation without metabolic activation positive (59).
Drosophila melanogaster sex-linked recessives positive (60).
Drosophila melanogaster aneuploidy without metabolic activation negative (61).

In vitro Chinese hamster cells sister chromatid exchange without metabolic activation negative, with positive (62).
In vitro human lymphocytes sister chromatid exchange without metabolic activation positive, with negative (63).
In vitro human cells micronucleus without metabolic activation positive, human lymphocytes chromosomal aberrations without metabolic activation positive (64).
In vivo animal bone marrow chromosomal aberrations negative (65).
In vitro human lymphoctyes chromosomal aberrations and sister chromatid exchange without metabolic activation negative (66).
In vitro human lymphocytes chromosomal aberrations without metabolic activation positive (67).

Other effects

Other adverse effects (human)

No toxicity noted when inhaled at 13 ppm (50 mg m^{-3}) for 6 hr. Exposure to 100 ppm led to slight irritation to the eyes and respiratory tract. Irritation occurred at 500 ppm. Higher concentrations led to depression of the central nervous system.
Tiredness, prolonged reaction time, loss of memory and decreased manual dexterity occur on chronic exposure to 100 ppm. Styrene sickness – pronounced dizziness, loss of appetite and coordination and nausea – occurs at 200 ppm (68).
Occupationally exposed workers showed irritative effects, skin genetic damage and slight neuropathies (69).
Genotoxic damage has been observed in furniture workers who use polyester resin laminating processes and are therefore exposed to styrene. Sister chromatid exchange and micronuclei have been observed in the peripheral lymphocytes (70).

Any other adverse effects

Acute deaths in rats and guinea pigs were due to central nervous system injury. Pneumonia was the cause of delayed deaths following lung irritation with the lungs showing congestion, oedema, haemorrhage and exudation (71).
Hepatic necrosis in hamster reported following intraperitoneal administration 2-3 g kg^{-1} (72).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (73).
WHO guideline value in drinking water 20 μg l^{-1}. At 4-2600 μg l^{-1} is likely to give rise to consumer complaints over odour and taste (74).

Other comments

NIOSH has designated styrene an ototoxin. It can impair hearing by causing hearing loss, ringing in the ears or total deafness and its toxicity can be exacerbated by combined exposure to noise (75).
Very active generator of photochemical smog (76).
Toxicity reviewed (77-80).
Autoignition temperature 490°C.
Found in various wastewater effluents and motor vehicle exhausts. Contaminant of freshwater and air. In cigarette smoke. In food stored in polystyrene containers (81-85).

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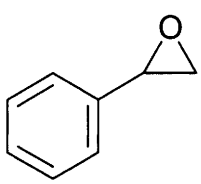
S127 styrene oxide



C_8H_8O **Mol. Wt.** 120.15 **CAS Registry No.** 96-09-3

Synonyms phenyloxirane; (epoxyethyl)benzene; 1,2-epoxy-1-phenylethane; epoxystyrene; phenethylene oxide; styryl oxide; phenyl oxirane

EINECS No. 202-476-7 **RTECS No.** CZ 9625000

Uses In manufacture of styrene glycol and derivatives. In manufacture of epoxy resins, β-phenethyl alcohol, polyols and agrochemicals. In treatment of textiles and fibres.

Physical properties

M. Pt. –35.6°C **B. Pt.** 194°C **Flash point** 79°C (open cup) **Specific gravity** 1.0523 at 16°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.61 **Volatility** v.p. 0.3 mmHg at 20°C ; v.den. 4.1
Solubility Water: 0.3%. Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol, heptane, methanol

Occupational exposure

Supply classification toxic
Risk phrases May cause cancer – Harmful in contact with skin – Irritating to the eyes (R45, R21, R36)
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)

Environmental fate

Abiotic removal
Wastewater treatment: activated carbon adsorbability, 0.19 g g^{-1} carbon; 95.3% reduction, influent 1000 mg l^{-1}, effluent 47 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 1500, 2000 mg kg^{-1}, respectively (2,3).
LC_{Lo} (4 hr) inhalation rat 500 ppm (4).
LD_{50} dermal rabbit 1060 mg kg^{-1} (4).
LD_{50} intraperitoneal rat 460 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Mortality was high in rats inhaling 97 or 300 ppm 7 hr day^{-1} for 3 wk pregestational period and on gestation days 1-19 (6,7).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity in humans, sufficient evidence for carcinogenicity in animals, IARC classification group 2A (8).
BDIV and Sprague-Dawley rats developed significantly increased incidence of forestomach tumours following oral administration (9,10).
In skin painting studies, mice showed no increased incidence of skin tumours (11).

Teratogenicity and reproductive effects
Inhalation exposure during gestation to 15-100 ppm reduced fecundity, foetal weight and length in rats and rabbits and gave rise to ossification defects in rats (6,12,13).
Reduced embryonic viability and malformations reported when administered to hens eggs (14,15).

Metabolism and toxicokinetics
Detected in the venous blood of workers exposed to styrene (16).
Following intraperitoneal injection of styrene to mice the highest concentrations were found in the kidneys, subcutaneous adipose tissue and blood 1-5 hr after administration (17,18).
Hydrolysed microsomal epoxide hydrolase from the liver, kidneys, lungs, intestine, and skin of several mammalian species to styrene glycol (19).
Other metabolic products include mandelic acid and glutathione conjugates (20,21).
Following a single oral dose to rabbits, ~80% was excreted (as metabolites) in the urine (22).
Binds covalently to microsomes, protein and nucleic-acid fractions of rat liver (*in vitro*) and to RNA and DNA in perfused rat liver (23,24).
Metabolism proceeds via styrene glycol to mandelic acid, phenylglyoxylic acid and hippuric acid (25).

Irritancy
Dermal rabbit (24 hr) 10 mg caused well defined erythema and slight oedema (open to the air) (2).
Skin irritant in humans (26).

Sensitisation

Guinea pig skin sensitised by intradermal injection (27).

Caused eye and skin irritation and skin sensitisation in humans (28).

Genotoxicity

Salmonella typhimurium TA100, TA1535 without metabolic activation positive (29-31).

Salmonella typhimurium TA98, TA1537, TA1538 with and without metabolic activation negative (29-31).

Saccharomyces cerevisiae mitotic gene conversion positive (32).

Drosophila melanogaster sex-linked recessive lethal mutations positive (33).

In vitro rat hepatocytes DNA single-strand breaks positive (34).

Mouse lymphoma L5178Y tk^+/tk^- positive (activity reduced by metabolic activation) (35).

Chinese hamster V79 cells forward mutations positive (32).

In vivo mouse induced single-strand breaks positive (32).

In vivo mouse induced single-strand breaks of the DNA in liver, lung, kidney, brain and testis (36).

In vivo mouse bone marrow cells chromosomal aberrations and micronuclei negative (37).

Other effects

Other adverse effects (human)

Inhalation may cause fatigue, headache, weakness, peripheral neuropathy, unsteady gait and central nervous system depression (26).

Human white blood cells exposed to styrene oxide in blood undergo high molecular weight DNA fragmentation. This may be caused by oxidation stress, similar to that caused by hydrogen peroxide (38).

Any other adverse effects

Activities of liver mixed function oxidases and cytochrome P_{450} content decreased following single intraperitoneal dose of 375 mg kg^{-1} body weight to rats (39).

Concentrations of 50 and 200 mg kg^{-1} body weight in rats decreased liver glutathione content (23).

Styrene oxide forms DNA adducts by alkylating purine bases primarily and pyrimidine bases only at higher concentrations. Adducts are found at the N7-, O6- and N2- positions of guanine and the nucleophilic sites of adenine (species unspecified) (40).

Other comments

Tentatively identified in US air samples (41,42).

In effluent from latex and chemical plants (16).

Genotoxicity reviewed (43,44).

Metabolism and pharmacokinetics reviewed (25).

Reviews on experimental toxicology, human health effects, physico-chemical properties and environmental effects are listed (45).

Autoignition temperature 498°C.

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S128 succinic acid

$$HO_2C(CH_2)_2CO_2H$$

$C_4H_6O_4$ **Mol. Wt.** 118.09 **CAS Registry No.** 110-15-6

Synonyms butanedioic acid; amber acid; dihydrofumaric acid; 1,2-ethanedicarboxylic acid; wormwood acid

EINECS No. 203-740-4 **RTECS No.** WM 4900000

Uses In photography. In the manufacture of dyes, lacquers and esters for perfumes and succinates.
Occurrence Found in fungi and lichens.

Physical properties

M. Pt. 185-187°C **B. Pt.** 235°C (decomp.) **Specific gravity** 1.572 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} –0.59 (1)
Solubility Water: 1 g 13 ml^{-1} (cold), 1 g ml^{-1} (boiling). Organic solvents: acetone, diethyl ether, ethanol, glycerol, methanol

Ecotoxicity

Invertebrate toxicity
No toxic effect *Pseudomonas* 125 mg l^{-1}, *Scenedesmus* 1 mg l^{-1} (duration unspecified) (2).
LC_0 *Colpoda* 125 mg l^{-1} (duration unspecified) (2).

Environmental fate

Degradation studies
ThOD, 1.305 mg O_2 l^{-1} (2).
BOD_5, 0.419 mg O_2 l^{-1} (2).
BOD, 35% ThOD (3).
COD, 1.85 mg O_2 l^{-1} (4).
Wastewater treatment (bench-scale activated sludge, fill and draw operations) after: 6 hr, 11.2% ThOD; 12 hr, 27.2% ThOD; 24 hr, 42.2% ThOD (5).
Degraded by *Azospirillum lipoferum* (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2260 mg kg^{-1} (7).

Irritancy
1179 µg instilled into rabbit eye caused severe irritation (duration unspecified) (8).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (9).

Other effects

Other adverse effects (human)
Caused significant physiological changes *in vitro* to the membrane proteins of erythrocytes (10).
Strongly inhibits alveolar macrophages (11).

Any other adverse effects
Causes non-selective glial and neural toxicity when injected into the dorsal hippocampus of rats (12).

Other comments

Detected in municipal wastewater (13).

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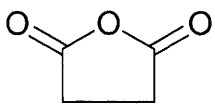
S129 succinic anhydride



$C_4H_4O_3$ **Mol. Wt.** 100.07 **CAS Registry No.** 108-30-5

Synonyms dihydro-2,5-furandione; butanedioic anhydride; 2,5-diketotetrahydrofuran; succinyl oxide; tetrahydro-2,5-dioxofuran; tetrahydro-2,5-furandione

EINECS No. 203-570-0 **RTECS No.** WM 0875000

Uses In manufacture of dyes, resins, polymeric materials, drugs, lubricant additives, photographic chemicals and agricultural chemicals. Used as a food starch modifier.

Physical properties

M. Pt. 119.6°C **B. Pt.** 261°C **Specific gravity** 1.503 **Volatility** v.p. 1 mmHg at 92°C ; v.den. 3.5
Solubility Organic solvents: carbon tetrachloride, chloroform, ethanol

Occupational exposure

Supply classification irritant
Risk phrases Irritating to eyes and respiratory system (R36/37)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the eyes (S2, S25)

Ecotoxicity

Fish toxicity
At 5 ppm killed trout and bluegill sunfish in 23 hr and caused sickness in goldfish within 4 hr. Water characteristics: pH, 7.0; dissolved oxygen, 7.5 ppm; total hardness (soap method) 300 ppm; methyl orange alkalinity, 310 ppm; free carbon dioxide, 5 ppm; temperature 12.8°C (1).

Invertebrate toxicity
Minimal detectable amounts by swarming inhibition of *Azospirillum brasilense* and *Proteus mirabilis* nerve, 0.5 and 0.1 mg ml^{-1}, respectively, and by growth inhibition of *Bacillus thuringiensis* 5.0 mg ml^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 96 mg kg^{-1} (3).
LD_{50} oral rat 1510 mg kg^{-1} (4).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).
Six ♂ rats were injected with 2 mg $animal^{-1}$ 2 × wk^{-1} for 65 wk (total dose, 260 mg). The 3 rats that survived for

93-106 wk showed injection-site subcutaneous sarcomas. Controls had no tumours (6,7).
US National Toxicology Program tested rats and mice via gavage. No evidence of carcinogenic activity (8).
In a 2-yr study 100 mg kg^{-1} given by gavage 5 day wk^{-1} led to 5-11% lower mean body weights (8).

Teratogenicity and reproductive effects
Minimum teratogenic dose, inducing major structural defects, in CD-1 mice 0.30 mmol kg^{-1} day^{-1} (9).

Irritancy
750 μg instilled into rabbit eye caused severe irritation (duration unspecified) (10).
Causes blisters or burns on prolonged skin contact in humans (11).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA135, TA1537 with and without metabolic activation negative (12).
Escherichia coli CHY832 RK-test without metabolic activation positive (13).

Other effects

Any other adverse effects
Necrosis and inflammation of the upper respiratory tract of 3/10 ♂ and 3/10 ♀ rats was seen following gavage administration of 750 mg kg^{-1} (8).

Legislation

No more than 4% may be used in the US for esterifying food starches (14).

Other comments

Reviews on experimental toxicology, human health effects and physico-chemical properties listed (15).

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S130 succinonitrile

$$NC(CH_2)_2CN$$

$C_4H_4N_2$ **Mol. Wt.** 80.09 **CAS Registry No.** 110-61-2

Synonyms butanedinitrile; sucinonitrile; *sym*-dicyanoethane; ethylene cyanide; succinic acid dinitrile; Succinil; Suxil

EINECS No. 203-783-9 **RTECS No.** WN 3850000

Physical properties

M. Pt. 57.15°C **B. Pt.** 265-267°C **Flash point** 132°C

Specific gravity 1.023 at 45°C with respect to water at 4°C **Volatility** v.p. 2 mmHg at 100°C ; v.den. 2.1

Solubility Water: slightly soluble. Organic solvents: acetone, chloroform, dioxane

Ecotoxicity

Toxicity to other species

LD_{Lo} subcutaneous frog 1000 mg kg^{-1} (1).

Environmental fate

Degradation studies

Wastewater treatment (bench-scale activated sludge, fill and draw operations) after: 6 hr, 1.5% ThOD; 12 hr, 2.4% ThOD; 24 hr, 3.8% ThOD (2).

Degraded by the soil bacterium *Pseudomonas putida* (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 129, 450 mg kg^{-1}, respectively (4,5).

LD_{50} intraperitoneal mouse 63 mg kg^{-1} (6).

LD_{Lo} subcutaneous rabbit, dog 36, 150 mg kg^{-1}, respectively (1).

LD_{Lo} subcutaneous pigeon 2200 mg kg^{-1} (1).

No toxic symptoms were seen in mice following inhalation of saturated vapour for 24 hr (7).

Teratogenicity and reproductive effects

Using logistic regression and discriminant analysis, no developmental toxicity in humans predicted.

Developmentally toxic in hamster (no further details given) (8).

Metabolism and toxicokinetics

Metabolised by rat nasal tissue enzymes to cyanide (9).

Other comments

Reviews on experimental toxicology, exposure and human health effects listed (10).

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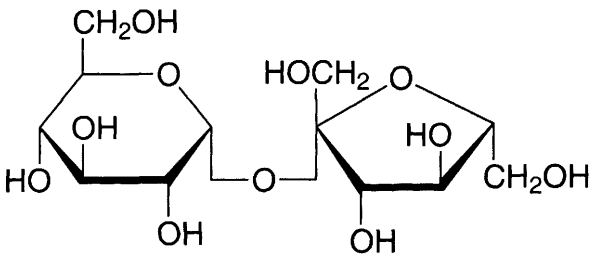
S131 sucrose



$C_{12}H_{22}O_{11}$ **Mol. Wt.** 342.30 **CAS Registry No.** 57-50-1

Synonyms β-D-fructofuranosyl α-D-glucopyranoside; beet sugar; cane sugar; confectioner's sugar; granulated sugar; saccharose; D-sucrose; sugar

EINECS No. 200-334-9 **RTECS No.** WN 6500000

Uses Sweetening agent. Starting material in fermentation for production of alcohols. As a drug preservative. In plastics and cellulose industry. In polyurethane foams. In manufacture of ink and soaps. In wound healing.
Occurrence From sugar cane and sugar beet.

Physical properties

M. Pt. 185-186°C (decomp.) **Specific gravity** 1.587 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} -3.67 (calc.) (1)
Solubility Water: 1 g 0.5 ml^{-1}. Organic solvents: ethanol, methanol

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
BOD^{25}_{35} 0.27 in seawater with cultures of hydrocarbon oxidising bacteria. ThOD, 1.12 mg O_2 l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 29.7 g kg^{-1} (3).
LD_{50} intraperitoneal mouse 14 g kg^{-1} (4).

Metabolism and toxicokinetics
Hydrolysed by sucrase, in the human small intestine, to give glucose and fructose which are then absorbed and metabolised. Excreted unchanged in the urine when given intravenously (5).

Other effects

Other adverse effects (human)

Increases frequency of dental caries (5).

The Panel on Dietary Sugars reviewed evidence on the health effects to the UK population. They found that it may contribute to the development of obesity, which has a significant role in the aetiology of a number of diseases. It was considered not to play a direct causal role in the development of cardiovascular disease, essential hypertension or diabetes mellitus. No specific evidence for effects on psychological function or behaviour were found. The evidence was inadequate to form recommendations in relation to suggested links with other diseases including colorectal cancer, Crohn's disease and renal and bilary calculi (6).

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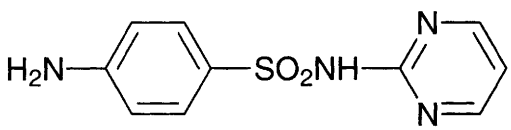
S132 sulfadiazine



$C_{10}H_{10}N_4O_2S$ **Mol. Wt.** 250.28 **CAS Registry No.** 68-35-9

Synonyms 4-amino-*N*-2-pyrimidinylbenzenesulfonamide; *N'*-2-pyrimidinylsulfanilamide; A306; Diazyl; Pirimal; Sterazine; Sulfazin; sulphadiazine

EINECS No. 200-685-8 **RTECS No.** WP 1925000

Uses Antibacterial agent.

Physical properties

M. Pt. 252-256°C

Solubility Water: 200 mg 100 mg^{-1} at pH 7.5, 13 mg 100 mg^{-1} at 37°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1500 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 750 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 1600 mg kg^{-1} (3).

LD_{50} intravenous mouse 180 mg kg^{-1} (4).

Teratogenicity and reproductive effects

When fed to ♂ rats at 10 × the human dose for 6 months, sperm concentration was unaffected and no significant effect on body or testis weight was seen (5).

Metabolism and toxicokinetics

Renal clearance decreased with an increase in dose: 89.3 and 14.8 ml min^{-1} for 500 and 1000 mg dose, respectively; active secretion was the major renal clearance route (6).

Mean elimination $t_{1/2}$ following intravenous administration to pigs was 4.9 hr. Plasma concentration of the unmetabolised compound was higher than that of the metabolites. The main metabolite, the acetylated derivative 4-hydroxysulfadiazine, was detected in the plasma. Acetylation was the major elimination pathway. Hydroxylation also occurred. These two processes increased elimination because their renal clearance values were greater than those of the unmetabolised drugs (7).

Readily absorbed from the human gastro-intestinal tract with peak blood concentrations being reached at 3 to 6 hours. Binding to plasma proteins accounts for 20-55%. Enters the cerebrospinal fluid within 4 hr of oral administration. The acetyl derivative makes up ≤40% of the drug in the blood. Following a single oral dose, ~50% is excreted via the urine in 24 hr; 15-40% is excreted as the acetyl derivative (8).

Excretion of the compound and the acetyl derivative in urine is pH-dependent. In acidic urine about 30% is excreted unchanged in both fast and slow acetylators, whereas 75% is excreted unchanged by slow acetylators. In alkaline urine, $t_{1/2}$ 7-12 hr; acetyl derivative, 8-12 hr (9).

Sensitisation

Rashes, exfoliative dermatitis, photosensitivity reactions, erythema nodosum and toxic epidermal necrolysis have occurred following administration of the drug. Contact with human skin may cause dermatitis. Systemic lupus erythematosus has occurred (8).

Other effects

Other adverse effects (human)

A woman taking the compound in eye-drops for about a year developed white stone-like concretions of the drug in the conjunctiva (10).

Vomiting, anorexia, nausea and diarrhoea may occur. Other effects include nephrotoxic reactions, back pain, agranulocytosis, leucopenia, hypoglycaemia, hypothyroidism and neurological reactions (convulsions, dizziness, insomnia, headache, mental depression and psychoses) (8).

Other comments

Resistance shown by *Salmonella* isolated from natural polluted waters (11).

Pharmacokinetics of the sulfonamide class of drugs reviewed (9).

Soluble in solutions of sodium and potassium hydroxides, dilute mineral acids and in ammonia water.

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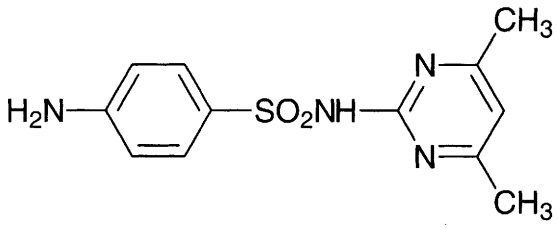
S133 sulfadimidine



$C_{12}H_{14}N_4O_2S$ **Mol. Wt.** 278.33 **CAS Registry No.** 57-68-1

Synonyms 4-amino-*N*-(4,6-dimethyl-2-pyrimidinyl)benzenesulfonamide; *N'*-(4,6-dimethyl-2-pyrimidinyl)sulfanilamide; 4,6-dimethyl-2-sulfanilamidopyrimidine; sulphadimidine; sulfamidine; Mefenal; Vertolan; Pirmazin; azolmetazin; Superseptyl

EINECS No. 200-346-4 **RTECS No.** WO 9275000

Uses Antibacterial agent.

Physical properties

M. Pt. 178-179°C

Solubility Water: 1.5 g l^{-1} at 29°C (pH 7). Organic solvents: acetone, diethyl ether

Ecotoxicity

Fish toxicity

Freshwater carp (duration unspecified) 20 mg day^{-1} fed to 100 g fish did not adversely affect the growth or survival of fish (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 50 g kg^{-1} (2).

LD_{50} intraperitoneal mouse 1060 mg kg^{-1} (3,4).

LD_{50} intravenous mouse 1770 mg kg^{-1} (5).

Carcinogenicity and chronic effects

Oral B6C3F1 mice (2 yr) 0 (control), 300, 600, 1200, 2400, 4800 ppm in feed (continuous dosing). Follicular cell adenomas of the thyroid gland in highest dose group occurred in 33% ♂ and 26% ♀, respectively. Non-neoplastic dose-related lesions observed in both sexes were follicular cell hyperplasia of the thyroid glands, haematopoietic cell proliferation of the spleen, and pigmentation of the spleen. Pigmentation of lymph nodes and hyperplasia of the mammary gland occurred (6).

Teratogenicity and reproductive effects

Oral rats 10 × human dose in corn oil reduced ♂ fertility by 34.3% (7).

Oral Swiss CD-1 ♂ mice 1% in diet, no significant effects on parameters examined: epididymis and testis weight, and spermmotility, abnormality and concentration (8).

Metabolism and toxicokinetics

Major metabolites in horses and cows included: N^4-acetylsulfadimidine, 6-hydroxymethylsulfadimidine, 5-hydroxysulfadimidine and 5-hydroxysulfadimidine glucuronide (9).

Major metabolic pathway in horses, ruminants and poultry was hydroxylation, while in humans and pigs, acetylation predominated (10).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Water solubility increases rapidly with increasing pH.

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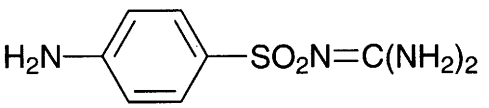
S134 sulfaguanidine



$C_7H_{10}N_4O_2S$ **Mol. Wt.** 214.25 **CAS Registry No.** 57-67-0

Synonyms 4-amino-*N*-(aminoiminomethyl)benzenesulfonamide; *N'*-amidinosulfanilamide; *p*-aminobenzenesulfoguanidide; Emanicil; Sulfaguine; Sulfoguanyl; Sulgin; sulphaguanidine

EINECS No. 200-345-9 **RTECS No.** WO 8575000

Uses Antibacterial drug.

Physical properties

M. Pt. 190-193°C

Solubility Water: 1 g 100 ml^{-1} at 25°C, 1 g 10 ml^{-1} at 100°C

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 500 mg kg^{-1} (1).

Teratogenicity and reproductive effects

Fecundity of ♂ rats was reduced to 55.6% of control when fed 10 × the human dose for 6 months (2).

Metabolism and toxicokinetics

Absorption from the gastro-intestinal tract of humans is limited (3).

Sensitisation
Rashes, photosensitivity reactions, toxic epidermal necrolysis, exfoliative dermatitis and erythema nodosum have occurred following administration of the drug. Contact with human skin may cause dermatitis. Systemic lupus erythematosus has occurred (3).

Other effects

Other adverse effects (human)
Vomiting, anorexia, nausea and diarrhoea may occur. Other effects include nephrotoxic reactions, haematuria, thrombocytopenia, eosinophilia, pancreatitis, hypoglycaemia and neurological reactions (aseptic meningitis, ataxia, convulsions, headache, peripheral or optic neuropathies and vertigo) (3).

Other comments

Pharmacokinetics of the sulfonamide class of drugs reviewed (4).
Soluble in dilute mineral acids.

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S135 sulfallate

$$CH_2=C(Cl)CH_2SC(S)N(CH_2CH_3)_2$$

$C_8H_{14}ClNS_2$ **Mol. Wt.** 223.79 **CAS Registry No.** 95-06-7

Synonyms diethylcarbamodithioic acid 2-chloro-2-propenyl ester; diethyldithiocarbamic acid, 2-chloroallyl ester; 2-chloroallyl diethyldithiocarbamate; CDEC; CP 4742; Vegadex; Thioallate

EINECS No. 202-388-9 **RTECS No.** EZ 5075000

Uses Superseded herbicide.

Physical properties

B. Pt. 128-130°C at 1 mmHg **Specific gravity** 1.088 at 25°C **Volatility** v.p. 3.2×10^{-2} mmHg at 20°C
Solubility Water: 100 ppm at 25°C. Organic solvents: acetone, benzene, ethanol

Occupational exposure

Supply classification toxic
Risk phrases May cause cancer – Harmful if swallowed (R45, 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)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 850 mg kg^{-1} (1).
LD_{50} dermal rabbit 2200 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rat (6 month) 250 ppm in feed caused eye irritation, toxic tubular nephropathy and acanthosis and hyperkeratosis of the forestomach (3).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (4).

Oral ♂, ♀ B6C3F1 mice (78 wk), time-weighted average concentrations in diet: low dose ♂ 949 mg kg^{-1}; high dose ♂ 1897 mg kg^{-1}; low dose ♀ 908 mg kg^{-1}; high dose ♀ 1815 mg kg^{-1}. Mammary adenocarcinomas, some of which metastasised to other sites, occurred in ♀. Low incidences of squamous cell carcinomas of the skin and forestomach, alveolar bronchiolar adenomas and carcinomas were observed in both sexes. Significant incidence in both low- and high-dose ♂ and low-dose ♀ (5).

Metabolism and toxicokinetics

In vitro rat liver microsomes, 2-chloroacrolein was formed as a metabolite (6).

Irritancy

Weak eye and skin irritant in rats (dose and duration unspecified) (7).

Genotoxicity

Escherichia coli pol with and without metabolic activation negative (8).
Bacillus subtilis rec assay without metabolic activation negative (9).
Salmonella typhimurium TA1535, TA100 with metabolic activation positive (10).
Aspergillus nidulans without metabolic activation strongly induced mitotic crossing over (11).
In vitro human lymphocytes short-term culture unscheduled DNA synthesis negative (12).

Other effects

Other adverse effects (human)

Prolonged contact with skin and eyes causes moderate irritation (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (13).
Included in Schedules 4 and 6 (Release into the Air and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).
Tolerance levels USA, residues in or on raw agricultural commodities 0.2 mg kg^{-1} (15).

Other comments

Present in air emissions from sulfallate manufacturing plants (at levels of 0.5 kg per 1000 kg pesticide produced) (16).
Hydrolysed by alkalis.

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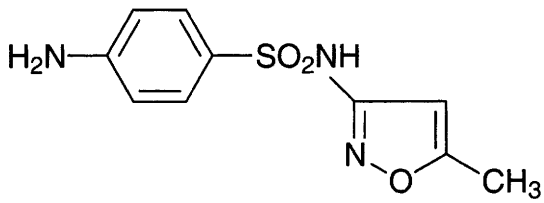
S136 sulfamethoxazole



$C_{10}H_{11}N_3O_3S$ **Mol. Wt.** 253.28 **CAS Registry No.** 723-46-6

Synonyms 4-amino-*N*-(5-methyl-3-isoxazolyl)benzenesulfonamide; *N'*-(5-methyl-3-isoxazolyl)sulfanilamide; 5-methyl-3-sulfanilamidoisoxazole; 3-(*p*-aminophenylsulfonamido)-5-methylisoxazole; sulfisomezole; sulfamethoxizole; Gantanol; Sinomin

EINECS No. 211-963-3 **RTECS No.** WP 0700000

Uses Antibacterial. Antipneumocytic.

Physical properties

M. Pt. 167-172°C
Solubility Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2650-3660 mg kg^{-1} (1,2).
LD_{50} oral rat 6370 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse, rat 2300, 2690 mg kg^{-1}, respectively (4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (5).
Oral rats (60 wk) 25, 50, 150, 300 or 600 mg kg^{-1} day^{-1} in diet. Thyroid nodules or adenomas were observed in the treated groups: 0/28, 7/30, 20/29, 19/27, 23/23, respectively. Lung metastases were observed in 4 animals of the 3 higher dose groups. No tumours were induced in controls (6).
1709 subjects receiving sulfamethoxazole medication between 1969 and 1973 were followed up for cancer development through 1976. A statistically significant number of nasopharyngeal and cervical cancers were noted (7).

Teratogenicity and reproductive effects

No increase in malformation rates in the offspring of 46 human pregnancies when treatment was given in the first 4 lunar months (8).

Metabolism and toxicokinetics

12 healthy adult subjects 100 mg kg^{-1} day^{-1} administered orally at 6 hr intervals for 3 days. Maximum serum drug concentration was 372 μg ml^{-1}, mean $t_{1/2}$ 14 hr (9).

In vivo ♂ human single unspecified dose, peak blood concentrations observed within 1.5-3.5 hr (10).

Maternal (human) administered 29.6 and 127.7 μg ml^{-1} gave foetal concentrations of 5.1 and 14.8 μg ml^{-1}, respectively. Readily crosses the placenta (11).

Oral mouse 1 g kg^{-1} body weight (single dose). Rapidly absorbed, peak plasma concentrations were achieved 1 hr after administration, plasma $t_{1/2}$ ~6 hr. Tissue distribution studies in rats showed high concentrations in kidneys, lung, liver, spleen and brain. Rate of elimination of the drug from most tissues paralleled that from the blood (12).

In humans, the plasma $t_{1/2}$ is ~9 hr whether administered alone or in combination with trimethoprim. Excretion is via the urine with complete elimination within 96 hr (13).

In humans, N^4-acetylsulfamethoxazole is the major metabolite; minor metabolites include sulfamethoxazole-N^1-glucuronide, sulfamethoxazole-N^2-glucuronide and hydroxysulfamethoxazole (12,14-16).

Crosses the human placenta, peak concentrations reached in 10 hr. After a few gestational wk, the concentration was lower in the amniotic fluid and foetus than in maternal serum (17).

Genotoxicity

In vitro human lymphocytes chromosomal aberrations negative (18).

In vitro human fibroblasts sister chromatid exchanges negative (19).

Other effects

Other adverse effects (human)

Oral human 100 mg total dose administered every 6 hr over a 3 day period. 5/12 subjects withdrew from testing because of intolerable gastro-intestinal and central nervous system toxicities (9).

Of 359 treated patients, 3.3% developed skin rashes, eosinophilia and drug fever which were severe enough to require discontinuance of treatment. No adverse effects on the thyroid were noted (20).

In humans, adverse effects include nausea, vomiting, anorexia and diarrhoea. Hypersensitivity reactions include rashes, photosensitivity reactions, exfoliative dermatitis, toxic epidermal necrolysis and erythema nodosum. A severe, potentially fatal, form of erythema multiforme has occurred in patients treated with sulfonamides. Dermatitis can also occur. Renal and blood disorders have also been reported (21).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (22).

Other comments

In the US, UK and most Western European countries, sulfamethoxazole is available in combination with trimethoprim (5:1 ratio sulfamethoxazole: trimethoprim) as Co-trimoxazole. Available as tablets, injections and mixtures.

Sensitive to oxidation and light.

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S137 sulfamic acid

NH_2SO_3H

H_3NO_3S **Mol. Wt.** 97.09 **CAS Registry No.** 5329-14-6

Synonyms amidosulfonic acid; sulfamidic acid; Dry Lightning; Liquid Lightning

EINECS No. 226-218-8 **RTECS No.** WO 5950000

Uses Standard reagent in alkalimetry. Used as a chlorine stabiliser in water treatment. Flameproofing fabrics and wood.

Physical properties

M. Pt. 205°C (decomp.) **Specific gravity** 2.15

Solubility Water: soluble in 6.5 parts water at 0°C, in 2 parts at 80°C. Organic solvents: freely soluble in pyridine, formamide, dimethylformamide. Also soluble in liquid ammonia

Occupational exposure

UN No. 2967 **HAZCHEM Code** 2Z **Conveyance classification** corrosive substance

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)

Environmental fate

Carbonaceous inhibition

Supports growth of *Chlorella fusca* 221-8b (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1.6-3.16 g kg^{-1} (2,3).

LD_{Lo} intraperitoneal rat 100 mg kg^{-1} (4).

Irritancy
250 µg instilled into rabbit eye (24 hr) caused severe irritation (3).
Dermal rabbit (24 hr) 500 mg caused severe irritation (3).
Dermal human 4% applied intermittently over 5 days caused mild irritation (4).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology and physico-chemical properties listed (6).

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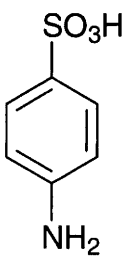
S138 sulfanilic acid



$C_6H_7NO_3S$ **Mol. Wt.** 173.19 **CAS Registry No.** 121-57-3

Synonyms aniline-4-sulfonic acid; *p*-aminophenylsulfonic acid; 4-aminobenzenesulfonic acid

EINECS No. 204-482-5 **RTECS No.** WP 3895500

Uses Antibacterial uses. Manufacture of dyestuffs and organic chemicals. Reagent for nitrate.

Physical properties

M. Pt. 288°C (decomp.) **Specific gravity** 1.485 at 25°C with respect to water at 4°C
Solubility Water: 10.8 g l^{-1} at 20°C, 66.7 g l^{-1} at 100°C. Organic solvents: hot methanol

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) – Avoid contact with the skin – Wear suitable gloves (S2, S24, S37)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 100.4 mg l^{-1} static bioassay (1).

Invertebrate toxicity

EC_{50} (5-30 min) *Photobacterium phosphoreum* 114 mg l^{-1} Microtox test (2).

IC_{50} *Saccharomyces cerevisiae* 533 mg l^{-1} (3).

Environmental fate

Degradation studies

Microbial decomposition in >64 days (4).

Sulfonic acid was utilised as the sole carbon source by adapted activated sludge at 20°C. COD 95%, 4 mg COD g^{-1} dry inoculum hr^{-1} (5).

BOD_5 1.1 mg l^{-1} oxygen consumed using standard dilute sewage (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse >3.2 g kg^{-1} (7).

LD_{50} intravenous rat 6 g kg^{-1} (8).

Metabolism and toxicokinetics

Following oral administration to rats 53% of the dose was excreted in the urine (9).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation, 100 mg instilled in rabbit eye caused moderate irritation (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (11).

Other effects

Any other adverse effects

Variable allergic response according to administration route in rats (12).

Other comments

Reviews on physico-chemical properties, experimental toxicology, human health effects, ecotoxicology, epidemiology, and workplace experience listed (13).

Currently available toxicological and ecotoxicological data reviewed (14).

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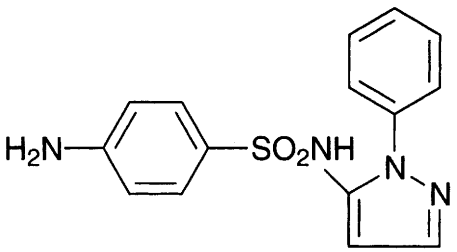
S139 sulfaphenazole



$C_{15}H_{14}N_4O_2S$ **Mol. Wt.** 314.37 **CAS Registry No.** 526-08-9

Synonyms 4-amino-*N*-(1-phenyl-1*H*-pyrazol-5-yl)benzenesulfonamide; *N'*-(1-phenylpyrazol-5-yl)sulfanilamidopyrazole; 3-(*p*-aminobenzenesulfonamido)-2-phenylpyrazole; 5-sulfanilamido-1-phenylpyrazole; Depocid; Isarol; Orisul; Sulfabid

EINECS No. 208-384-3 **RTECS No.** DA 9520000

Uses Antibacterial. Antimicrobial.

Physical properties

M. Pt. 179-183°C

Solubility Water: 1.5 g l^{-1} at pH 7 and 25°C. Organic solvents: glacial acetic acid, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 5800 mg kg^{-1} (1).

LD_{50} intravenous rabbit, mouse, rat 440, 470, 525 mg kg^{-1}, respectively (2).

LD_{50} subcutaneous mouse, rat, rabbit 660, 900, 950 mg kg^{-1}, respectively (2).

Metabolism and toxicokinetics

Oral red-eared turtle 100 mg (single dose) excreted 27% as the unchanged compound and 3.8% as the N^4-acetylsulfaphenazole metabolite. The expected glucuronide conjugate sulfaphenazole-*N*-glucuronide was not formed (3).

Oral, intravenous injection ruminants 82.5-90% was bound to plasma proteins; bioavailability 53.3% (4).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicity and physico-chemical properties listed (6). Commercial medicinal grades also contain 5-sulfanilimido-1-phenyl-2*H*-pyrazolene.

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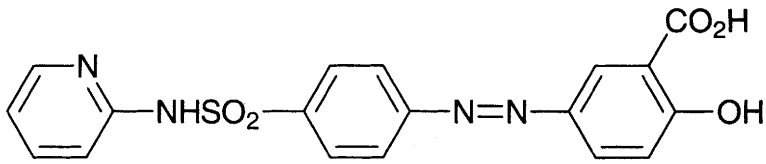
S140 sulfasalazine



$C_{18}H_{14}N_4O_5S$ **Mol. Wt.** 398.40 **CAS Registry No.** 599-79-1

Synonyms 2-hydroxy-5-[[4-[(2-pyridinylamino)sulfonyl]phenyl]azo]benzoic acid; 5-[*p*-(2-pyridylsulfamoyl)phenylazo]salicylic acid; salazosulfapyridine; 5-[4-(2-pyridylsulfamoyl)phenylazo]-2-hydroxybenzoic acid; 4-(pyridyl-2-amidosulfonyl)-3'-carboxy-4'-hydroxyazobenzene; salicylazosulfapyridine; Sulphaxalazine; Colo-Pleon; Azopyrin; Azulfidine; Salazopyrin

EINECS No. 209-974-3 **RTECS No.** VO 6250000

Uses Treatment of Crohn's disease and ulcerative colitis.

Physical properties

M. Pt. 240-245°C (decomp.)
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 1250 mg kg^{-1} (1).
LD_{50} intravenous mouse 1100 mg kg^{-1} (1).

Carcinogenicity and chronic effects
The National Toxicology Program tested rats and mice via gavage: Some evidence of carcinogenicity in rats, clear evidence of carcinogenicity in mice (2).

Teratogenicity and reproductive effects
Gavage rats (28 day) unspecified dose (daily) caused reduced body weights in treated animals. Testes, prostate or seminal vesicle weights were not altered. Sperm motility and the number of spermatozoa were reduced (3). Sulfapyridine, a metabolite of sulfasalazine, caused adverse effects at ovulation in ♀ rats. A greater number of potentially available oocytes were available in treated animals compared with controls (4).
♂ humans receiving sulfasalazine in treatment for ulcerative colitis became infertile. The effect was completely reversed after drug withdrawal (5).

Metabolism and toxicokinetics
Metabolites include sulfapyridine, 5-aminosalicylic acid and olsalzine (humans) (6,7).
♂ humans were given 500, 1000 and 2000 mg (single doses). Metabolites identified included: 5-aminosalicylic acid and sulfapyridine in the large intestine; N^4-acetylsulfapyridine, N^4-acetyl-5'-hydroxysulfapyridine, N^4-acetyl-5'-hydroxysulfapyridine-*O*-glucuronide and acetyl-5-aminosalicylic acid in blood, serum, urine and faeces. $t_{1/2}$ 3-4 hr, urinary excretion 3.8%. Blood metabolites were cleared within 72 hr of administration (8).
In vitro human red blood cells and mononuclear leukocytes; only the sulfapyridine metabolite was bioactivated by human liver microsomes in the presence of NADPH to a metabolite which caused methaemoglobinaemia and leucocyte cell death (9).
Poorly absorbed, ~10% following oral dosing in mice, ~40% was hydrolysed to sulfapyridine in the gastro-intestinal tract and 74% was absorbed. Multiple dosing did not alter the patterns or rate of metabolism and elimination (2).

Genotoxicity

In vitro Chinese hamster ovary cells chromosomal aberrations and sister chromatid exchanges negative (10).
In vivo mice (single gavage dose 100 mg kg^{-1}) did not increase chromosomal aberrations. However, mice given 675, 1350 or 2700 mg kg^{-1} by gavage for 90 days had increased levels of micronuclei in peripheral blood erythrocytes (10).
In vivo human lymphocytes, induced sister chromatid exchanges and micronuclei (10).
In vivo cytogenetic assays micronuclei positive (species unspecified) (2).

Other effects

Other adverse effects (human)
♂ human volunteers given single doses of 500, 1000 and 2000 mg reported mild discomfort in the stomach, lower abdominal pain and mucocutaneous stomatitis (8).
Oligospermia has been reported, reversible on withdrawal. Can interfere with the absorption of digoxin or folic acid from the gastro-intestinal tract (11).
Adverse effects in humans included nausea, vomiting, headache, haemolytic anaemia and methaemoglobinaemia. Hypersensitivity reactions included skin rash, aplastic anaemia, hepatic and pulmonary dysfunction and autoimmune haemolysis (11).
In humans, pulmonary complications occur rarely, although one fatality has been reported (12).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).

Other comments

Reproductive effects reviewed (14).

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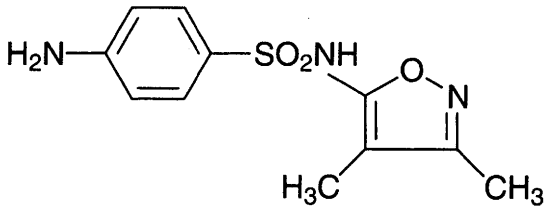
S141 sulfisoxazole



$C_{11}H_{13}N_3O_3S$ **Mol. Wt.** 267.31 **CAS Registry No.** 127-69-5

Synonyms 4-amino-*N*-(3,4-dimethyl-5-isoxazolyl)benzenesulfonamide; *N'*-(3,4-dimethyl-5-isoxazolyl) sulfanilamide; 5-(*p*-aminobenzenesulfonamido)-3,4-dimethylisooxazole; Sulfafurazole; Entusil; Sulfoxol; Gantrosan; Uritrisin

EINECS No. 204-858-9 **RTECS No.** WO 9100000

Uses Antibacterial (humans); antimicrobial in veterinary medicine.

Physical properties

M. Pt. 194-198°C

Solubility Water: 3.5 g l^{-1} at pH 6.0. Organic solvents: acetone, chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

Following oral administration to rainbow trout, bile samples were taken at 48 hr, and urinary samples throughout 72 hr. Metabolites included unchanged form, N^4-acetylated forms, and glucuronides (1).

Environmental fate

Abiotic removal

Sensitive to oxidation and light (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 6800 mg kg^{-1} (3).

LD_{50} oral rabbit 1000 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Insufficient evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).

Gavage ♂, ♀ mice, ♂, ♀ rats (103 wk) 0, 500 or 2000 mg kg^{-1} body weight (mice) and 0, 100 or 400 mg kg^{-1} body weight (rats). No significant incidence of tumours observed (6).

Teratogenicity and reproductive effects

Oral mice, rats 1000 mg kg^{-1} body weight on days 7-12 and 9-14 of gestation, respectively, caused a significant increase in cleft palate and skeletal defects in the offspring of both species. Rat foetuses also showed mandibular defects (7).

~800 humans treated with sulfisoxazole during the first 4 months of pregnancy showed no increase in the rate of malformations (8).

In vitro teratogen screening, rat embryo limb bud cells positive teratogen (9).

Gavage ♂, ♀ rats (6 wk) 150 and 450 mg kg^{-1} (diet) in corn oil, no anti-fertility activity detected (10).

Metabolism and toxicokinetics

Following oral administration to rats 67% of the unchanged compound and 16% of its acetyl derivative were excreted in the urine within 48 hr (11).

Following administration to mice of 1 g kg^{-1} peak plasma levels of 2 mg ml^{-1} were reached within 1 hr (12).

Oral dog single dose 250 mg, 72-82% excreted via urine in 24 hr. Intravenous dog single dose 9 mg kg^{-1} body weight 88-96% excreted via urine in 24 hr (13).

Following oral, intravenous or intramuscular doses of 2 g to humans, >90% of dose was excreted in the urine; of this, 40-60% was unchanged compound, $t_{1/2}$ ~6 hr (14).

Urinary metabolites included: acetylsulfisoxazole, sulfisoxazole-*N*-glucuronide, sulfisoxazole-*N*-sulfonate and sulfanilamide (15).

Genotoxicity

Escherichia coli without metabolic activation negative (16).

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (17,18).

Multivariate statistical methods used to determine genotoxicity potential in short-term *in vitro* tests. *In vitro* mouse lymphoma positive; Chinese hamster ovary sister chromatid exchanges positive; CHO chromosomal aberrations negative; *Salmonella typhimurium* negative (19).

In vitro mouse lymphoma L5178Y tk^+/tk^- without metabolic activation positive (at toxic doses) (20).

Other effects

Other adverse effects (human)

Of 1000 patients treated with sulfisoxazole, treatment was discontinued in 3.1% after skin rashes, eosinophilia and fever developed (21).

In an epidemiological study of 11,659 patients given sulfisoxazole (doses and duration unspecified) with a 3 yr follow-up, no significant excess of any cancers was noted (22).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).

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S142 sulfluramid

$$CF_3(CF_2)_7SO_2NHCH_2CH_3$$

$C_{10}H_6F_{17}NO_2S$ **Mol. Wt.** 527.20 **CAS Registry No.** 4151-50-2

Synonyms *N*-ethylperfluoro-octane-1-sulfonamide; *N*-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-1-octanesulfonamide

EINECS No. 223-980-3

Uses Insecticide used for household control of Formicidae and Blattellidae.

Physical properties

M. Pt. 96°C **B. Pt.** 196°C **Flash point** >93°C **Specific gravity** 1.21 g ml^{-1} at 20°C
Partition coefficient log P_{ow} >6.8 **Volatility** v.p. 0.057 mPa at 25°C
Solubility Water: insoluble at 25°C. Organic solvents: dichloromethane, hexane, methanol

Ecotoxicity

Invertebrate toxicity
Oral LD_{50} *Blattella germanica* (5th instar) 4.1 μg g^{-1} (1).
Topical LD_{50} *Blattella germanica* (5th instar) 14.5 μg g^{-1} (1).
Oral LD_{50} *Blattella germanica* adult ♂ 175.6, adult ♀ 117.8, gravid adult ♀ 122.3 μg g^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail 4733 mg kg^{-1} (2).
LD_{50} oral rat 543 mg kg^{-1} (2).

Sub-acute and sub-chronic data
LC_{50} (8 day) bobwhite quail, mallard duck 460, 165 mg kg^{-1} in diet, respectively (2).

Irritancy
Not irritating to skin (species unspecified) (2).

Legislation

WHO Toxicity Class III (3).
Limited under EC Directive on Drinking Water Quality 80/788/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedules 5 and 6 (Release into Water and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

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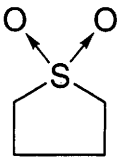
S143 sulfolane



$C_4H_8O_2S$ **Mol. Wt.** 120.17 **CAS Registry No.** 126-33-0

Synonyms tetrahydrothiophene 1,1-dioxide; thiophan sulfone; cyclic tetramethylene sulfone

EINECS No. 204-783-1 **RTECS No.** WN 0700000

Uses Solvent for liquid-vapour extractions.

Physical properties

M. Pt. 27.4-27.8°C **B. Pt.** 285°C **Flash point** 176-177°C (open cup) **Specific gravity** 1.2606 (liquid) at 30°C with respect to water at 4°C **Volatility** v.p. 5 mmHg at 118°C

Solubility Water: miscible at 30°C. Organic solvents: miscible with acetone and toluene, octanes, olefins and naphthenes

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 eyes (S2, S25)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) goldfish 4.8 g l^{-1} (1).

Bioaccumulation

Confirmed non-accumulative or low accumulative (2).

Environmental fate

Degradation studies

Confirmed non-biodegradable (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1900-1940 mg kg^{-1} (3,4).

LC_{Lo} (24 hr) inhalation rat 4700 mg m^{-3} (5).

LD_{50} dermal rabbit 4000 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse, rat 1250, 1600 mg kg^{-1}, respectively (6,7).

LD_{50} intravenous mouse 1080 mg kg^{-1} (8).

Metabolism and toxicokinetics

Following oral administration to rats, rapidly and completely absorbed from the gastro-intestinal tract, mainly in the small intestine, $t_{1/2}$ for urinary and faecal excretion were 36 and 59 hr, respectively. Distributed to various organs and systems. Highest concentrations observed in liver, followed by kidney, lung, thyroid and adrenal glands, pancreas, spleen, heart, muscle, brain, testis and fat. Crosses blood-brain and placental barriers (9).

Irritancy
250 mg instilled into rabbit eye caused mild irritation (duration unspecified) (4).

Legislation

Recommended for testing for chemical fate, health and ecological effects under the Federal Toxic Substances Control Act (10).
Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology, physico-chemical properties and environmental effects listed (12).

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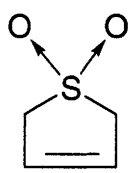
S144 3-sulfolene



$C_4H_6O_2S$ **Mol. Wt.** 118.16 **CAS Registry No.** 77-79-2

Synonyms 2,5-dihydrothiophene 1,1-dioxide; 1-thia-3-cyclopentene 1,1-dioxide; butadiene sulfone; β-sulfolene

EINECS No. 201-059-7 **RTECS No.** XM 9100000

Physical properties

M. Pt. 64-65.5°C **Flash point** >110°C
Solubility Water: soluble. Organic solvents: acetone, ethanol, diethyl ether

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2830 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 1700 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 without metabolic activation negative (3,4).

Legislation

Recommended for testing for chemical fate, health and/or ecological effects under the US Federal Toxic Substances Control Act (5).

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

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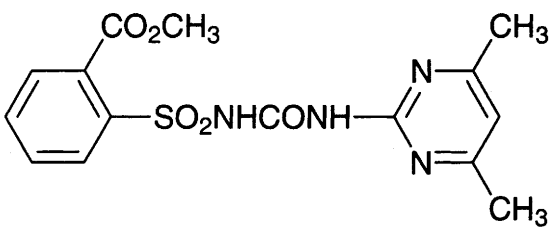
S145 sulfometuron-methyl



$C_{15}H_{16}N_4O_5S$ **Mol. Wt.** 364.38 **CAS Registry No.** 74222-97-2

Synonyms 2-[[[[(4,6-dimethyl-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]benzoic acid methyl ester; *N*-[(4,6-dimethylpyrimidin-2-yl)aminocarboxyl]-2-methoxycarbonylbenzenesulfonamide; 2-[3-(4,6-dimethylpyrimidin-2-yl)ureidosulfonyl]benzoic acid methyl ester

EINECS No. 277-780-6 **RTECS No.** DG 9096550

Uses Nonselective pre- and post-emergence herbicide.

Physical properties

M. Pt. 203-205°C **Specific gravity** 1.48 **Partition coefficient** log P_{ow} 1.176 at pH 5; –0.509 at pH 7 (1)

Volatility v.p. 6×10^{-5} mmHg at 25°C

Solubility Water: 244 mg l^{-1} at 25°C, pH 7. Organic solvents: acetone, acetonitrile, dimethyl sulfoxide, methanol, methylene chloride

Occupational exposure

US-TWA 5 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish >12.5 mg l^{-1} (2).

Invertebrate toxicity

Adult crayfish exposed to concentrations ≤60,000 ppm (duration unspecified) suffered no mortalites. LC_{50} values could not be calculated. However, published LC_{50} values for pesticides indicate freshwater crayfish are more tolerant than marine decapods *Crangon septemspinosa* and *Mysidopsis bahia* (3).

LC_{50} (48 hr) *Diaptomus, Eucyclops, Celonella* and *Cypria* microcrustaceans 1315, 1320, 802 and 2241 ppm, respectively (static test) (3).

Environmental fate

Degradation studies

Degraded by microbial action and by hydrolysis. $t_{1/2}$ in soil ~4 wk (1).

Degraded rapidly at four field sites following application at the maximum rate. Calculated $t_{1/2}$ 12-25 days.

At 359 days after treatment the highest degradate concentration present (at 40 ppb) was the herbicidally inactive 2-amino-4,6-dimethylpyrimidine (4).

Adsorption and retention

Moistening air-dried chernozem or sod-podzolic soil to 90% water capacity decreased adsorption. However, increasing the soil organic carbon content and decreasing the pH increased adsorption. Increasing the temperature from 11 to 41°C also promoted adsorption. The pH and temperature effects were due to hydrogen bonding (5).

Laboratory experiments studied the effects of application rates, grass cover and formulation type on herbicide loss in run-off. Concentration of 0.4 kg ha^{-1} (suspension concentrate and emulsifiable concentrate) was applied to loamy sand soil. 24 hr after application, rainfall equivalent to 2 mm run-off was simulated. Formulation loss was 1-2% of applied herbicide concentration regardless of grass cover. Total losses of both formulations were sensitive to duration between rainfall initiation and run-off initiation, indicating that leaching made the compound unavailable for run-off (6).

Sulfometuron-methyl and its degradates were immobile under field conditions (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂, ♀ rats >5000 mg kg^{-1} (7).

LC_{50} (4 hr) inhalation rat >5.3 mg l^{-1} (air) (1).

LD_{50} dermal rabbit >200 mg kg^{-1} (1).

Carcinogenicity and chronic effects

In 2-yr feeding trials in rats the no-effect-level was 50 mg kg^{-1} diet (1).

Teratogenicity and reproductive effects

NOEL: in reproduction (2-generation) study in rats 500 mg kg^{-1} diet; teratogenicity in rats 1000 mg kg^{-1} diet, in rabbits 300 mg kg^{-1} diet (1).

Metabolism and toxicokinetics

Oral goats 25 or 60 ppm in diet, >93% of administered dose excreted in urine and faeces after 7 days. ~60% of dose was rapidly metabolised to (hydroxymethyl)pyrimidine sulfometuron-methyl, which was eliminated in the urine. Cleavage of the sulfonylurea bridge occurred giving sulfonamide and (hydroxymethyl)pyrimidinamine, which were found bound to protein residues, in liver and kidney (8).

Irritancy
10 mg instilled into rabbit eye caused mild irritation (duration unspecified) (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 Schedules 4 and 6 (Release into the Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Herbicidal activity discussed (12).
Metabolic pathways reviewed (13).

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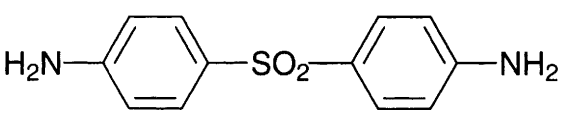
S146 4,4′-sulfonyldianiline



$C_{12}H_{12}N_2O_2S$ **Mol. Wt.** 248.31 **CAS Registry No.** 80-08-0

Synonyms 4,4′-sulfonylbisbenzeneamine; bis(4-aminophenyl)sulfone; 4,4′-diamino diphenyl sulfone; DDS; DADPS; Dapsone; Croysulfone; Novophone; Udolac; Avlosulfon; Eporal

EINECS No. 201-248-4 **RTECS No.** BY 8925000

Uses Hardening agent for epoxy resins. Antibacterial, antiprotozoan in veterinary medicine. Used in the treatment of multibacillary and paucibacillary leprosy. Malaria prophylaxis treatment.

Physical properties

M. Pt. 175-180°C
Solubility Organic solvents: acetone, ethanol, 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) – Do not breathe dust (S2, S22)

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 59 ppm Microtox test (1).

Mammalian & avian toxicity

Sub-acute and sub-chronic data
LD_{50} oral mouse 375 mg kg^{-1} (2).
LD_{Lo} oral cat 357 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 200 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 310 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 330 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 (5).
Potential carcinogenicity investigated in ♂, ♀ rats and mice (2-yr feeding study). Positive results in ♂ rats tumour sites integumentary system, pancreas and stomach. Negative in ♀ rats, ♂, ♀ mice (6).

Teratogenicity and reproductive effects
Oral rat (6 month) in feed 10 × the human dose (suspended in corn oil) reduced fecundity of ♂ rats by 38.3% compared with controls (7).

Metabolism and toxicokinetics
In vitro human leucocytes NADPH-dependent toxicity range 8.8-27%. Metabolised to a hydroxylamine (3.1%) which was further oxidised to a cytotoxic metabolite (8).
Oral human volunteers 100 mg; peak serum concentrations of 1.10-2.33 mg l^{-1} were reached within 0.5 to 4 hr; elimination $t_{1/2}$ 11-29 hr (9).

Genotoxicity

Salmonella typhimurium (strains and metabolic activation unspecified) negative (10).
In vitro primary hepatocytes DNA repair test negative (11).
In vitro mouse lymphoma L-5178Y tk^+/tk^- without metabolic activation negative (12).
In vitro Chinese hamster ovary cells chromosomal aberrations weakly positive (metabolic activation unspecified) (13).

Other effects

Other adverse effects (human)
In vitro human leucocytes irreversible binding to cells was reduced by omission of NADPH or addition of glutathione (14).
Dose-related haemolysis and methaemoglobinaemia occur in most subjects given more than 200 mg daily; doses of ≤100 mg daily do not cause significant haemolysis but subjects deficient in glucose-6-phosphate dehydrogenase are affected by doses above about 50 mg daily. Agranulocytosis has been reported when used with other agents in the prophylaxis of malaria. Rash and pruritus may develop. Serious cutaneous hypersensitivity reactions occur rarely and include maculopapular rash, exfoliate dermatitis, toxic epidermal necrolysis and Stevens-Johnson syndrome. Fixed drug eruptions have occurred. Other adverse effects occur infrequently and include nausea, vomiting, anorexia, headache, hepatitis and psychosis (15).

1678 leprosy patients admitted for treatment to the National Hansen's Disease Center in Carville between 1939 and 1977 indicated that, although 4,4'-sulfonyldianiline has been implicated as a carcinogen in animals, no significant cancer risk was found in these patients (16).
Eye damage in two patients was associated with acute or sub-acute 4,4'-sulfonyldianiline poisoning (17).

Any other adverse effects
In vivo ♂ rat liver no changes in xenobiotic biotransformation except for induction of aniline hydroxylation (18).
In vivo ♂, ♀ rats; ♂ developed methaemoglobinaemia while ♀ were protected because they do not produce the toxic *N*-hydroxylamine metabolites (19).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (20).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology and physico-chemical properties listed (21).

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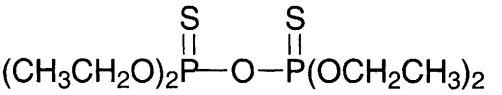
S147 sulfotep



$C_8H_{20}O_5P_2S_2$ **Mol. Wt.** 322.32 **CAS Registry No.** 3689-24-5

Synonyms thiodiphosphoric acid, *O,O,O',O'*-tetraethyl ester; thiopyrophosphoric acid, tetraethyl ester; thiotepp; dithiophos; TEDP; Bladafum; Dithion

EINECS No. 222-995-2 **RTECS No.** XN 4375000

Uses Insecticide. Miticide.

Physical properties

B. Pt. 136-139°C at 2 mmHg **Specific gravity** 1.196 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.99 at 20°C **Volatility** v.p. 1.7×10^{-4} mmHg at 20°C
Solubility Water: 10 mg l^{-1} at 20°C. Organic solvents: miscible with acetone, chloroform, ethanol

Occupational exposure

DE-MAK 0.0075 ppm (0.1 mg m^{-3})
FR-VME 0.2 mg m^{-3}
UK-LTEL 0.2 mg m^{-3}
US-TWA 0.2 mg m^{-3}

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) – Do not breathe fumes – 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) rainbow trout, golden orfe 3.61, 71 μg l^{-1}, respectively (1).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* 0.002 mg l^{-1} (1).

Environmental fate

Degradation studies
Anaerobic leachate from two subsoils was used to determine degradation rates. The study duration was 10 months, temperature 8-10°C, $t_{1/2}$ 10-20 days (2).
Metabolised by hydrolytic and oxidative mechanisms. Cleavage products include diethyl phosphate, monoethyl phosphate and phosphoric acid (3).

Abiotic removal
Photochemically stable under most environmental conditions, in the absence of humic acid, no degradation occurs. $t_{1/2}$ (10 mg l^{-1} humic acid) 38.4 hr; (100 mg l^{-1} humic acid) 12.4 hr (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 100 mg kg^{-1} (5).
LD_{50} oral rat, rabbit 10, 25 mg kg^{-1}, respectively (3,6).
LD_{50} dermal rabbit 20 mg kg^{-1} (7).
LC_{50} (4 hr) inhalation mouse 40 mg kg^{-1} (6).
LD_{50} subcutaneous mouse 8 mg kg^{-1} (8).
LD_{50} intraperitoneal mouse 940 μg kg^{-1} (9).

Carcinogenicity and chronic effects

In 2-yr feeding trials, no-effect level for rats 10 mg kg^{-1} diet (3).

Genotoxicity

Salmonella typhimurium TA1535 with metabolic activation positive (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 Schedules 4 and 6 (Release into the Air and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).
Log P_{ow} exceeds the European Community recommended level of 3.0 (13).
WHO Toxicity Class Ia (14).
EPA Toxicity Class I (formulation) (1).
ADI (BGA) 0.001 mg kg^{-1} body weight (1).

Other comments

Not harmful to bees when used as recommended (3).
Reviews on human health effects, experimental toxicology, ecotoxicology and physico-chemical properties listed (15).

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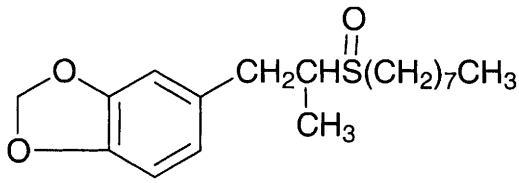
S148 sulfoxide



$C_{18}H_{28}O_3S$ **Mol. Wt.** 324.48 **CAS Registry No.** 120-62-7

Synonyms piperonyl sulfoxide; isosafrole *n*-octylsulfoxide; 1,2-methylenedioxy-4-[2-(octylsulfinyl)propyl]benzene; 1-methyl-2-(3,4-methylenedioxyphenyl)ethyloctyl sulfoxide; sulfoxyl

EINECS No. 204-412-3 **RTECS No.** DA 5775000

Uses Superseded synergist for pyrethroid insecticides.

Physical properties

Specific gravity 1.06 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 2.81 (1)
Solubility Organic solvents: diethyl ether, ethanol, methylene chloride, petroleum oils, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 0.75 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, waterfowl 2000, 4000 mg kg^{-1}, respectively (3,4).
LD_{50} dermal rabbit 9000 mg kg^{-1} (5).

Carcinogenicity and chronic effects
Oral rat, mouse (2 yr) 0, 1500, 3000 or 6000 mg kg^{-1} diet for rats and 0, 350, 700 or 1400 mg kg^{-1} diet for mice. An increase in the incidence of hepatocellular carcinomas was observed in ♂ mice. There was no significant increase in tumour incidence in ♀ mice and ♂ and ♀ rats. All treated animals showed a decrease in body weight gain (6).
Oral rat, no-adverse-effect-level 2000 mg kg^{-1} diet (7).

Teratogenicity and reproductive effects
Subcutaneous mouse, lowest toxic dose 90 mg kg^{-1} day^{-1} on days 6-14 of gestation (foetotoxicity and craniofacial malformations) (8).

Metabolism and toxicokinetics
Following oral administration to mice metabolism involves cleavage of the methylenedioxyphenyl moiety, and expiration of the methylene carbon as carbon dioxide. Mixed-function oxidases of the liver microsomes demethylated several compounds containing the methylenedioxyphenyl moiety (9).

Irritancy
Dermal rabbit 9000 mg kg^{-1} (LD_{50}) caused slight irritation (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (11).
Drosophila melanogaster sex-linked recessive lethal assay and reciprocal translations negative (12).
In vitro mouse lymphoma L5178Y cells with metabolic activation positive (13).

In vitro human lymphoblast TK6 cells with and without metabolic activation negative (13).
In vitro Chinese hamster ovary cells with and without metabolic activation, sister chromatid exchanges and chromosomal aberrations negative (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (15).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).

Other comments

Physical properties and toxicity reviewed (17).

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S149 sulfur

S

S **Mol. Wt.** 32.07 **CAS Registry No.** 7704-34-9

Synonyms brimstone; atomic sulfur; Cosan; Sufran; Thiosol

EINECS No. 231-722-6 **RTECS No.** WS 4250000

Uses Used in the manufacture of sulfuric acid, carbon disulfide, sulfites, insecticides, plastics, enamels, and metal-glass cements. Also used in the manufacture of dyes, gunpowder, and matches. In the bleaching of wood pulp and textiles. In vulcanising rubber. Non-systemic contact acaricide and fungicide.
Occurrence Four naturally occurring isotopes exist: ^{32}S (95%), ^{33}S (0.76%) ^{34}S (4.22%) and ^{36}S (0.014%). Free sulfur, sulfide and sulfate ores constitute 0.05% of the Earth's crust.

Physical properties

M. Pt. 114.5°C (rhombic 112°C; monoclinic 119°C) **B. Pt.** 444.6°C (rhombic) **Flash point** 207°C (closed cup)
Specific gravity 2.06 (α-form); 1.96 (β-form) **Volatility** v.p. 1 mmHg at 183.8°C
Solubility Organic solvents: acetone, benzene, carbon disulfide, chloroform, toluene

Occupational exposure

UN No. 1350 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid

Ecotoxicity

Bioaccumulation
Sulfur accumulation from the air in 50 species of plants and suburban soil were investigated. Highest concentrations occurred in *Salix matsudana*. Sulfur content was as follows: mosses, deciduous broad-leaf trees >herbs >deciduous shrubs >evergreen coniferous trees. Extent of purification by plants was also determined (1).

Environmental fate

Anaerobic effects
The rate of S and SO_4^{2-} reduction and the number of S and SO_4^{2-} reducing bacteria in sludge and water of fish hatchery ponds were determined. The rate of SO_4^{2-} reduction reached 2 mg S^{2-} l^{-1} day^{-1} in the upper sludge layers. In the bottom layers SO_4^{2-} was reduced to pyrite and elemental S, the latter being formed as a result of oxidative processes. The rate of S reduction was 10 × higher than that of SO_4^{2-} reduction. The number of bacterial cells reducing S and SO_4^{2-} was highest in August and September, *Desulfovibrio desulfuricans* 20,000-90,000 ml^{-1} of sludge. The processes of S and SO_4^{2-} reduction amounted to 3.2 and 14.6%, respectively, of the overall anaerobic decomposition in sludge (2).

Degradation studies
Degradation proceeds primarily by microbial reduction in and on plants (3).
Beads of elemental sulfur and glass beads were placed in sulfur-treated and control soils and studied for 10 days. Principal colonisers detected were heterotrophic microorganisms, which under *in vitro* conditions oxidised sulfur to thiosulfate, tetrathionate or sulfate. Heterotrophs which reduced sulfur and thiosulfate to H_2S were also detected. Autotrophic elemental sulfur oxidisers were not detected, but autotrophic thiosulfate reducers were found. Heterotrophic colonisation appeared non-specific whereas autotrophic colonisation was selective (4).
Two sterilised soils were amended with *Arthrobacter globiformis* or *Enterobacter gerogenes* or bacteria and amoebas (soil isolate) and held at 25°C. The protozoa enhance the mineralisation of nutrients immobilised in the microbial biomass by consuming bacteria and excreting excess nutrients, peaking on day 17. A significant negative correlation was observed between microbial biomass sulfur and extractable SO_4^{2-} in soil (5).

Abiotic removal
Some oxidation to the volatile oxides occurs in the environment (3).

Adsorption and retention
Liming sandy-loamy podzol at a single and double hydrolytic acidity increased sulfur leaching under annual crops from 180 to 240 and 270 kg ha^{-1} over a 4-yr period, respectively. This was balanced by an input at 336 kg ha^{-1} over a 4-yr period from atmospheric precipitation (6).
Probably persistent, unlikely to leach from soil and is unlikely to reach water (7).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rabbit 175 mg kg^{-1} (form unspecified) (8).
LD_{Lo} intravenous rabbit, rat, dog 5, 8 and 10 mg kg^{-1}, respectively (form unspecified) (8).
LD_{Lo} intraperitoneal guinea pig 55 mg kg^{-1} (form unspecified) (8).

Irritancy

In humans, inhalation of sulfur dusts is not known to cause systemic poisoning, but may irritate the respiratory tract. Chronic exposure can cause lung irritation; the dust can cause eye irritation (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with and without metabolic activation negative (10).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
No advisory value necessary under The Water Supply (Water Quality) Regulations 1989 (7).

Other comments

$CaCO_3$ applications were not effective in promoting plant growth in soils with total sulfur levels >4% (12).
The role of anaerobic bacteria in sulfur metabolism and the influence on organic decomposition in aquatic sediments reviewed (13).
Toxicity reviewed (14,15).
Reviews on human health effects, experimental toxicology and ecotoxicology listed (16).
Sulfur and its compounds reviewed (17).
Exists in several allotropic modifications but at standard temperatures and pressures only the orthorhombic (Sα) crystal structure is thermodynamically stable. Ignites in air at 261°C; in oxygen at 260°C.

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S150 sulfur dioxide

SO_2

O_2S **Mol. Wt.** 64.06 **CAS Registry No.** 7446-09-5

Synonyms sulfurous anhydride; sulfur superoxide; sulfurous oxide; fermenticide liquid

EINECS No. 231-195-2 **RTECS No.** WS 4550000

Uses Preservative in vegetables, fruits, and cooked meats. Disinfectant used in food factories and breweries. Bleaching agent used especially for textiles, gelatin, sugar beet and glue. The liquid is used as a solvent.

Physical properties

M. Pt. –72°C **B. Pt.** –10°C **Specific gravity** 1.50 (liquid)
Volatility v.p. 2538 mmHg at 21°C ; v.den. 2.26 at 0°C
Solubility Water: 85 g l^{-1} at 25°C. Organic solvents: chloroform, diethyl ether, ethanol, methanol

Occupational exposure

DE-MAK 0.5 ppm (1.3 mg m^{-3})
FR-VME 2 ppm (5 mg m^{-3}) **FR-VLE** 5 ppm (10 mg m^{-3})
JP-OEL (pending)
SE-LEVL 2 ppm (5 mg m^{-3}) **SE-CEIL** 5 ppm (13 mg m^{-3})
UK-LTEL 2 ppm (5.3 mg m^{-3}) **UK-STEL** 5 ppm (13 mg m^{-3})
US-TWA 2 ppm (5.2 mg m^{-3}) **US-STEL** 5 ppm (13 mg m^{-3})

UN No. 1079 (liquefied) **HAZCHEM Code** 2RE (liquefied) **Conveyance classification** toxic gas, corrosive (liquefied)
Supply classification toxic
Risk phrases Toxic by inhalation – Causes burns (R23, 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 – 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

Toxicity to other species
Young *Arbutus unedo* and *Viburnum tinus* plants exposed (80-120 days) to 25-60 ppb sulfur dioxide suffered no visible symptoms to leaves. The photosynthetic activity and growth of *A. unedo* was greatly reduced and a partial stomatal closure was observed. Stomatal conductance significantly decreased at the end of treatment for *V. tinus* but no change in CO_2 assimilation occurred. A mechanism of repair was thought to operate (1).
One-month-old *Quercus rotundifolia Lam.* were exposed to 0.23 ppm for 14 hr day^{-1} for 130 days in a growth chamber. The plants showed a significant decrease in growth rate (2).

Environmental fate

Nitrification inhibition
Injury to spruce by acid rain was associated with inhibition of ammonification in the litter and the soil A horizon at 500-600 and 800-900 metres above sea level. The increased SO_4^{2-} content caused the number of sulfite-resistant heterotrophs, thiosulfate oxidisers and bacteria oxidising elemental S to SO_4^{2-} to increase. Levels of aerobes and ammonifers decreased (3).

Carbonaceous inhibition

Soil acidification due to air pollutants (SO_2 and NO_x) was studied in Brown Forest soil. Carbon dioxide production rate decreased, and the activity of microbial biomass increased with decreasing pH. Population sizes did not increase wtih acidification but some groups (anaerobic nitrogen fixers, and sulfur oxidisers) tolerated pH change (4).

Abiotic removal

A 1981/1982 survey determined the atmospheric decay, deposition and reaction of SO_2 to be 15, 18.5 and 78.8 hr, respectively (5).

Mammalian & avian toxicity

Acute data

LC_{50} (1 hr) inhalation rat 2520 ppm (6).
LC_{50} (30 min) inhalation mouse 3000 ppm (7).
TC_{Lo} (5 day) inhalation human 3 ppm (pulmonary effects) (8).

Sub-acute and sub-chronic data

Inhalation guinea pig (30 day) 5 ppm 4 hr day^{-1} caused a reduction in respiratory rate (9).
Inhalation rabbit (3-12 month), exposure to 0.5 ppm NO_2 and 0.1 ppm SO_2 mixture caused morphological changes to the respiratory system. Changes in glutathione peroxidase, glucose-6-phosphate dehydrogenase, malate dehydrogenase activities, and nonprotein SH group levels in the blood, liver and lung were observed (10).

Carcinogenicity and chronic effects

An association between occupational exposure and lung cancer deaths has been suggested (11).
National Institute for Occupational Safety and Health (NIOSH) found no data to suggest that sulfur dioxide was a primary carcinogen (12).

Teratogenicity and reproductive effects

Inhalation ♀ CD-1 mice 0, 32 or 65 ppm SO_2 from gestational days 7 to 18. SO_2 air flow was set at 500 ml min^{-1}. Litter size was not affected, but 65 ppm caused significant decrease in pup weight. Maternal exposure affected neuromuscular coordination and caused deficits in the functional capacity of the developing offspring (13).

Metabolism and toxicokinetics

Inhalation rabbit 0.1 ppm (duration unspecified) 40% was absorbed in the nose and pharynx. At higher concentrations 10-100 ppm, absorption was 95% (14).
Absorbed from the respiratory tract into the blood stream. It is then widely distributed throughout the body, where it is metabolised then excreted via the urine (species unspecified) (15).

Irritancy

Eye and respiratory tract irritant (humans) (16).
10,000 ppm caused irritation to moist areas of the skin within a few minutes (17).
A person suffered severe burns following the bursting of a cylinder containing sulfur dioxide (18).

Sensitisation

Four groups of human volunteers (normal, atopics sensitive to allergens, mild asthmatics, and moderate-severe asthmatics) were exposed to SO_2 inhalation during exercise. Following exposure to 0.6 ppm all groups showed airway resistance, which was most marked in mild asthmatics (19).
Humans aged 55+ yr exposed to aerosols containing 1 ppm sulfur dioxide showed significant sensitivity (20).

Genotoxicity

In vitro human lymphocytes chromosomal aberrations and sister chromatid exchanges positive (21).
Vicia faba chromosomal aberrations positive (22).

Other effects

Other adverse effects (human)

The genotoxic effects of an average concentration of 41.7 mg m^{-3} of sulfur dioxide (SO_2) exposure on 42 workers in a fertilizer factory were investigated. Mitotic index (MI), chromosomal aberrations (CAs), sister-chromatid exchanges (SCEs) and satellite associations (SA) were observed. In exposed workers, a higher MI was recorded in comparison with controls, but this declined with duration of exposure. Satellite associations mean frequency of CAs and SCEs per cell were higher in exposed workers. In smokers, alcoholics and smoker-alcoholics, the frequency of CAs and SCEs per cell was significantly higher than for the non-smokers and non-alcoholics, both in the controls and the SO_2-exposed workers and showed a correlation with the duration of exposure. SO_2 is therefore a clastogenic and genotoxic agent for which necessary precautions must be taken (23).

Non-smoking women, aged 40-65 yr who used coal with a high-sulfur content as a cooking fuel had higher incidences of respiratory complaints and higher carboxyhaemoglobin levels (24).

143 smelter workers who processed a high sulfide ore were studied on 4 days of their working wk. Exposure to SO_2 and particulates was monitored and compared with the results from 117 control workers. Smelter workers were exposed to 0.374 mg m^{-3} particulates and 0.67 ppm SO_2. No excess of chronic respiratory symptoms was found (25).

Epidemiological studies investigating the effects of air pollution on the respiratory tract showed that acute symptoms were caused by SO_2 and smoke at levels below the recommended European standards and that the susceptibility to air pollution related respiratory diseases was linked to sex, age, tobacco smoking and alcohol consumption. Meteorological factors and pollens also contributed (26).

Studies on 10-12 yr old children in Germany showed that the air pollutants SO_2, NO_2, carbon monoxide and dust may contribute to obstructive bronchitis (27).

In humans, inhalation causes irritation of the respiratory tract which may lead to bronchoconstriction and pulmonary oedema. Very high concentrations (unspecified) may cause respiratory arrest and asphyxia. Contact with liquid sulfur dioxide results in acid burns. Allergic reactions including anaphylaxis and deaths have been reported (28,29).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (30).

Other comments

Environmental acidification mechanisms by NO_2 and SO_2 reviewed (31,32).

Air pollutant, contributes to acid rain in the atmosphere.

Air pollutants including sulfur dioxide were investigated to determine the potential risk of cancer mortality from environmental pollution (33).

Health and environmental pollution reviewed (34).

Toxicity to terrestrial wildlife resulting from environmental pollution reviewed (35).

Health, safety precautions and toxicity reviewed (36).

Reviews on human health effects, experimental toxicology, ecotoxicology, physico-chemical properties, exposure levels, epidemiology and workplace experience listed (37).

Synergistic effects with sulfuric acid have been reported (14).

Environmental fate of sulfur oxides and suspended particulate matter reviewed (14).

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S151 sulfur hexafluoride

SF_6

F_6S **Mol. Wt.** 146.06 **CAS Registry No.** 2551-62-4

Synonyms sulfur fluoride (SF_6); Elegas

EINECS No. 219-854-2 **RTECS No.** WS 4900000

Uses Used in electronic ultra-high frequency piping and electrical circuits.

Physical properties

M. Pt. –50.8°C **B. Pt.** –63.8°C (sublimes) **Specific gravity** 1.88 (liquid) at –50.8°C
Solubility Organic solvents: ethanol

Occupational exposure

DE-MAK 1000 ppm (6100 mg m^{-3})
SE-LEVL 1000 ppm (6000 mg m^{-3})
UK-LTEL 1000 ppm (6070 mg m^{-3}) **UK-STEL** 1250 ppm (7590 mg m^{-3})
US-TWA 1000 ppm (5970 mg m^{-3})

UN No. 1080 **HAZCHEM Code** 2RE **Conveyance classification** non-flammable non-toxic gas

Mammalian & avian toxicity

Metabolism and toxicokinetics

Inhalation rat (5 hr) 80 vol% in blood, a significant amount accumulated in fatty tissues despite its low solubility. Sulfur hexafluoride also accumulated in the spinal cord and brain, but to a lesser extent (1).

Genotoxicity

In vitro Chinese hamster ovary cells HGPRT with and without metabolic activation non-cytotoxic, non-mutagenic; however, the spark-decomposed compound was strongly cytotoxic both with and without metabolic activation (2).

Other effects

Other adverse effects (human)

Six workers were accidentally exposed to degradation products of sulfur hexafluoride during electrical repair work. Unprotected exposure in an underground enclosed space occurred for 6 hr over a 12 hr period. Initial symptoms included shortness of breath, chest-tightness, productive cough, nose and eye irritation, headache, fatigue, nausea and vomiting. Although exposure ended after several hr, 4 workers remained symptomatic for 1 wk to 1 month. Some pulmonary damage was seen. At follow-up, after 1 yr, no persistent abnormalities were found (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluorides: maximum admissible concentration 1500 μg l^{-1} at 8-12°C; 700 μg l^{-1} at 25-30°C (4).

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Other comments

Influence of sulfur hexafluoride gas on the rate and yield of ozone formation in air and in oxygen was investigated by using a single pulse ozoniser system at a total pressure of 1 atmosphere. Addition of sulfur hexafluoride into air attained about 270% increase of the maximum ozone yield at 1% of sulfur hexafluoride concentration, while the rate of ozone formation remained unaffected. In pure O_2, sulfur hexafluoride resulted in a decrease in ozone yield with increase of the rate. Addition of sulfur hexafluoride into N_2 enhanced the emission, while the addition into the air had little effect (6).

The toxicities of its decomposition by-products are discussed (7).

The safety aspects in handling, storage and emergencies are discussed (8).

Reviews on human health effects, epidemiology, workplace experience, experimental toxicology and environmental effects listed (9).

Its density is ~5 times that of air (gas). Kinetically stable, thermodynamically unstable. No fluorine exchanges with hydrogen fluoride.

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S152 sulfuric acid

H_2SO_4

H_2O_4S **Mol. Wt.** 98.08 **CAS Registry No.** 7664-93-9

Synonyms oil of vitriol; dihydrogen sulfate; vitriol brown oil

EINECS No. 231-639-5 **RTECS No.** WS 5600000

Uses Used in the manufacture of fertilizers, paper, glue and dyes. Also used in petroleum purification processes and metal pickling. Dilute acid formerly used in the treatment of gastric hypoacidity, while the concentrated acid was used as a topical caustic. Also used in the manufacture of phosphoric acid for detergents.

Physical properties

M. Pt. 10°C (anhydrous acid) **B. Pt.** ~290°C **Specific gravity** 1.84 at 25°C **Volatility** v.p. 1 mmHg at 145.8°C
Solubility Water: miscible. Organic solvents: miscible with ethanol

Occupational exposure

DE-MAK 1 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 1 mg m^{-3} **FR-VLE** 3 mg m^{-3}
JP-OEL 1 mg m^{-3}
SE-LEVL 1 mg m^{-3} (mist) **SE-STEL** 3 mg m^{-3} (mist)
UK-LTEL 1 mg m^{-3}
US-TWA 1 mg m^{-3} **US-STEL** 3 mg m^{-3}

UN No. 1830 **HAZCHEM Code** 2P **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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Never add water to this product – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S30, S45)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) flounder 100-330 mg l^{-1} (1).
Experimental acidification of a freshwater lake was carried out in 1976. Response of fish population species – lake trout, white sucker, fathead minnow, shiny sculpin, pearl dace – was observed during progressive reduction in pH. No changes in growth of lake trout and white sucker occurred during the initial years of acidification but during the period 1979-1982 a decline in numbers of all species was noted (2).
Brook trout embryos and fry were exposed to lethal and sublethal levels of acidity (pH 7.0, 6.2, 4.7, 4.3 and 3.9) beginning at fertilisation. Significant differences in mortality between the strains suggested a genetic component to acid tolerance. Only at pH 4.3 did substantial mortality occur at hatching (3).

Invertebrate toxicity
LC_{50} (48 hr) brown shrimp 60-70 mg l^{-1} (1).
Between 1976 and 1983 pH in a freshwater lake was lowered 0.5 pH yr^{-1} from pH 6.7 to pH 5.0 and held there for 3 yr. The decrease in pH caused major changes in epilimnetic phytoplankton community in this lake. Biomass increased as pH decreased. *Chlorella* abundance increased as pH decreased from 6.1 to 5.6, wherein *Merismopedia*, *Chroococcus*, *Gymnodinium* and *Peridinium* dominated once pH decreased below 5.6. The amount of edible biomass increased as the pH decreased from 6.7 to 5.6, then declined as pH decreased to 5.0 (4).
A chronically acidic stream, pH 5.2, was subjected to an induced episode of acidity, during which acid, aluminium

and limestone were added at different points along the stream length. Four zones were set up: a control zone (A); an acid zone (B); an acid plus aluminium zone (C); and downstream a zone of aluminium at low pH with added limestone to increase pH (D), were created over a 24-hr period. Fish mortalities were highest in zones B and C. Overall mortality was low among invertebrate species found in acid waters. Highest mortality was observed for *Gammarus pulex* (5).

Increased acidity adversely affected protozoan communities; however biomass, algal biomass, fungal biomass and net oxygen metabolism were not sensitive to increases in acidity (6).

Environmental fate

Nitrification inhibition

In a greenhouse, 7 identical small-scale ecosystems, simulating hydrologically isolated lentic soft waters, were exposed to different artificial rain solutions during a 2-yr period. Two major types of rain were used, H_2SO_4 rain (pH 5.6-3.5) containing nitrate, and $(NH_4)_2SO_4$ rain (pH 5.6). The treatments with $(NH_4)_2SO_4$, particularly, caused remarkable changes in water quality and flora. The pH decreased to 3.5, and both ammonium and sulfate accumulated. Nitrification of ammonium was the dominant acidifying process (7).

Abiotic removal

Air samples were collected from above oceans and land to determine air pollution levels. Particles containing H_2SO_4, sulfate, HNO_3 and nitrate were identified. A diurnal solar radiation effect on concentration and chemical composition of small sulfate-containing particles (0.2-0.7 μm size) was observed, indicating photochemical reaction. H_2SO_4 particles were most frequently observed near noon and $(NH_4)_2SO_4$ particles dominated at night. The concentration of sulfate particles depended on air trajectories, wind direction and wind speed. Numbers of sulfate particles were higher at low altitudes (<150 m) than at high altitudes (2600 m) (8).

Adsorption and retention

Reconstructed Spodosol and intact Alfisol soil columns were used to examine the effects of 52 wk of additions of various simulated throughfall solutions on base cation, Al, acid neutralising capacity, and pH levels in soil leachates. For leachates collected from the forest floor after H_2SO_4 additions, H^+ exchange for Ca^{2+} was the major buffering mechanism of acid inputs (9).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2.14 g kg^{-1} (10).

LC_{50} (2 hr) inhalation mouse, rat 320, 510 mg m^{-3}, respectively (11).

Sub-acute and sub-chronic data

Inhalation rabbits 2 hr day^{-1} exposure to 0.5 mg m^{-3} H_2SO_4 and NO_2 at 0.3 (low) or 1 ppm (high) concentrations. Animals were killed 24 hr after 2, 6 or 13 exposures. 1 ppm NO_2 with sulfuric acid caused increased neutrophil and phagocytic capacity while 0.3 ppm NO_2 mixtures depressed phagocytic capacity and mobility. The results were compared with those for NO_2 or H_2SO_4 alone (12).

Inhalation monkey (78 wk) 0.38-4.79 mg m^{-3} and particle sizes of 0.54 to 3.60 μm. At concentrations of 2.43 and 4.79 mg m^{-3} and particle sizes of 3.60 and 0.73 μm, definite damage to the pulmonary structure was evident and there was deterioration in pulmonary function. No detectable effects were seen in guinea pigs (52 wk) 0.08-0.1 mg m^{-3} and particle sizes of 0.84 and 2.78 μm (13).

Inhalation guinea pig (120 hr) 2, 4.2 and 8 mg m^{-3}. Exposure to the highest concentration caused oedema of the lungs, changes in the interalveolar walls and increased histamine content in lung tissue. 3 wk after exposure, sclerosis appeared (14).

Teratogenicity and reproductive effects

No teratogenic effects were observed in rabbits and mice exposed to sulfuric acid aerosol (≤20 mg m^{-3}) (15).

Irritancy

5% H_2SO_4 classified as irritant; defined as producing inflammation of the skin persisting for at least 24 hr after an exposure period of ≤4 hr. 15% H_2SO_4 classified as corrosive; defined as producing full thickness destruction of skin tissue in at least one animal during the test for skin irritation (16).

100 μl of 10% solution instilled into rabbit eye, results scored at 24, 48 and 72 hr, classified as non-irritant (17).

Sensitisation

In humans, frequent skin contact with dilute solutions can cause dermatitis (18).

Other effects

Other adverse effects (human)

Corrosive to all body tissues. Inhalation of the concentrated vapour can cause serious lung damage. Contact with eyes can cause blindness. Skin contact can cause severe necrosis. Ingestion can cause severe internal injury and death (19).

112 workers exposed to H_2SO_4 were investigated for tooth erosion compared with 513 controls. The rate of erosion in exposed workers was 2.4% higher than in controls. The prevalence rate of teeth erosion was significantly higher in the group who worked longer than 3 yr (20).

22 normal and 22 asthmatic adult volunteers were exposed in an environmental control chamber to light fogs (~0.1 g m^{-3} liquid water content, 10 μm median droplet diameter) containing nominally 0, 500, 1000, 2000 μg m^{-3} H_2SO_4. Exposures were random, 1 hr duration at 1 wk intervals and included three 10 min periods of moderately heavy exercise. H_2SO_4 had only a slight effect on pulmonary function, even at the highest concentration. Asthmatics experienced bronchioconstriction attributed to exercise under all exposure conditions (21).

Inhalation adolescents 68 μg m^{-3} H_2SO_4 alone and in combination with SO_2 caused significant changes in pulmonary function, whereas exposure to air or SO_2 alone did not (22).

The mortality rate from lung cancer was found to be significantly elevated in workers exposed to sulfuric acid mist (and in workers exposed to other acids) during steel-pickling operations (23).

The possibility of a carcinogenic effect is also suggested by a study which found higher (but not statistically significant) mortality from lung and laryngeal cancer in soap production workers (24).

A positive association has been shown between the development of upper respiratory tract cancer and exposure to sulfuric acid mist at an oil refinery (25).

A mortality study, together with an incidence study for laryngeal cancer, was made among 361 workers with a minimum employment of 1 yr in soap production in Italy. Mortality from all causes was lower than expected, but lung cancer and laryngeal cancer deaths were increased, although without statistical significance. Five new laryngeal cancer cases were detected during the study period, whereas ~1 was expected. All men with respiratory cancer had been working for several years, and the latency time was >10 yr. Even though the mechanism of a causal link is difficult to assess, the possibility of a carcinogenic effect of H_2SO_4 is suggested (26).

Any other adverse effects

Intradermal mice (duration and dose unspecified) caused necrotic foci which rapidly regressed (27).

Inhalation rats 0.1 or 1.0 mg m^{-3} H_2SO_4 exposure 6 hr to 7 days, no significant difference from controls. Pulmonary damage was demonstrated when exposure was to H_2SO_4 and ozone combined (28).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Hydrogen ion concentration guide level 6.5<pH<8.5. Sulfates: maximum admissible concentration 250 mg l^{-1} SO_4; guide level 25 mg l^{-1} (29).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (30).

Other comments

Chronic health effects from airborne exposure in humans and animals reviewed (31-33).

Atmospheric pollution by sulfuric acid and sulfates reviewed (34).

Sulfuric acid as a water treatment agent reviewed (35).

Reviews on human health effects, experimental toxicology, ecotoxicology, physico-chemical properties, epidemiology, workplace experience and exposure listed (36).

Synergistic effects with sulfur dioxide have been reported (37).

Environmental fate of sulfur oxides and suspended particulate matter reviewed (37).

Physical and chemical properties, hazards and current legislation in France reviewed (38).

Very corrosive. Strong affinity for water abstracts it from air and organic substances. Decomposes at 340°C to

sulfur trioxide and water. Freezes at 3°C. The toxicity of sulfuric acid is based on the acidity and therefore is dependent on the buffer capacity of the water dilution. Commercial sulfuric acid contains 93-98% sulfuric acid and 2-7% water.

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S153 sulfuric acid (fuming)

$$H_2SO_4 \cdot SO_3$$

$H_2O_7S_2$ **Mol. Wt.** 178.14 **CAS Registry No.** 8014-95-7

Synonyms disulfuric acid; oleum; dithionic acid; pyrosulfuric acid

RTECS No. WS 5605000

Uses Used in chemical industry to manufacture other acids. Dehydrating agent in explosives.

Physical properties

M. Pt. –11°C to 35°C according to concentration **Specific gravity** 1.94
Solubility Water: miscible. Organic solvents: ethanol

Occupational exposure

UN No. 1831 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance, toxic
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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Never add water to this product – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S30, S45)

Mammalian & avian toxicity

Acute data
LC_{50} (1 hr) inhalation rat 347 ppm (1).

Other effects

Other adverse effects (human)
Following an oleum spillage in a populated industrial area in Delhi, India in 1985, worst affected regions were downwind of the accident where ground level concentrations reached 2.3 ppm (2).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

Other comments

An oleum spillage in India in 1985 (65% sulfur trioxide and 35% sulfuric acid mixture) resulted in 55 tons of oleum being released within 40 min. When oleum is spilt SO_3 gas is liberated, which is highly volatile and unstable. It reacts with atmospheric moisture and forms a fine sulfuric acid mist. A mathematical model used to predict impact of future similar incidents, showed that maximum concentrations could be expected 1 km from spill in downwind direction. People within this radius would suffer eye irritation, pain and burning sensations and breathlessness (1).
Reviews on human health effects, experimental toxicology, ecotoxicology and physico-chemical properties listed (4).
Environmental fate of sulfur oxides and suspended particulate matter reviewed (5).
Commercial grade oleum contains ~80% free SO_3.
Very corrosive. Hygroscopic.

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S154 sulfur monochloride

S_2Cl_2

Cl_2S_2 **Mol. Wt.** 135.04 **CAS Registry No.** 10025-67-9

Synonyms disulfur dichloride; sulfur subchloride

EINECS No. 233-036-2 **RTECS No.** WS 4300000

Uses Insecticide. Intermediate and chlorinating agent in the manufacture of organic chemicals, sulfur dyes, synthetic rubbers. Used in cold vulcanisation of rubber. Polymerisation catalyst for vegetable oils and for hardening soft woods.

Physical properties

M. Pt. -77°C **B. Pt.** 138°C at 760 mmHg **Flash point** 119°C **Specific gravity** 1.6885 at 15.5°C with respect to water at 15.5°C **Volatility** v.p. 10 mmHg at 27.5°C ; v.den. 4.66
Solubility Water: decomposes. Organic solvents: benzene, carbon disulfide, carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

DE-MAK 1 ppm (5.6 mg m^{-3})
JP-OEL ceiling limit 1 ppm (5.5 mg m^{-3})
UK-STEL 1 ppm (5.6 mg m^{-3})
US-STEL ceiling limit 1 ppm (5.5 mg m^{-3})
Supply classification corrosive
Risk phrases Reacts violently with water – Causes burns – Irritating to the respiratory system (R14, R34, R37)
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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Other effects

Other adverse effects (human)
Vapours are corrosive and irritate eyes, nose and throat, cause tears and affect breathing (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

Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology and workplace experience listed (4).

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S155 sulfurous acid

$$H_2SO_3$$

H_2O_3S **Mol. Wt.** 82.08 **CAS Registry No.** 7782-99-2

Synonyms sulfur dioxide solution

EINECS No. 231-973-1 **RTECS No.** WT 2775000

Uses Dental bleach. Antiseptic.

Physical properties

Specific gravity 1.03

Occupational exposure

UN No. 1833 **HAZCHEM Code** 2R **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Acute data

TD_{Lo} oral human 500 μg kg^{-1} (gastro-intestinal disturbances) (1).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Environmental fate of sulfur oxides and suspended particulate matter reviewed (3).

Sulfurous acid is a ~6% solution of sulfur dioxide in water. Gradually oxidises in air to sulfuric acid.

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S156 sulfur tetrafluoride

SF_4

F_4S **Mol. Wt.** 108.06 **CAS Registry No.** 7783-60-0

Synonyms tetrafluorosulfurane

EINECS No. 232-013-4 **RTECS No.** WT 4800000

Uses Selective fluorinating agent.

Physical properties

M. Pt. –121°C **B. Pt.** –38°C **Specific gravity** 1.95 (liquid) at –78°C, 2.35 (solid) at –183°C
Solubility Organic solvents: freely soluble in benzene

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
SE-CEIL 0.1 ppm (0.4 mg m^{-3})
UK-LTEL 0.1 ppm (0.45 mg m^{-3}) **UK-STEL** 0.3 ppm (1.3 mg m^{-3})
US-STEL ceiling limit 0.1 ppm (0.44 mg m^{-3})

UN No. 2418 **Conveyance classification** toxic gas, corrosive

Mammalian & avian toxicity

Acute data
LC_{Lo} (4 hr) inhalation rat 19 ppm (1).

Other effects

Other adverse effects (human)
Very toxic, corrosive. Strong irritant (2).
Six workers were accidentally exposed to sulfur tetrafluoride, a degradation product of sulfur hexafluoride, during electrical repair work. Workers were exposed for 6 hr over a 12 hr period. Initial symptoms included shortness of breath, chest tightness, productive cough, nose and eye irritation, headache, fatigue, nausea and vomiting. Four workers remained symptomatic for 1 wk to 1 month after exposure. No persistent abnormalities present after 1 yr (3).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

New uses in organic synthesis reviewed (5).
Reviews on human health effects, experimental toxicology, ecotoxicology and physico-chemical properties listed (6).
Degradation product of sulfur hexafluoride. Thermostable to 600°C. Reacts violently with water.

References

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S157 sulfur trioxide

SO_3

O_3S **Mol. Wt.** 80.06 **CAS Registry No.** 7446-11-9

Synonyms sulfuric anhydride; Sulfan

EINECS No. 231-197-3 **RTECS No.** WT 4830000

Uses In the manufacture of sulfuric acid and explosives. Sulfonation reagent.

Physical properties

M. Pt. 62.3°C (α); 32.5°C (β); 16.8°C (γ) **B. Pt.** 44.8°C (γ) **Specific gravity** 1.9224 (liquid γ)
Volatility v.p. 73 mmHg (α) 25°C, 344 mmHg (β) 25°C, 433 mmHg (γ) 25°C

Occupational exposure

UN No. 1829 (inhibited) **HAZCHEM Code** 4WE (inhibited) **Conveyance classification** corrosive substance (inhibited)

Environmental fate

Abiotic removal

Highly reactive gas which rapidly hydrolyses to sulfuric acid in the presence of moisture in the air (1).

Other effects

Other adverse effects (human)

Concentrations of 1 ppm can cause coughing, choking and severe discomfort. Corrosive to mucous membranes, irritant (2).

47 copper flotation workers who were exposed to SO_2 and SO_3 (in addition to lead, copper, zinc, silicon dioxide and carbon disulfide) had higher concentrations of serum copper and lactic acid and higher activities of phosphohexoisomerase, glucose-6-phosphate dehydrogenase and pyruvate kinase compared with 34 non-exposed controls. Lower haematocrit value, number of erythrocytes and concentrations of Mg and Ca were also observed in the blood (3).

Legislation

Included in Schedule 4 (Release into the Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

Flue gas treatment reviewed (5).

Disposal methods, handling, storage and toxic effects discussed (6,7).

Reviews on human health effects, experimental toxicology and ecotoxicology listed (8).

Environmental fate of sulfur oxides and suspended particulate matter reviewed (9).

Exists in three forms: α, β, γ. The α-form is stable, the β and γ forms are metastable. The commercial product Sulfan A consists mainly of β-SO_3 and melts at 30-35°C. Sulfan B consists mainly of γ-SO_3 and melts at 17°C. Sulfan C contains no stabiliser and polymerises to α-SO_3.

Absorbs moisture rapidly from air, emitting dense white fumes. Combines explosively with water.

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S158 sulfuryl fluoride

SO_2F_2

F_2O_2S **Mol. Wt.** 102.06 **CAS Registry No.** 2699-79-8

Synonyms sulfuryl difluoride; Vikane

EINECS No. 220-281-5 **RTECS No.** WT 5075000

Uses Fumigant insecticide.

Physical properties

M. Pt. –135.82°C **B. Pt.** –55.38°C **Specific gravity** 1.349 **Volatility** v.p. 21.1°C at 1275 mmHg
Solubility Water: 750 mg kg^{-1} at 25°C. Organic solvents: carbon tetrachloride, ethanol, toluene

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (inhalable dust fraction)
FR-VME 5 ppm (20 mg m^{-3})
UK-LTEL 5 ppm (21 mg m^{-3}) **UK-STEL** 10 ppm (42 mg m^{-3})
US-TWA 5 ppm (21 mg m^{-3}) **US-STEL** 10 ppm (42 mg m^{-3})

UN No. 2191 **Conveyance classification** toxic gas
Supply classification toxic
Risk phrases Toxic by inhalation and if swallowed – Irritating to eyes, respiratory system and skin (R23/25, R36/37/38)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe gas – Wear suitable 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, S37/39, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 100 mg kg^{-1} (1).
LD_{50} oral guinea pig 100 mg kg^{-1} (2).
LC_{50} (4 hr) inhalation ♂ rat, ♀ rat 5.1, 4.92 mg l^{-1}, respectively (1).
LC_{Lo} (1 hr) inhalation mouse, rabbit 1200, 2000 ppm, respectively (3).

Sub-acute and sub-chronic data
Inhalation (13 wk) ♂ and ♀ Fischer 344 rats at 300 ppm for 6 hr day^{-1}, 5 days wk^{-1} reduced weight gain, and caused dental fluorosis, a slight decrease in grooming, decreased flicker fusion threshold, slowing of flash, auditory and somatosensory evoked potentials, mild nasal and pulmonary inflammation, mild kidney effects, and mild vacuolation in the brain (4).
Inhalation (2 wk) rat and rabbit, 6 hr day^{-1}, 5 days wk^{-1} to 0, 100, 300 or 600 ppm. 9/10 rats at 600 ppm died or

were moribund between the second and sixth exposure. Rabbits exposed to 600 ppm were hyperactive and one animal had a convulsion. Exposure to 300 or 600 ppm resulted in vacuolation and/or malacia in the cerebrum of all rabbits and most of the rabbits had moderate inflammation of nasal tissues (5).

Teratogenicity and reproductive effects

Inhalation Fischer 344 rats and New Zealand White rabbits 0, 25, 75 or 225 ppm for 6 hr day^{-1}, water consumption was increased in the 225 ppm group, but no indication of embryotoxicity, foetotoxicity in any of the groups. Among rabbits, maternal weight loss was observed in the 225 ppm group. Decreased foetal body weights were observed. No evidence of embryotoxicity or teratogenicity were observed (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).

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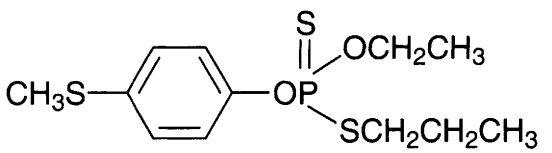
S159 sulprofos



$C_{12}H_{19}O_2PS_3$ **Mol. Wt.** 322.45 **CAS Registry No.** 35400-43-2

Synonyms *O*-ethyl *O*-[4-(methylthio)phenyl]-phosphorodithioic acid *S*-propyl ester; *O*-ethyl *O*-[4-(methylmercapto)phenyl] *S*-*n*-propyl phosphorothionothiolate; BAY NTN 9306; Bolstar

EINECS No. 252-545-0 **RTECS No.** TE 4165000

Uses Insecticide.

Physical properties

M. Pt. -15°C (tech.) **B. Pt.** 155-158°C at 0.1 mmHg **Specific gravity** 1.20 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} 5.48 **Volatility** v.p. $<7.5 \times 10^{-6}$ mmHg at 20°C
Solubility Water: 0.31 mg l^{-1} at 20°C. Organic solvents: dichloromethane, *n*-hexane, isopropanol, toluene

Occupational exposure

FR-VME 1 mg m^{-3}
US-TWA 1 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 23-38 mg l^{-1} (1).
LC_{50} (96 hr) carp 5.2 mg l^{-1} (2).
LC_{50} (96 hr) bluegill sunfish 11-14 mg l^{-1} (1).

Environmental fate

Degradation studies

Degradation was increased in the presence of non-sterile sediment compared with sterile sediment. Biodegradation was significantly faster in flasks containing sediment than in those with water alone (3).

Abiotic removal

Rapid photolytic degradation; $t_{1/2}$ of a 0.5 mg l^{-1} solution in sunlight 0.5 days, metabolites include the corresponding sulfoxide and sulfone of the phosphate and thiophosphate compounds (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂,♀ rat 304, 176 mg kg^{-1}, respectively (1).
LD_{50} oral mouse 1700 mg kg^{-1} (1).
LD_{50} dermal ♂,♀ rat 5491, 1064 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation rat >4.1 mg l^{-1}(1).

Metabolism and toxicokinetics

~92% is eliminated within 24 hr in rats (4).

Other effects

Any other adverse effects

In isolated mitochondria of rat liver, exposure to 10-50 μM prevented swelling in 1 mM phosphate or 20 μM $CaCl_2$, increased calcium accumulation in the mitochondria, and decreased calcium release from the mitochondria. It prevents activation of mitochondrial phospholipase A_2 by calcium and phosphate. Hepatotoxicity may be due to the modification of calcium transport system of internal mitochondrial membranes (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).
Log P_{ow} exceeds the European Union recommended limit of 3.0 (8).
WHO Toxicity Class II (9).
EPA Toxicity Class II (formulation) (1).
ADI 0.003 mg kg^{-1} body weight (1).

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