The Dictionary of Substances and their Effects

DOSE

Second Edition

Editor
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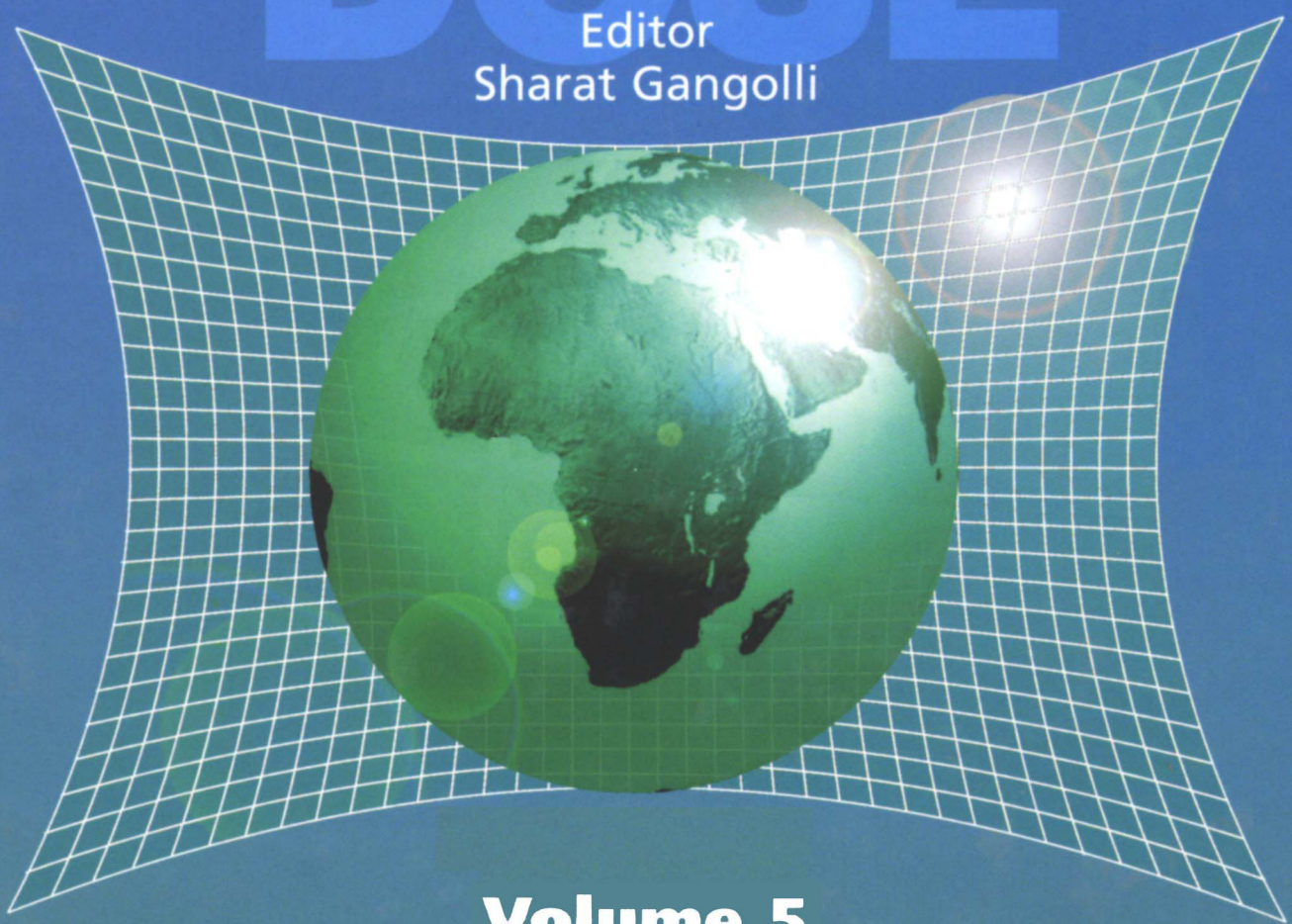

Volume 5
K–N

The Dictionary of Substances and their Effects

Second Edition

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

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

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

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

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

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

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

EINECS No.
This number is assigned by the European Commission to each record in the EINECS (European Inventory of Existing Commercial Chemical Substances) inventory. The numbers are in the format XXX-XXX-X, for example, *202-716-0* for *nitrobenzene*.

RTECS No.
The RTECS (Registry of Toxic Effects of Chemical Substances) number is a unique identifier assigned by NIOSH (National Institute of Occupational Safety and Health in the US) to every substance in the RTECS database. The number is in the format of two alphabetic characters followed by seven numeric characters, for example, *DA 6475000* for *nitrobenzene*.

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

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

Physical properties

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

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

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

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

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

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

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

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

Occupational exposure

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

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

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

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

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

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

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

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

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

UN number

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

HAZCHEM code

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

Conveyance classification

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

Supply classification

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

Risk and safety phrases

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

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

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

Ecotoxicity

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

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

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

Fish toxicity

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

Invertebrate toxicity

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

Toxicity to other species

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

Bioaccumulation

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

Environmental Fate

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

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

Nitrification inhibition

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

Carbonaceous inhibition

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

Anaerobic effects

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

Degradation studies

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

Abiotic removal

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

Adsorption and retention

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

Mammalian and avian toxicity

Studies on mammalian species are carried out to determine the potential toxicity of substances to humans. Avian species are studied primarily to assess the environmental impact on the ecosystem, however data from avian studies are also used for assessing human toxicity. This is specifically applied to pesticides, with neurotoxicology studies.
Procedures involve undertaking a series of established exposure studies on a particular substance using specific routes, oral, inhalation, dermal or injection for variable durations. Exposure durations include acute or single exposure to a given concentration of substance. Sub-acute or sub-chronic exposure, i.e. repeat doses over an intermediate time period, up to 4 weeks for sub-acute and 90 day/13 week (in rodents) or 1 year (in dogs) for sub-chronic studies. Chronic/long-term studies involve exposure to specific concentrations of chemical for a duration of 18 month-2 years. A variety of species are used in toxicity testing, most commonly rodents (rats, mice, hamsters) and rabbits, but tests can also be carried out on monkeys, domestic animals and birds.

Acute data

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

Sub-acute and sub-chronic data

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

Carcinogenicity and chronic effects

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

Teratogenicity and reproductive effects

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

Metabolism and toxicokinetics

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

Irritancy

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

Sensitisation

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

Genotoxicity

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

Other effects

Other adverse effects (human)

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

Any other adverse effects

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

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

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

References
Contains references to data from above sections.

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

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

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

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

Note

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

If you have any relevant information, please contact:

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Thomas Graham House
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Cambridge CB4 0WF
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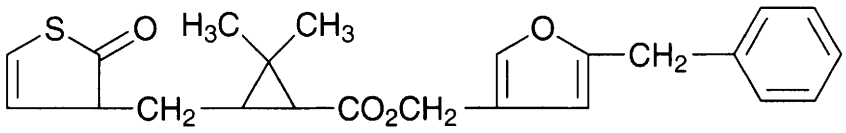
Document Delivery

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.

Telephone: +44 (0)20 7437 8656
Fax: + 44 (0)20 7287 9798
Email: library@rsc.org

K1 kadethrin



$C_{23}H_{24}O_4S$ **Mol. Wt.** 396.51 **CAS Registry No.** 58769-20-3

Synonyms cyclopropanecarboxylic acid, 3-[(dihydro-2-oxo-3(2*H*)-thienylidene)methyl]-2,2-dimethyl-, [5-(phenylmethyl)-3-furanyl]methyl ester, [1*R*-[1α,3α(*E*)]]-

EINECS No. 261-433-0 **RTECS No.** GZ 1266550

Uses Insecticide used in aerosols and sprays in combination with other insecticides.

Physical properties

M. Pt. 31°C **Volatility** v.p. 7.52×10^{-7} mmHg at 20°C

Solubility Organic solvents: acetone, benzene, dichloromethane, ethanol, piperonyl butoxide, toluene, xylene

Mammalian & avian toxicity

Acute data

LD_{50} oral ♀ rat, dog, ♂ rat >1000, 650, 1324 mg kg^{-1}, respectively (1).

LD_{50} percutaneous ♀ rat >3200 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral (90 day) no-effect level dog, rat 15, 25 mg kg^{-1}, respectively (1).

Inhalation rat, guinea pig 200 × normal aerosol dose (exposure unspecified) caused no adverse effects (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).

Other comments

Unstable in heat. Hydrolysed by aqueous alkalis. Rapidly decomposes in light (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. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

K2 kaolin

$Al_2H_4O_9Si_2$ **Mol. Wt.** 258.16 **CAS Registry No.** 1332-58-7

Synonyms Argiflex; Hydrogloss; Lustra; Porcelain clay; Satintone; Suprex clay; aluminium silicate hydroxide

RTECS No. GF 1670500

Uses Treatment for diarrhoea and for reducing inflammation and pain when applied in a poultice. Manufacture of porcelain, pottery and bricks.

Occupational exposure

UK-LTEL 2 mg m^{-3} (respirable dust)
US-TWA 2 mg m^{-3} (respirable fraction, containing no asbestos and <1% crystalline silica)

Mammalian & avian toxicity

Acute data
TD_{Lo} oral rat 590 g kg^{-1} (1).

Carcinogenicity and chronic effects
Inhalation hamster (6 hr day^{-1}, 5 days $week^{-1}$ for 18 months) 30 mg m^{-3} kaolin ceramic fibre. At 3 months macrophage infiltration, bronchiolisation of proximal alveoli and microgranuloma formation were observed. At 6 months interstitial and focal pleural fibrosis were observed. The severity of pulmonary lesions reached a plateau at 12 months, however the fibrosis continued to the end of the study. No lung neoplasms were observed, but 42% of the hamsters had pleural mesotheliomas (2).

References

1. *J. Nutr.* 1977, **107**, 2027.
2. Mast, R. W. et al *Inhalation Toxicol.* 1995, **7**(4), 503-532

K3 karaya gum

CAS Registry No. 9000-36-6

Synonyms Indian tragacanth gum; katilo gum; Lame gum; Muccira; Siltex gum; Tab gum

EINECS No. 232-539-4 **RTECS No.** WI 9370000

Uses Denture adhesive. Binder in paper manufacture. Emulsifier and stabiliser in food. Laxative.
Occurrence As a dried exudate from tree *Sterculia urens* Roxbo.
Sterculiqceae, which grows in S. E. Asia.

Physical properties

Solubility Water: swells to form gel

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 30 g kg^{-1} (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (2).

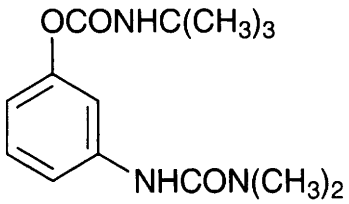
Other comments

DNA damaging activity reviewed (3).

References

1. *Food Res.* 1948, **13**, 29.
2. Prival, M. J. et al *Mutat. Res.* 1991, **260**(4), 321-329.
3. Ishizaki, M. et al *Shokuhin Eiseigaku Zasshi* 1987, **28**(6), 498-501 (Japan.) (*Chem. Abstr.* **109**, 5417v)

K4 karbutilate



$C_{14}H_{21}N_3O_3$ **Mol. Wt.** 279.34 **CAS Registry No.** 4849-32-5

Synonyms carbamic acid, (1,1-dimethylethyl)-, 3-[[(dimethylamino)carbonyl]amino]phenyl ester; Tandex

EINECS No. 225-439-7 **RTECS No.** EY 9980000

Uses Superseded non-selective herbicide used for residual control of most annual and perennial broad-leaved weeds and grasses.

Physical properties

M. Pt. 169-169.5°C

Solubility Water: 325 mg l^{-1}. Organic solvents: acetone, dimethyl sulfoxide, propan-2-ol, xylene

Environmental fate

Abiotic removal

Degraded in soil, $t_{1/2}$ 20-120 day (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3000 mg kg^{-1} (2).

LD_{50} intravenous mouse 320 mg kg^{-1} (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

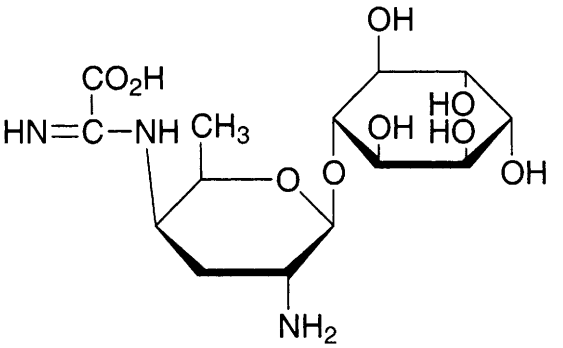
Other comments

Stable in acid media.

References

1. *The Pesticide Manual* 9th ed., 1993, British Crop Protection Council, Farnham, Surrey, UK.
2. *Guide to Chemicals Used in Crop Protection* 1972, Information Canada, Ottawa, Canada.
3. U.S. Army Armament Research and Development Command, Report: NX 03896, Chemical Systems Laboratory, NIOSH Exchange Chemicals.
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

K5 kasugamycin



$C_{14}H_{25}N_3O_9$ **Mol. Wt.** 379.37 **CAS Registry No.** 6980-18-3

Synonyms D-*chiro*-inositol, 3-*O*-[2-amino-4-[(carboxyiminomethyl)amino]-2,3,4,6-tetradeoxy-α-D-*arabino*-hexopyranosyl]-; Kasumin

RTECS No. NM 7521650

Uses Control of diseases in rice, especially rice blast. Also the control of other plant diseases such as leaf mould, leaf spot and scab on apples and pears.

Occurrence Produced by the fermentation of *Streptomyces kasugaensis*.

Physical properties

M. Pt. 202-204°C (decomp.) (hydrochloride hydrate)

Solubility Water: 125 g l^{-1} (hydrochloride hydrate). Organic solvents: acetone, methanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp, goldfish >40 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (6 hr) *Daphnia pulex* >40 mg l^{-1} (1).

Toxicity to other species

LC_{50} frog tadpoles (duration unspecified) >100 ppm (2).

Environmental fate

Abiotic removal

At 50°C, $t_{1/2}$ 47 day at pH 5 and $t_{1/2}$ 14 day at pH 9 (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral Japanese quail >4000 mg kg^{-1} (3).

LD_{50} oral ♂ rat, ♀ mouse 20,000-20,500 mg kg^{-1} (3).

LD_{50} dermal rat, mouse 4000, 10,000 mg kg^{-1}, respectively (3).

Carcinogenicity and chronic effects

Oral (2 yr) rat, dog no-effect level 1000, 800 mg kg^{-1}, respectively (3).

Genotoxicity

In vitro Chinese hamster ovary cells (metabolic activation unspecified) in combination with carbendazim sister chromatid exchanges negative, chromosomal aberrations positive (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. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
WHO Toxicity Class Table 5 (7).
EPA Toxicity Class IV (3).

Other comments

No adverse effects observed in adult fireflies (dose duration unspecified) (8).
Levels of 0.2 g kg^{-1} daily for 7 days to carp with bacterial infection resulted in 98% cure during this period (9).
Very stable at room temperature. Stable in weak acids, but is unstable in strong acids and alkalis.

References

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3. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
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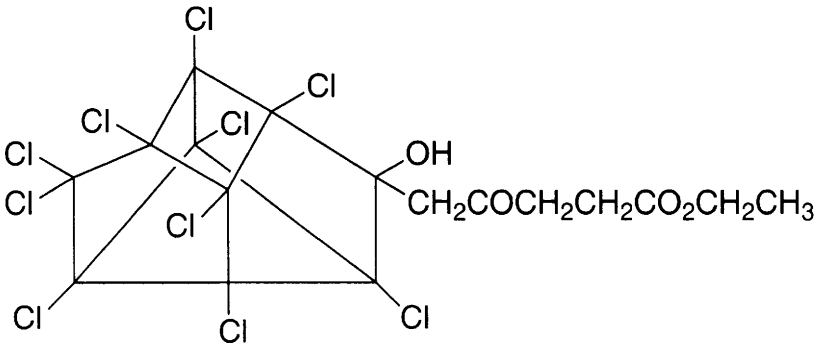
K6 kelevan



$C_{17}H_{12}Cl_{10}O_4$ **Mol. Wt.** 634.81 **CAS Registry No.** 4234-79-1

Synonyms 1,3,4-metheno-1*H*-cyclobuta[*cd*]pentalene-2-pentanoic acid, 1,1a,3,3a,4,5,5,5a,5b,6-decachloro-octahydro-2-hydroxy-γ-oxo-, ethyl ester; Despirol

RTECS No. PC 8400000

Physical properties

M. Pt. 89-90°C

Occupational exposure

Supply classification toxic

Risk phrases Harmful if swallowed – Toxic in contact with skin (R22, R24)

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

Environmental fate

Degradation studies

Supported growth of three *Pseudomonas* spp. (1).

Abiotic removal

Photooxidation by UV light in aqueous medium at 90-95°C, time for the formation of CO_2 (% of theoretical); 25%: 1.2 hr, 50%: 9.6 hr, 75%: 19 hr (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >104 mg kg^{-1} (3).

Other comments

Toxicity, human health effects, environmental effects comprehensively reviewed (4).

References

1. George, S. et al *Xenobiotica* 1988, **18**(4), 407-416.
2. Knoevenagel, K. et al *Arch. Environ. Contam. Toxicol.* 1976, **4**, 324-333.
3. Schafer, E. W. et al *Arch. Environ. Toxicol.* 1983, **12**, 355-382.
4. *Environmental Health Criteria: Kelevan* No. **66**, 1986, World Health Organisation, Geneva, Switzerland

K7 kerosene

CAS Registry No. 8008-20-6

Synonyms kerosine; jet fuel

EINECS No. 232-366-4 **RTECS No.** OA 5500000

Uses Fuel in lamps, stoves. Cleaner and degreaser. Jet fuel.

Occurrence Mixture of petroleum hydrocarbons, it constitutes the fifth fraction in petroleum distillation.

Physical properties

B. Pt. 175-325°C **Flash point** 81°C **Specific gravity** ~0.80

Solubility Organic solvents: miscible with other petroleum solvents

Occupational exposure

UN No. 1223 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Supply classification harmful

Risk phrases Harmful: may cause lung damage if swallowed (R65)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour – Avoid contact with the skin – If swallowed, do not induce vomiting: seek medical advice immediately and show this container or label (S2, S23, S24, S62)

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit 28 ml kg^{-1} (1).

LD_{50} oral guinea pig 20 g kg^{-1} (2).

LD_{50} oral ♂ rat >60 ml kg^{-1} (3).

LD_{50} intravenous, intratracheal rabbit 180, 200 mg kg^{-1}, respectively (4,5).

LD_{50} intraperitoneal rabbit 6600 mg kg^{-1} (4).

Gavage ♂ rat 24 ml kg^{-1} showed moderate renal and hepatic functional alterations 1-3 days later (3).

Sub-acute and sub-chronic data

Inhalation (90 days) ♂ Fischer 344 rats continuous exposure to 150 and 750 mg m^{-3} developed dose-related kidney damage with cytoplasmic hyaline droplets, necrosis of proximal tubular cells and accumulation of intratubular necrotic debris (6,7).

Dermal (60 wk) mice 5 µl 3 × wk^{-1} developed atrophied and degenerating nephrons as well as papillary necrosis (8).

Carcinogenicity and chronic effects

Dermal (2 yr) B6C3F1 mice 250 or 500 mg kg^{-1}, no evidence of carcinogenicity (9).

Teratogenicity and reproductive effects

Charles River CD rats, 6-15 days of gestation inhalation 6 hr day^{-1} 100, 400 ppm, no embryotoxic, foetotoxic or teratogenic effects observed (10).

Application to the shell surface of duck embryos, day-6 of incubation, 1-20 µl of weathered or unweathered aviation kerosene no toxic effects observed (11).

Metabolism and toxicokinetics

In baboons given radiolabelled kerosene via a nasogastric tube after tracheostomy, radiolabel was found localised in the kidney, brain, liver, lungs and spleen (12).

Irritancy

Dermal rabbit (duration not specified) 500 mg caused severe irritation (2).

Dermal (90 wk) ♀ B6C3F1 mice 500 mg kg^{-1} caused excessive irritation and ulceration at site of application (9).

Dermal B6C3F1 mice 250 or 500 mg kg^{-1} (unspecified duration) caused dose-related increased incidence of chronic dermatitis, identified by acanthosis, hyperkeratosis, necrosis and ulceration of the overlying epidermis. Dermal changes frequently included fibrosis, increased amounts of melanin and acute and chronic inflammatory cell infiltrates (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (9).

Other effects

Other adverse effects (human)

A group of human ♂ exposed to levels in air >350 mg m^{-3} were studied for 8 yrs; no increase in incidences of cancer were seen (13).

Case-control study of cancer in Canada revealed an increased incidence of kidney cancer in human ♂ with occupational exposure (14).

Other comments

Reviews on human health effects and experimental toxicology listed (15).

Autoignition temperature 210°C.

References

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15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

K8 ketene

$$CH_2=C=O$$

C_2H_2O **Mol. Wt.** 42.04 **CAS Registry No.** 463-51-4

Synonyms ethenone; carbomethene

EINECS No. 207-336-9 **RTECS No.** OA 7700000

Uses For acetylation in the manufacture of cellulose acetate and aspirin.

Physical properties

M. Pt. –150°C **B. Pt.** –56°C **Flash point** –107°C **Volatility** v.den. 1.45

Solubility Organic solvents: acetone (decomposes in ethanol), diethyl ether

Occupational exposure

DE-MAK 0.5 ppm (0.87 mg m^{-3})

UK-LTEL 0.5 ppm (0.87 mg m^{-3}) **UK-STEL** 1.5 ppm (2.6 mg m^{-3})

US-TWA 0.5 ppm (0.86 mg m^{-3}) **US-STEL** 1.5 ppm (2.6 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1300 mg kg^{-1} (1).

LC_{Lo} (10 min) inhalation monkey 200 ppm (2).

LC_{Lo} (10 min) inhalation cat 750 ppm (2).

LC_{Lo} (30 min) inhalation mouse 23 ppm (2).

LC_{Lo} (100 min) inhalation rat, guinea pig 53 ppm (2).

Other comments

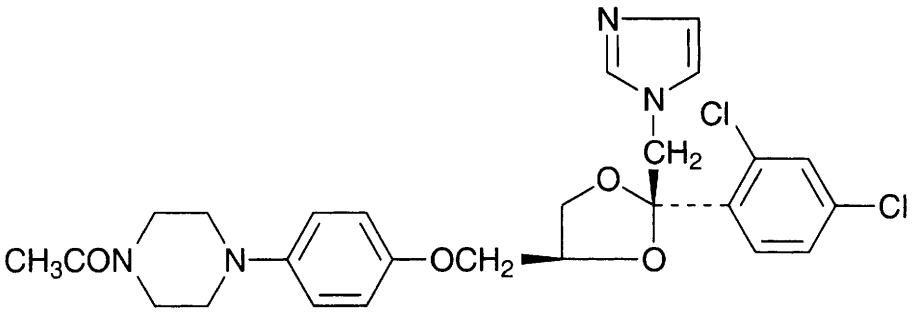
Reviews on human health effects, epidemiology and experimental toxicology listed (3).

Autoignition temperature 528°C.

References

1. *Union Carbide Data Sheet* Industrial Medicine and Toxicology Department, Union Carbide Corp., 270 Park Avenue, New York, NY10017, USA.
2. *J. Ind. Hyg. Toxicol.* **1949**, **31**, 209.
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

K9 ketoconazole



$C_{26}H_{28}Cl_2N_4O_4$ **Mol. Wt.** 531.44 **CAS Registry No.** 65277-42-1

Synonyms *cis*-1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]-phenyl]piperazine

EINECS No. 265-667-4 **RTECS No.** TK 7912300

Uses Oral broad-spectrum antimycotic. Possible treatment for prostate carcinoma (1).

Physical properties

M. Pt. 146°C

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, mouse, rat, dog 202-780 mg kg^{-1} (2).

LD_{50} intravenous guinea pig, mouse, rat, dog 28-86 mg kg^{-1} (2).

Teratogenicity and reproductive effects

Healthy human ♂, oral doses caused a transitory decrease in circulating levels of both total and free testosterone without affecting oestradiol concentrations. The time of maximum effect was dose related, being maximum at 4 hr after 200 or 400 mg and 8 hr after 600 mg. No effect on circulating levels of testosterone or oestradiol in women (3).

Teratogenic potential assessed using post-implantation rat embryo culture system, malformations at concentrations well below those affecting embryonic growth and differentiation were observed (4).

Oral (72 hr) ♂ rats 200 mg kg^{-1} reduced fertility compared to the controls. 400 mg kg^{-1} caused complete loss of fertility. Sperm motility and forward progression was reduced but there was no change in testicular weight, epididymal sperm concentrations or epididymal weight (5).

In vitro rat embryos (48 hr) with metabolic activation, ketoconazole was determined to have relatively high teratogenic potential (6).

Metabolism and toxicokinetics

Elimination is reported to be biphasic in humans, with an initial $t_{1/2}$ of 2 hr and a terminal $t_{1/2}$ 8 hr (7).

Oral (1-6 month) humans 200 mg daily. Mean elimination $t_{1/2}$ 3.3 hr 0.22% excreted in urine unchanged, suggesting almost complete metabolism (8).

Human adults 2% cream single application (5 g). Skin absorption rate was calculated to be 2.5-12.5%. Haematological and biochemical parameters remained normal, no unchanged drug was detected in blood or urine. Ketoconazole may be accumulated mainly in cutaneous layer and has no clinical safety problem (9).

Rats, rabbits, absorbed rapidly by the skin and then gradually distributed throughout the body. Excretion in urine and faeces was 0.4 and 2.1% of applied dose, respectively, after skin absorption (10).

Irritancy

Healthy adult subjects 2% cream single application (5 g) did not cause skin irritation (9).

Other effects

Other adverse effects (human)

Nausea and vomiting reported in 3-10% of patients administered orally, and topical administration has resulted in irritation or dermatitis (11).

Demonstrated to inhibit testosterone biosynthesis in human ♂ (12).

Shown to have immunosuppressive effects (13,14).

Any other adverse effects

In rat testes testosterone formation inhibited via inhibition of cytochrome P_{450}-dependent C17,20-lyase (15).

Intraperitoneal administration caused a rapid dose-dependent reduction of bile acid synthesis in eight-day bile-diverted rats, single dose 50 mg kg^{-1} reduced bile synthesis to 5% of the control value (16).

Other comments

Toxicity and pharmacokinetics reviewed (17).

Has dose/time related cytotoxic effects against malignant cell lines *in vitro* (18).

References

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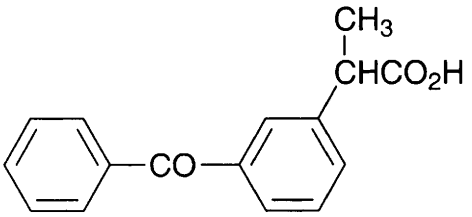
K10 ketoprofen



$C_{16}H_{14}O_3$ **Mol. Wt.** 254.29 **CAS Registry No.** 22071-15-4

Synonyms 3-benzoyl-α-methylbenzeneacetic acid; Oruvail; Epatec; Alrheumun; Orudis; Profenid; *m*-benzoylhydratopic acid; 3-benzoylhydratropic acid

EINECS No. 244-759-8 **RTECS No.** UE 7570000

Uses Analgesic, anti-inflammatory and antipyretic. Inhibitor of cyclo-oxygenase activity. Used in musculoskeletal and joint disorders.

Physical properties

M. Pt. 94°C

Solubility Organic solvents: acetone, chloroform, diethyl ether, dimethylformamide, ethanol, ethyl acetate

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 101 mg kg^{-1} (1).

Metabolism and toxicokinetics

Readily absorbed from the gastro-intestinal tract in humans; peak plasma concentrations occur about 0.5-2 hr after a dose. When taken with food, total bioavailability is not altered but rate of absorption is slowed. It is well absorbed from intramuscular and rectal routes, though only a small amount is absorbed via topical application. Extensively bound to plasma proteins and substantial concentrations are found in synovial fluid. Plasma $t_{1/2}$ 2-4 hr. Metabolised mainly by conjugation with glucuronic acid and excreted mainly in urine (2).

Seven elderly subjects were administered a single rectal dose of 75 mg. No abnormalities were seen in clinical and physical findings. Maximum plasma concentration was reached at 0.5-2.0 hr. Urinary excretion of total ketoprofen during 72 hr after administration was 35-82% of dose, and 97% of the urinary total ketoprofen was in the form of glucuronide (3).

Ten healthy volunteers received daily 15 g of 2.5% ketoprofen topical gel, corresponding to 375 mg of ketoprofen on skin. The peak plasma concentration was 144 mg ml^{-1} after the first administration with apparent absorption and elimination $t_{1/2}$ 3.2 and 27.7 hr, respectively. The total quantities eliminated in the urine represented about 2.6% of the first dose applied. Apparent $t_{1/2}$ of ketoprofen was 17.1 hr and there was no accumulation (4).

Irritancy

0.3% adhesive agent was tested in ♂ rabbits for both primary and cumulative skin irritations. In the primary test hardly any irritation occurred and no irritation occurred in the cumulative test (5).

Sensitisation

In photopatch tests for skin photosensitisation to UVA plus UVB light 3.8% of the subjects gave a positive reaction with ketoprofen (6).

Other effects

Other adverse effects (human)

Life threatening asthma, urticaria and angioedema developed in two aspirin-sensitive patients after taking ketoprofen, 50 mg by mouth (7).

Cardiac and respiratory arrest occurred in an asthmatic patient (8).
Reported to cause photosensitivity reactions (9).

Any other adverse effects
Oral rat (concentration unspecified) increased incidence of gastric ulcers (10).
DNA damage, single strand breaks was photoinduced by ketoprofen. No particular base specificity observed (11).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

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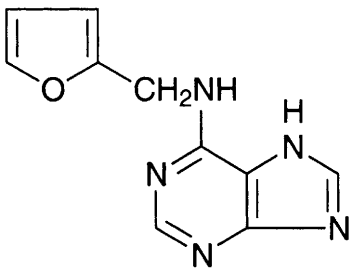
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

K11 kinetin



$C_{10}H_9N_5O$ **Mol. Wt.** 215.21 **CAS Registry No.** 525-79-1

Synonyms 1*H*-purin-6-amine, *N*-(2-furanylmethyl); adenine, N^6-furfuryl-; FAP; *N*-furfuryladenine; 6-(furfurylamino)purine

EINECS No. 208-382-2 **RTECS No.** AU 6270000

Uses Plant growth regulator. To augment growth of microbial cultures.
Occurrence A cell division factor found in various plant parts and in yeasts. Isolation from autoclaved water slurries of deoxyribonucleic acid (1).

Physical properties

M. Pt. 266-267°C (sealed tube)

Environmental fate

Adsorption and retention

Activated carbon was effective in adsorbing plant growth regulators including kinetin (2).

Genotoxicity

In vitro wheat cell cultures, no significant effect on sister chromatid exchange induction (3).

Legislation

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

Other comments

Sublimes at 220°C.

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L1 lactic acid

$$CH_3CH(OH)CO_2H$$

$C_3H_6O_3$ **Mol. Wt.** 90.08 **CAS Registry No.** 50-21-5

Synonyms Milk acid; 2-hydroxypropionic acid

EINECS No. 200-018-0 **RTECS No.** OD 2800000

Uses In the treatment of infective skin and vaginal disorders. Infusions to provide a source of bicarbonate for treatment of metabolic acidosis. Food preservatives and cosmetics.

Occurrence In sour milk as a result of fermentation by lactic acid bacteria

Physical properties

M. Pt. 16.8°C **B. Pt.** 122°C at 15 mmHg **Flash point** 110°C (closed cup) **Specific gravity** 1.249

Solubility Water: miscible. Organic solvents: ethanol, furfurol

Occupational exposure

Safety phrases Avoid contact with skin and eyes (S24/25)

Ecotoxicity

Fish toxicity

LC_{50}(18 hr) trout 100 mg l^{-1} (1).

Mechanism of hepatic lactate uptake was studied in the gulf toadfish by following the accumulation of ^{14}C lactate by isolated hepatocytes *in vitro*. Lactate uptake is by passive diffusion in toadfish hepatocytes. Lactate uptake by toadfish hepatocytes further differed from lactate uptake by mammalian tissues in that rates were not altered by

changes in either extracellular pH or extracellular sodium ion concentration. Rates of lactate conversion into glucose and carbon dioxide were measured and compared with uptake rates; it appears the rates of lactate metabolism are not limited by passive diffusion (2).

Invertebrate toxicity

LC_0 (26-72 hr) *Daphnia* 170 mg l^{-1} (3).

Environmental fate

Degradation studies

Methanogenic bacteria *Methanosarcina* spp. and *Methanobacterium* spp. were capable of metabolising lactate under methanogenic conditions (4).

Biodegradation occurs in anaerobic environments with transformation rate constants decreased as the food chain ascends acetate >lactate >glucose (5).

Anaerobic degradation by a mixed microbial culture, without sulfate and with both sulfate and molybdate, lactate was rapidly consumed and propionate and acetate were produced, whereas with sulfate alone, only acetate accumulated. Propionate oxidation was strongly accelerated by the presence of sulfate (6).

BOD_5 0.63 mg l^{-1} O_2 Warburg Sewage (7).

BOD_{10} 0.88 mg l^{-1} O_2 standard dilution sp. culture (8).

COD 100% ThOD (8).

Tubifex tubifex (0-2 hr), 80-85% of ^{14}C lactate was found in the intermediary products, with glutamate and malate as the main constituents. During aerobic long-term incubation (12-24 hr) the largest proportion of label was incorporated into proteins. In the absence of oxygen most of the radioactivity remained in the intermediaries, mainly in alanine and succinate; during initial period of aerobic incubation, high amounts of ^{14}C-carbon dioxide were released (9).

100 ppm was treated by activated sludge process in a rotary cylinder type biological treatment at 20°C for 120 hr. 70-100% of lactic acid was removed (rotating tube) (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3730 mg kg^{-1} (11).

LD_{50} oral mouse 4875 mg kg^{-1} (12).

LD_{50} oral guinea pig 1.81 g kg^{-1} (1).

LD_{Lo} oral rabbit 500 mg kg^{-1} (13).

LD_{50} subcutaneous mouse 4500 mg kg^{-1} (14).

Injection of 22.5 mg l^{-1} into jugular vein of anaesthetised rabbits initially increased breathing rate but no change or decrease in tidal volume. This was followed by deep and fast respiration (15).

Carcinogenicity and chronic effects

Subcutaneous 16 mice (18 months) 125 mg, 2 lymphomas, 1 sarcoma and 1 pulmonary tumour were observed (16).

Metabolism and toxicokinetics

Bacterial metabolites (lactate) in the gut contents and the blood in relation to the faecal excretory cycle were studied in anaesthetised rabbits. The level of organic acids in the alimentary tract varied cyclically with the faecal excretion pattern. Lactate originates from the stomach; it was available for extrahepatic tissue metabolism (17).

The effect of glucose concentration (0-20 ml) on lactate uptake at low lactate concentrations was studied in perfused livers from 48-hr starved rats with perfusate pH values of 7.4 and 6.8. Lactate uptake was independent of glucose concentration (0.18-1.80 mg l^{-1}), but was slightly inhibited with time at 3.60 mg l^{-1} glucose (18).

Irritancy

Dermal rabbit 500 mg (4 hr) caused severe irritation and 750 mg (24 hr) caused severe irritation (19).

Genotoxicity

Saccharomyces cerevisiae and *Salmonella typhimurium* with and without metabolic activation, negative (16).
Salmonella typhimurium TA97, TA98, TA100, TA104 with and without metabolic activation, negative (20).
In vitro Chinese hamster ovary K1 cells 900-1261 mg l^{-1} induced chromosomal aberrations at the initial pH of ~6.0 with and without metabolic activation. No clastogenic activity was observed when the culture medium was first acidified with each of the acids and then neutralised with sodium hydroxide (21).

Other effects

Any other adverse effects

Lactic acidosis has been proposed to be one factor promoting cell death following cerebral ischaemia. It has been demonstrated that cultured neurons and glia are killed by relatively brief (10 min) exposure to acidic solutions of pH <5. The onset of death after exposure to moderately acidic solutions was delayed in some cells, such that death of the entire cell population became evident only 48 hr after acid exposure (22).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (23).

Other comments

Toxicity reviewed (24).
Reviews on experimental toxicity and human health effects listed (25).
Analysis of the concentration of low molecular weight organic acids in soil, in the unsaturated zone, and in groundwater was undertaken. An unexpectedly high concentration of organic substances in natural surroundings that had significant dependence on the extractable amount of organic acids and on the pH value of the extract was observed. A clear connection between the spectrum of extractable organic acids and the microbiological activity was found in a depth profile from the soil down to the groundwater. In general, the spectrum of organic acids reduces to increasingly simpler substances with increasing depth (26).
Metabolism reviewed (27).

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L2 lactonitrile

$CH_3CH(OH)CN$

C_3H_5NO **Mol. Wt.** 71.08 **CAS Registry No.** 78-97-7

Synonyms acetocyanohydrin; 2-hydroxypropionitrile

EINECS No. 201-163-2 **RTECS No.** OD 8225000

Uses Solvent, intermediate in production of lactate and lactic acid.

Physical properties

M. Pt. –40°C **B. Pt.** 183°C **Flash point** 76.6°C **Specific gravity** 0.9834 at 20°C with respect to water at 25°C
Volatility v.den. 2.45
Solubility Organic solvents: ethanol

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) pinperch 0.215 mg kg^{-1} (1).
LC_{50} (96 hr) fathead minnow 0.9 mg kg^{-1} (2).
LC_{50} (96 hr) guppy 1.37 mg kg^{-1} (3).
Median threshold limit (24-96 hr) bluegill sunfish 4.0 mg l^{-1} (3).

Toxicity to other species
LD_{Lo} subcutaneous frog 200 mg kg^{-1} (4).

Environmental fate

Degradation studies
60% ThOD after 8 days at 20°C, 10 mg l^{-1} of feed (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 87 mg kg^{-1} (6).
LD_{50} dermal rabbit 20 mg kg^{-1} (6).
LD_{Lo} subcutaneous rabbit 5 mg kg^{-1} (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

A retrospective structure-activity relationship (SAR) comparison has been reported of acute, sub-chronic toxicity,

teratogenicity and biochemical mechanism studies of a series of structurally similar aliphatic nitriles, including lactonitrile (8).

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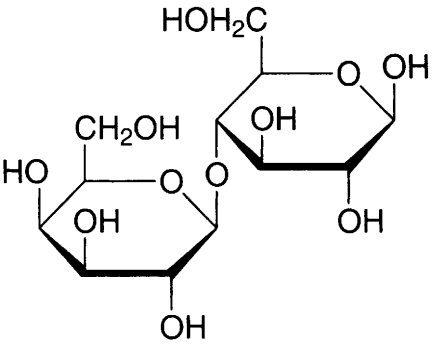
L3 β-lactose



$C_{12}H_{22}O_{11}$ **Mol. Wt.** 342.30 **CAS Registry No.** 5965-66-2

Synonyms β-D-glucopyranose, 4-*O*-β-D-galactopyranosyl; lactose, β; β-D-lactose

EINECS No. 227-751-9 **RTECS No.** OD 9625000

Physical properties

M. Pt. 253-255°C

Other effects

Any other adverse effects

It is a potent inhibitor of the lytic activity of natural killer cells as well as of the cytotoxic T-lymphocytes activated in mixed lymphocyte cultures (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Oral preclinical and clinical safety data are reviewed (3).

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L4 lanthanum

La

La **Mol. Wt.** 138.91 **CAS Registry No.** 7439-91-0

EINECS No. 231-099-0

Uses La^{3+} used in experimental biology as a specific antagonist of Ca^{2+} (1).
Oxide in glass to improve optical properties.
Occurrence Estimated abundance in earth's crust: 5-18 ppm in ores monazite, bastnaesite and cerite.

Physical properties

M. Pt. 920°C **B. Pt.** 3454°C **Specific gravity** 6.166 at 25°C

Ecotoxicity

Fish toxicity
LC_{50} (28 day) rainbow trout 0.02 mg kg^{-1} as lanthanum salt (2).

Bioaccumulation
Adult rainbow trout were exposed to various unspecified concentrations of $^{140}La^{3+}$. The dissociation constant for gill metal binding was 43 mg l^{-1} for La^{3+} (3).
Accumulation within mussels and limpets was 0.904 and 1.14 μg g^{-1} La^{3+}, respectively. The highest concentration within the mussel was 6.89 μg g^{-1} La^{3+} in the digestive gland (4).

Genotoxicity

Drosophila melanogaster yw and mus 302^{D1} strain at 10, 20 or 30 Gy, chromosome loss 0.31, 0.89 or 0.46% respectively; recessive lethals 0.40, 1.3 or 2.4%, respectively, and translocations 0.69% at 10 Gy and 0% at 20 and 30 Gy (5).

Other effects

Other adverse effects (human)
High levels of lanthanum, antimony, arsenic, cadmium and lead and low levels of selenium salts found in the lung tissues of smelter workers who died from lung cancer, compared with control groups, suggested a multifactorial genesis for the development of lung cancer and a protective effect of selenium in occupational exposure to certain carcinogens (6).

Any other adverse effects
Intravenous, mice (concentration unspecified) as lanthanum salt caused significant elevation in alanine transaminase activity and serum lipid peroxide 24 hr later. Degradation of hepatocytes and disappearance of glycogen in the cytoplasm were observed (7).

Legislation

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

Other comments

Cytoxicity reviewed (9).
Four field studies detailing application of lanthanum salts in ecological research are reported. Studies covered:
(I) Accretion and erosion of sediment in wetlands;
(II) Fire ant behaviour in a crop;
(III) Adsorption of chelated and nonchelated ions to aquatic roots;
(IV) Sorption by aquatic insect larvae (10).
Effects on cell growth and reproduction were studied in the unicellular cellular organism *Tetrahymena pyriformis*. Elements with higher molecular weights showed lower nutritive values and higher toxicities (11).
If radioactive lanthanum was released in sufficiently large quantities from nuclear power stations it could contribute significantly to early bone marrow damage in humans (12).

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L5 lanthanum trichloride

$LaCl_3$

Cl_3La **Mol. Wt.** 245.26 **CAS Registry No.** 10099-58-8

Synonyms lanthanum chloride ($LaCl_3$); lanthanum chloride (La_2Cl_6)

EINECS No. 233-237-5 **RTECS No.** OE 4375000

Uses Reagent for the conversion of carbonyls into thioacetal under mild conditions.

Physical properties

M. Pt. 907°C
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4180 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 106 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 2420 mg kg^{-1} (1).
LD_{50} intravenous rabbit 148 mg kg^{-1} (1).

Other effects

Any other adverse effects

Intravenous mice (concentration unspecified) as lanthanum chloride caused significant elevation in alanine transaminase activity and serum lipid peroxide 24 hr later. Degradation of hepatocytes and disappearance of glycogen in the cytoplasm were observed (3).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
Limited under EC Directive on Drinking Water Quality 80/778/EEC, guide level 25 mg chloride l^{-1}. Approximate concentration above which effects might occur 200 mg l^{-1} (5).

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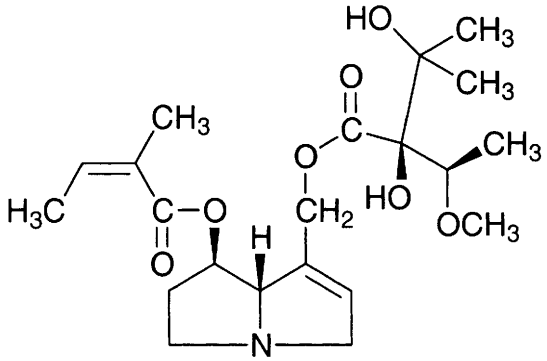
L6 lasiocarpine



$C_{21}H_{33}NO_7$ **Mol. Wt.** 411.50 **CAS Registry No.** 303-34-4

Synonyms 2-methyl-2-butenoic acid 7-[(2,3-dihydroxy-2-(1-methoxyethyl)-3-methyl-1-oxobutoxy]methyl]-2,3,5,7a-tetrahydro-1*H*-pyrrolizin-1-yl ester, [1*S*-[1α(*Z*),7(2*S**,3*R**),7aα]]-

RTECS No. OE 7875000

Uses As an emetic and in the treatment of snake bites in South East Asia.

Occurrence Isolated only from plant species of the family Boraginaceae; *Heliotropium europaeum, Heliotropium lasiocarpum* and *Symphytum caucasicums.*

Physical properties

M. Pt. 94-95.5°C
Solubility Organic solvents: benzene, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 150 mg kg^{-1} (1).
LD_{Lo} intravenous mouse 85 mg kg^{-1} (2).
LD_{Lo} intravenous guinea pig 50 mg kg^{-1} (3)
LD_{Lo} intravenous monkey 20 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 (4).
Oral (104 wk) ♂, ♀ Fischer 344 rats at 7, 15 or 30 ppm in diet. Mean body weights of the high-dose ♂, ♀ rats were lower than the control groups, weights of mid-dose rats were lower only in second year and weights of low-dose rats were unaffected. All surviving ♂ rats developed tumours except for one low-dose and one high-dose animal. Among ♀ rats 23 low-dose and 22 high-dose animals developed tumours. It is carcinogenic in Fischer 344 rats, producing hepatocellular tumours and angiosarcomas of the liver in both sexes and haematopoietic tumours in ♀ animals (5).
Intraperitoneal injections (dose unspecified) were given to rats fed aflatoxin B_1 in the diet and also pretreated with lasiocarpine to produce an antimitotic effect. Liver tumours developed after a similar time (18 wk) and in similar numbers to those in rats given aflatoxin alone. The tumours were associated with post-necrotic cirrhosis or advanced portal scarring not seen in rats receiving aflatoxin alone (6).

Teratogenicity and reproductive effects
Suckling rats showed toxic signs and died with severe liver lesions when their mothers were given total doses of 125 mg kg^{-1} body weight twice wkly. The mothers showed no outward ill effects (7).

Metabolism and toxicokinetics
In vivo rats, metabolised via pyrrole formation (8).
Most of the toxic effects appeared to be mediated via the very reactive dehydroalkaloid metabolites that are produced by the liver mixed function oxidases. The toxicity is not related to the level of activity of this enzyme system (9,10).
Dehydroheliotridine has been isolated and identified as a product of microsomal oxidation (11).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (12).
Salmonella typhimurium TA98, TA1535, TA1537 with and without metabolic activation negative (12).
Salmonella typhimurium TA1535 with and without metabolic activation negative (13).

Other effects

Any other adverse effects
In vitro rat hepatocytes significant toxicity observed (14).
Low doses produce severe haemorrhagic necrosis of the liver, gastro-intestinal haemorrhage, sometimes congestion and oedema of the lungs, congestion of the adrenals and sometimes pyloric, duodenal and rectal ulceration (species unspecified) (15-17).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Reviews on environmental toxicology and human health effects listed (19).
It is a pyrrolizidine alkaloid.

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L7 lauramide DEA

$$CH_3(CH_2)_{10}C(O)N[(CH_2)_2OH]_2$$

$C_{16}H_{33}NO_3$ **Mol. Wt.** 287.44 **CAS Registry No.** 120-40-1

Synonyms lauridiethanolamide; lauroyl diethanolamide; lauric acid diethanolamide; *N,N*-bis(hydroxyethyl)lauramide; *N,N*-bis(β-hydroxyethyl)lauramide; *N,N*-bis(2-hydroxyethyl)dodecanamide; Ablumide DEA; Emalex NN-7; Amidex L-9

EINECS No. 204-393-1 **RTECS No.** JR 1925000

Uses In pharmaceuticals and cosmetics. Detergents and cleansers. Acaricide and mite repellent.

Physical properties

Solubility Water: <1 mg ml^{-1} at 24°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2700 mg kg^{-1} (1).

Carcinogenicity and chronic effects

National Toxicology Program skin painting study on rats and mice, no evidence of carcinogenicity (2).

Genotoxicity

Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges positive and chromosome aberrations negative (3).

Other effects

Any other adverse effects

The Toxicology Design Committee has approved prechronic testing of lauric acid diethanolamine condensate, a detergent, in rats and mice by skin painting (4).

Toxicity has been evaluated (5).

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L8 lauric acid

$$CH_3(CH_2)_{10}CO_2H$$

$C_{12}H_{24}O_2$ **Mol. Wt.** 200.32 **CAS Registry No.** 143-07-7

Synonyms dodecanoic acid; ABL; Aliphat No.4; Vulvic acid; Laurostearic acid; Neo-Fat 12

EINECS No. 205-582-1 **RTECS No.** OE 9800000

Physical properties

M. Pt. 44-46°C **B. Pt.** 225°C at 100 mmHg **Flash point** >110°C (closed cup) **Specific gravity** 0.869 at 50°C with respect to water at 4°C **Partition coefficient** log P_{ow} 4.6

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

Ecotoxicity

Fish toxicity

LC_{50} red killifish (seawater) no mortality occurred at saturation (unspecified duration) (1).

LC_{50} red killifish (freshwater) 20 mg l^{-1} (unspecified duration) (1).

Invertebrate toxicity

Untreated retort waters were highly toxic to *Nitzschia closterium*, growth inhibited by concentration as low as 0.01% of retort water in sea water. Aliphatic acids are one of the many toxic components of retort waters (2).

Environmental fate

Anaerobic effects

The effect of lauric acid on the microbial formation of methane was investigated using *Methanothrix* sp. Inhibition commenced at 320 and 861 mg l^{-1}, the maximum specific acetoclastic methanogenic activity was reduced to 50%. Synergistic toxicity observed with capric acid and myristic acid (3).

Under laboratory conditions 60-90% degradation occurred. Results obtained by measuring the amount of fermentation gas and methane concentration (4).

Degradation studies

Activated sludge (6 hr) 4.1% ThOD; (12 hr) 4.3% ThOD; (24 hr) 6.1% ThOD (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 12 g kg^{-1} (6).

LD_{50} intravenous mouse 131 mg kg^{-1} (7).

Irritancy

Based on the available data for studies in animals and humans it was concluded that lauric acid is non-irritant and is safe in present practice of use and concentration in cosmetics (8).

Genotoxicity

Salmonella typhimurium TA97, TA89, TA100, TA1535, TA1537 with and without metabolic activation negative (9).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Log P_{ow} exceeds European Union recommended limit of 3.0 (11).

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L9 lauroyl peroxide

$$[CH_3(CH_2)_{10}C(O)O]_2$$

$C_{24}H_{46}O_4$ **Mol. Wt.** 398.63 **CAS Registry No.** 105-74-8

Synonyms bis(oxododecyl) peroxide; didodecanoyl peroxide; dodecanoyl peroxide; Alperox C; dilauroyl peroxide; Laurox Q; laurydol; LYP 97

EINECS No. 203-326-3 **RTECS No.** OF 2625000

Uses Catalyst. Cross-linking agent.

Physical properties

M. Pt. 55°C

Solubility Organic solvents: acetone, benzene, carbon tetrachloride, chloroform, diethyl ether, ethanol, methanol

Occupational exposure

Supply classification oxidising
Risk phrases May cause fire (R7)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container tightly closed in a cool place – Keep away from acids – Wear suitable protective clothing, gloves and eye/face protection (S2, S3/7, S14, S36/37/39)

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate data for evaluation of carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (1).
Subcutaneous mouse 0.1 or 10 mg animal^{-1} wk^{-1} throughout life span. Median survival time was 324-331 and 368-535 days for the low-dose, high-dose and control groups, respectively. No tumours were observed in controls or the high-dose group. In the low-dose group 3/50 mice developed a fibrosarcoma at the site of injection (2,3).
Subcutaneous mouse (18 month) 0.05 mg animal^{-1} 2 × wk^{-1} for 12 months. No tumours were observed in treated mice. One fibrosarcoma was found at the injection site in the control group (3).
Subcutaneous rat (18 month) 11 mg animal^{-1} wk^{-1}. Median survival times were 537 days for controls and 488 days for treated rats. No tumours were observed at the injection site in any group, although local palpable masses associated with tissue necrosis, inflammatory reaction and vascular thrombosis were noted in the treated group (4).
Mice were tested to evaluate tumour-promoting, tumour initiating and complete carcinogenic activity for dermal application. In the tumour promoting study, mice were given a single dermal application of 0.2 mg 7,12-dimethylbenz[*a*]anthracene (DMBA) followed 1 wk later by applications of 1, 10 or 20 mg dilauroyl peroxide 2 × wk^{-1} for 25 wk. A dose-related incidence of papillomas was observed at this time. In the tumour-initiation study mice received a single dermal application of 20 mg lauroyl peroxide, followed by 2 μg 12-*O*-tetradecanoylphorbol 13-acetate 2 × wk^{-1} for 25 wk. At this time 4/29 controls and 4/28 treated animals had papillomas. In the complete carcinogenic study, mice received 20 mg animal^{-1} 2 × wk^{-1} for 25 wk. 1/28 treated animals and 0/29 controls had papillomas at that time. At 50 wk no squamous-cell carcinoma was observed in any animal (5).

Teratogenicity and reproductive effects
Tested for embryotoxicity in three-day chicken embryos using the air-chamber method. ED_{50} 50-1070 μg egg^{-1}. Malformations occurred, although dilauroyl peroxide was least potent of the nine peroxides tested (6).

Irritancy
500 mg instilled into rabbit eye for 24 hr caused mild irritation (7).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation negative (8).

Other effects

Any other adverse effects
Dermal mouse, single application of 20 or 40 mg animal^{-1} induced mild hypoplasia and a temporaory increase in the number of dark basal keratinocytes. No major inflammatory or vascular change was noted (5).

Legislation

Oxidising agents are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

Physical properties, use, analysis, carcinogenicity, mammalian toxicity, teratogenicity and mutagenicity reviewed (10).

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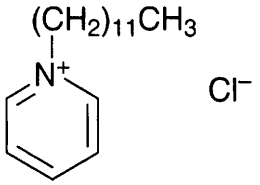
L10 laurylpyridinium chloride



$C_{17}H_{30}ClN$ **Mol. Wt.** 283.88 **CAS Registry No.** 104-74-5

Synonyms Dehyquart C; DPC; Eltren; 1-dodecylpyridinium chloride; Quaternario LPC

EINECS No. 203-232-2 **RTECS No.** UU 4017070

Physical properties

M. Pt. 66-70°C

Environmental fate

Adsorption and retention

Adsorption of laurylpyridinium chloride on sodium kaolinite was studied (1).

The adsorption of laurylpyridinium chloride onto different adsorbents was examined at equilibrium concentrations from 10 to 300 μmol l^{-1}. The adsorption maximum for soils and compost was less than 10 μmol g^{-1}. There is no significant correlation between adsorption behaviour and organic matter contents in soils and composts (2).

The reaction of the cationic surfactant laurylpyridinium chloride with model humic substances was studied. The compound was bound to the humic substance, whereby the products contained between 25-70% of the surfactant. Reaction with *in situ* generated model humic substance gave products containing higher laurylpyridinium chloride contents than those prepared by precipitation reactions with the various humic substances, indicative of multilayer binding. Both the former and the sodium hydroxide extract revealed a drastic reduction of free carboxylic groups following reaction with laurylpyridinium chloride (3).

Mammalian & avian toxicity

Irritancy

Eye guinea pig 5% (w/v) was found to be extremely irritating (4).

Other effects

Other adverse effects (human)
Human mixed lymphocyte reaction 94% inhibition and toxic to cells (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. Guide level 1 $\mu g\ l^{-1}$ (7).

Other comments

Cationic surfactant biodegradability was studied in river waters (8).
With increase in the ionic strength of the medium, which contained 2 ml sheep red blood cells in a buffer, haemolytic activity of laurylpyridinium chloride decreased (9).

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L11 lead

Pb

Pb **Mol. Wt.** 207.20 **CAS Registry No.** 7439-92-1

Synonyms C.I. 77575; C.I. pigment metal 4; lead flake

EINECS No. 231-100-4 **RTECS No.** OF 7525000

Uses Construction material for tank linings, piping. For x-ray and atomic radiation protection. Pigments for paints. Bearing metal and alloys. Storage batteries. Solder and other lead alloys.
Occurrence Occurs in galena, galenite, lead sulfide, cerussite, anglesite, lancarksite, massicot and matlockite ores. Extent of occurrence in earth's crust ~15 g ton^{-1}, or 0.002%.

Physical properties

M. Pt. 327.4°C **B. Pt.** 1740°C **Specific gravity** 11.34 at 20°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 973°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 0.15 mg m^{-3}
JP-OEL 0.1 mg m^{-3}

SE-LEVL 0.1 mg m^{-3} (total dust); 0.05 mg m^{-3} (respirable dust)
UK-LTEL 0.15 mg m^{-3}
US-TWA 0.05 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (28 day) rainbow trout 0.22 mg kg^{-1} (Pb salt) (1).
EC_{50} (96 hr) giant gourami 26 mg kg^{-1} (Pb salt) (2).
LOEC chronic survival rainbow trout 0.0007 mg kg^{-1} (Pb salt) (3).
In preference-avoidance response determinations under uniform illumination in a countercurrent trough, lake Whitefish *Coregonus clupeaformis* avoided lead ion concentrations >10 μg l^{-1} (4).

Invertebrate toxicity

EC_{50} (96 hr) reproduction *Navicula incerta* 11 mg kg^{-1} (Pb salt) (5).
LC_{50} (48 hr) *Daphnia magna* 0.3 mg kg^{-1} (Pb salt) (6).
LC_{50} (48 hr) *Bufo arenarum* 0.47-0.90 mg l^{-1}. Concentrations ≥0.25 mg Pb^{2+} (Pb salt) l^{-1} interfered with normal embryo development (7).
EC_{50} (96 hr) *Perna viridis* 8820 μg l^{-1} (Pb salt) (8).
EC_{50} (48 hr) *Daphnia magna* 3.61 ppm (Pb salt) (9).

Toxicity to other species

Pickerel frogs *Rana palustris* and bullfrogs *Rana catesbeiana* were exposed from the egg stage to lead-contaminated surface water from a trap and skeet range. 100% range water containted 840-3150 μg l^{-1} with the filterable from accounting for ~4-5% of the total. Hatching was not affected in either species. *R. pallustris* tadpoles exhibited 100 and 98% mortality after 10 days of exposure to 100 and 75% range water, respectively. Range water did not significantly effect the mortality of *R. catesbeiana* during 10 days of exposure. Exposure to lead in the range water did not adversely affect the growth of surviving tadpoles of either species after 10 wk. In both species the intestinal mucosa of tadpoles exposed to range water was reduced in thickness. *R. palustris* tadpoles that died in 100% range water had stunted tail growth, incurvation of the spine, hydropsy, and generally reduced body size (10).

Bioaccumulation

Lead uptake is slow and reaches equilibrium only after prolonged exposure. *Crassostrea virginica* (49 day) exposed to 25, 50, 100, 200 mg Pb^{2+} l^{-1} in water, final concentrations in soft tissues were 17, 35, 75 and 200 mg kg^{-1} lead, respectively (11).
A bioconcentration factor of less than 1 was observed in earthworms in soils with 15-50 mg lead kg^{-1} soil (12,13).
Arca granosa accumulated lead in soft tissue and blood. Distribution order: internal organs >gill >mantle >blood. Positive correlation with lead concentration in seawater (14).
Artemia salina exposed to concentrations of 5 μg l^{-1} accumulated 250 μg l^{-1}. Lead had a synergistic effect on heavy metal uptake in combined heavy metal element solution (15).
Several species of fish, molluscs and crustacea accumulate lead. Main storage tissues are digestive tract and exoskeleton. Spherocrystals and lysosomes are prominent in accumulation and elimination (16).
Tissue distribution of lead was studied in four species of raptor from Southeast Spain. The bone was found to be the principal organ of accumulation followed by kidney, liver and brain. This distribution suggested that the birds had been exposed to a low level of lead over a long period of time. Relationships were found among bird size, age and nearness to areas of human activity (17).

Environmental fate

Nitrification inhibition

20 mg (Pb salt) l^{-1} inhibited denitrification in rotating disc and 20 mg (Pb salt) l^{-1} inhibited nitrification and denitrification in activated sludge (18).
0.5 mg l^{-1} was toxic to *Nitrosomonas* (19).

Azotobacter exposed to high concentrations showed inhibited urease activity. Inhibition threshold concentration range 30-500 ppm (20).

Adsorption and retention

Cores of marine sediment were used as model systems to examine the degradation of digested sewage sludge in the marine environment at the sediment-water interface. Lead added to the model systems in the sludge was immobilised by the sediment and not exported from the model (21).

Adsorption to sediment occurs rapidly and almost quantitatively (22).

Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestrial plants is drastically reduced and effects to plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} (23).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral pigeon 160 mg kg^{-1} (24).

TD_{Lo} oral mouse 4800 mg kg^{-1} (25).

Lowest lethal dose oral woman 450 mg kg^{-1} (26).

LD_{Lo} intraperitoneal rat 1000 mg kg^{-1} (27).

LD_{50} intraperitoneal rat 400 mg kg^{-1} body weight lead oxide (371 as lead) (28).

LD_{50} intraperitoneal rat 220 mg kg^{-1} body weight lead tetroxide (20 as lead) (28).

LD_{50} intraperitoneal guinea-pig 2000 mg kg^{-1} body weight lead chloride (1490 as lead) (28).

Sub-acute and sub-chronic data

American kestrel (7 month) 0, 10 or 50 mg kg^{-1}. Lead levels increased in liver and bones though no adverse effects were observed (29).

Oral American kestrel (10 day) 125 or 625 mg kg^{-1} body weight. Reduced haematocrit, haemoglobin levels and plasma creatine phosphorylase activity was observed (30).

Oral ♂ bobwhite quail (4 wk) 10 lead shot. Increased mortality was observed, >90% of ♂ dosed with 30 lead shots wk^{-1} died within 4 wk (31).

Oral rat (6 month) single concentration lead or combined heavy metals in non-toxic, minimal or toxic concentrations. Every single metal affected the concentrations of some of the other metals in the liver, brain, femoral bone, spleen and kidney. The changes are due to compensatory mechanism and/or toxic effects of the metal (32).

Carcinogenicity and chronic effects

Renal tumours have been induced in rats following administration of large doses (33).

Gavage (12 month) ♂, ♀ Fischer 344 rat, 10 mg twice a month. One lymphoma and 4 leukaemias in 47 treated rats. No significant difference from control rate (34).

Teratogenicity and reproductive effects

Lead salts are gonadotoxic and embryotoxic (35,36).

Caused a reduction in the number of pregnancies in successfully mated mice compared with controls (37).

Reduced foetal birth weight, neonatal body weight and motor activity and induced skeletal deformities in mice (38).

Developmental toxicity in humans not determined; in rabbits negative; and in rats, mice and hamsters positive (39).

♂ rats were injected intraperitoneally with 10 mg kg^{-1} body weight of lead acetate weekly for 6 or 9 weeks. After 6 weeks of lead exposure epididymal sperm counts were unchanged, as was percentage of motile sperm. After 9 weeks of exposure numbers of motile sperm and epididymal sperm counts were reduced. An increase in reactive oxygen species was observed (via chemiluminescence) and a decrease in sperm-oocyte penetration rate (40).

Sequentially administered stable lead isotopes were used to investigate changes in blood lead during pregnancy in five cynomolgus monkeys. Bone lead mobilisation decreased during the first trimester by 29-56% and then increased during the second and third trimesters, up to 44% above base levels. From 7-39% of lead found in the foetal skeleton originated from the maternal skeleton (41).

Semen and blood samples from 5 workers with long-term lead exposure (in a lead battery manufacturing factory) and 8 workers not exposed to lead were compared. Lead concentrations were significantly higher in the exposed group, but no significant differences were found in comparisons based on sperm count, motility, and viscosity. A significant negative relationship existed for the exposed group between motility and blood-Pb and semen-Pb concentrations. Comparing sperm count and blood-Pb and semen-Pb concentrations, there was a non-significant negative relationship. Semen-Pb concentrations and semen pH were significant factors that explained semen count and semen motility results. The authors propose that prolonged Pb exposure may have harmful effects on the body's reproductive functions (42).
In 90 occupationally exposed men, the lead exposure levels may have resulted in a subclinical increase in follicle-stimulating hormone (FSH), which was related to blood lead levels. This suggests that lead may be causing some subclinical primary damage to the seminiferous tubules in the testes. However, at blood levels of >47 $\mu g\ ml^{-1}$ this effect on serum FSH level was not apparent (43).
Lead concentrations (Pb salts) were above normal in women with spontaneous abortions and were above normal in mothers of newborn with intra-uterine growth retardation (44).

Metabolism and toxicokinetics
Uptake by mallard ducks (14 day) 178 $g\ m^{-2}$ of lead shot. The liver contained 28.4 $mg\ kg^{-1}$ wet weight and bones contained 176 $mg\ kg^{-1}$ dry weight (45).
Lead crosses placental barrier (46).
Inhalation (different periods) rats 0.05, 77, 249 and 1546 μg (Pb salt) m^{-3}. Blood Pb levels declined with a $t_{1/2}$ of between 3 and 5 days. Baseline blood concentration was reached by 25 and 50 days for the 2 smallest doses of lead. The most heavily contaminated groups had not returned to initial concentration after 180 days (47).
Single oral dose (unspecified) of ^{203}Pb radiolabel to pregnant mice. Effects differed depending on which gestation period the animals were treated; retention was markedly increased in later stages of pregnancy. Lead accumulated in bone and kidney (48).
Absorbed from the gastro-intestinal tract, also absorbed by the lungs from dust particles. Inorganic lead is not absorbed through intact skin whilst organic lead is absorbed rapidly. Distributed in soft tissues, higher concentrations in liver and kidneys. Associated with erythrocytes in blood. Accumulates in body, deposited in calcified bone, hair and teeth. It crosses placental barrier. Excreted in faeces, urine, sweat and milk (49).
A level of 0.20 $mg\ l^{-1}$ was associated with a 75% decrease in δ-aminolevulinic acid dehydratase activity (50).
Single oral dose of 0.5 and 1.5 mg ^{204}Pb, kinetic data were derived to estimate degree of human intestinal absorption from the empty stomach which varied from 10 to 80%, $t_{1/2}$ of lead in blood was in the range of 39 to 53 days (51).
75 volunteers from plastic industry had lead blood levels of 15-20 mg 100 ml^{-1}. The δ-aminolevulinic acid excretion in urine was 2-8.4 mg in 24 hr (52).

Genotoxicity

Salmonella typhimurium TA98, TA102, TA1535, TA1537 with metabolic activation and *Salmonella typhimurium* TA102 without metabolic activation positive (53).
In vitro Chinese hamster cells induced an increased number of UV-induced mutations and sister chromatid exchange (54).
In vitro mice bone marrow induced chromosomal aberrations and increased frequency of sister chromatid exchanges (55).
Monopterus albus, *Cyprinus carpio* and *Aristichthys nobilis* micronucleus test positive (56).
In vitro human peripheral lymphocytes (72 hr) 0.05 $\mu g\ l^{-1}$ increased number of sister chromatid exchanges (57).

Other effects

Other adverse effects (human)
Acute toxicity – anorexia, vomiting, malaise, convulsions due to increased intercranial pressure, common in young children with a history of pica. Children with chronic toxicity show weight loss, weakness, anaemia. Lead poisoning in adults is usually occupational, due mainly to inhalation of lead dust or fumes (58).

Organic lead poisoning produces mainly central nervous system symptoms, there can be gastro-intestinal and cardiovascular effects, renal and hepatic damage (49).
Higher mortality from malignant neoplasms has been reported in smelter workers. In battery workers no association was found between lead exposure and cancer (59,60).
Chromosomal aberrations have been reported in occupationally exposed workers (61).
Lung cancer mortality was examined in 4393 men employed in a lead smelter. There was an excess of lung cancer which was particularly evident for those employed for >20 yr. Lung cancer mortality was associated with estimates of cumulative exposure to arsenic and lead. It was not possible to determine whether the increased risk might be due to arsenic, lead or other contaminants in the smelter (62).
A case reference study has shown an increased risk for glassworks employees to die from stomach cancer, lung cancer and cardiovascular disorders. A follow-up study covering the entire glass-producing industry of Sweden confirmed the earlier results and, furthermore, an excess risk for colon cancer was also identified. The grouping of glassworks employees according to type of metal contamination showed an excess risk of stomach cancer, colon cancer and cardiovascular deaths related to glassworks with a high consumption of lead, arsenic, antimony and manganese. Their exposure might be oral, involving the glassblowers pipe as a vector for the exposure to various metals (63).
A study of working conditions at all stages of lead production showed that the worker morbidity was affected by chemical factors involving complex polymetallic dust and sulfur dioxide (64).
The relationship between blood lead concentration and blood pressure was examined in a survey of 7371 men aged 40 to 59 in UK. There exists a very weak but statistically significant positive association between blood lead and both systolic and diastolic blood pressure. After 6 years of follow-up, 316 of these men had major ischaemic heart disease and 66 had had a stroke. There is no evidence that blood lead is a risk factor for these cardiovascular events. This and other surveys provided reasonably consistent evidence of the relationship between lead and blood pressure (65).
Workers occupationally exposed to lead (mean blood lead concentrations 19 $\mu g\ dl^{-1}$) showed significantly reduced numbers of memory T cells and a significant expansion in the percentage of CB8+ cells compared with controls (66).
A study of 141 middle-aged men showed that subjects with higher bone and blood lead concentrations showed reduced cognitive functions such as attention, perceptional speed, memory, language and spatial copying (67).

Any other adverse effects

The effects of atmospheric lead concentrations were investigated in Madrid city pigeons. Renal tissues contained >30 $\mu g\ g^{-1}$ (dry weight). Inclusions present in proximal convoluted tubules and hepatic haemosiderosis were observed (68).
Lead significantly inhibited *N*-methyl-D-aspartate specific glutamate receptor binding, in neonate and adult rat brain, in a dose-dependent manner (69).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (70).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Maximum admissible concentration 50 μg Pb l^{-1} (in running water). Where lead pipes are present, content should not exceed 50 $\mu g\ l^{-1}$ in a sample after flushing. If the sample is taken either directly or after flushing and lead content exceeds 100 $\mu g\ l^{-1}$, measures must be taken to reduce the exposure (71).
A maximum admissible concentration of 10 $\mu g\ dl^{-1}$ was established for Canadian drinking water in Autumn 1989. Lead was classified as a possible carcinogen and the concentration evaluated using threshold concentrations (72).

Other comments

Soluble lead salts are more toxic than insoluble salts.
Environmental pollutant through surface runoff and airborne lead. Lead, in the form of simple salts, is acutely toxic to aquatic invertebrates at concentrations between 0.1->40 mg l^{-1} (freshwater) and 2.5->500 mg l^{-1} (marine). However, lead salts are poorly soluble in water and the presence of other salts reduces the bioavailability because of precipitation. Concentrations of lead in water are nominal in most studies; the contribution to toxicity of factors

such as pH, water hardness, anions and complexing agents cannot be fully evaluated.
Plant-available lead found in 87 garden soils in England and Wales ranged from 10-680 μg g^{-1} dry soil (73).
Samples of topsoil were taken and the total content of 19 elements determined. Mean lead values for uncontaminated soil in the 30-40 mg kg^{-1} range were calculated (74).
Calculated concentration below which biological effects were minimal in sediment quality criteria was 50 μg Pb g^{-1} (dry weight sediment) (75).
NIOSH has designated lead an ototoxin. It can cause hearing loss, ringing in the ears or total deafness, and its toxicity can be exacerbated by combined exposure with noise (76).
Carcinogenicity, sources, environmental levels, human exposure and absorption reviewed (77-80).
Environmental exposure to humans and related blood effects reviewed (81).
The biogeochemical availability to aquatic and semiaquatic wildlife reviewed (82).
Lead ingestion and inhibition studies in humans 1937-1971 reviewed (83).
Environmental fate, toxicity and genotoxicity reviewed (84).
Toxicity to terrestrial animals reviewed (85).
Health hazards of airborne particulate matter reviewed (86).
Toxicology, metabolism, teratogenicity, neurotoxicity and carcinogenicity reviewed (87-92).
Toxicity profile lead (93).
Lead and lead compounds comprehensively reviewed (94).
Carcinogenicity, mutagenicity, teratogenicity and neurotoxicology reviewed (95-98).
Reviews on ecotoxicity, epidemiology, environmental effects, environmental toxicity, exposure, exposure levels, human health effects, physico-chemical properties and work exposure listed (99).
Killing of 34 simian primates and 3 fruit bats in Washington Zoo by lead in paint on their cages has been reported (22).
Environmental health criteria reviewed (100).

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L12 lead acetate

$$(CH_3CO_2)_2Pb$$

$C_4H_6O_4Pb$ **Mol. Wt.** 325.29 **CAS Registry No.** 301-04-2

Synonyms lead methanoate; neutral lead acetate; normal lead acetate; salt of saturn; sugar of lead

EINECS No. 206-104-4 **RTECS No.** AI 5250000

Uses In the manufacture of lead salts. In the dyeing and printing of cotton.

Physical properties

M. Pt. 75°C (when rapidly heated), decomposes completely above 200°C **Specific gravity** 2.55 at 20°C with respect to water at 4°C

Solubility Water: 625 g l^{-1} at 20°C. Organic solvents: ethanol, glycerol

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
UK-LTEL 0.15 mg m^{-3} (as Pb)

UN No. 1616 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Danger of cumulative effects – Possible risk of irreversible effects – Harmful: danger of serious damage to health by prolonged exposure if swallowed (R61, R62, R33, R40, R48/22)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 400 ppm. No lethal effects up to 300 ppm (1).

Invertebrate toxicity

Cell multiplication inhibition test *Uronema parduczi* 0.07 mg l^{-1}, *Pseudomonas putida* 1.8 mg l^{-1} (1,2).
Microcystis aeruginosa lowest effective concentration observed to cause reproductive effects 0.45 mg l^{-1} (2).
LC_{50} (96 hr) freshwater crabs 20 ppm. On exposure the haemolymph, pH, lactate and carbon dioxide levels increased while the oxygen level decreased (3).
EC_{50} (24-48 hr) *Daphnia magna* 5-2.7 mg l^{-1} (4).

Environmental fate

Nitrification inhibition

Threshold inhibition at 0.5 mg l^{-1} (5).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 200 mg kg^{-1} (6).

Sub-acute and sub-chronic data

Intraperitoneal ♂ mice 0.5 mg kg^{-1} body weight lead acetate daily for 30 days caused a significant reduction in the activities of serum 3,3',5-triiodothyronine and type 1 iodothyronine 5'-monodeiodinase and of antioxidant enzymes of the liver. Peroxidative reactions involving membrane components increased (7).
Rats receiving 10 mg kg^{-1} daily (unspecified route) for 3 months exhibited reticulocytosis within 36 days (6).
An oral dose of lead acetate at 0.2 mg kg^{-1} to rats for 21 days caused growth retardation, blood haemoglobin decrease and metabolic disorders (8).
Rats receiving 1000 ppm in drinking water for six weeks showed a tenfold increase of lead levels in the parotid gland. Ultrastructural examinations revealed impaired secretion of alveolar cells, damaged mitochondria and disturbed lipid balance (9).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals for inorganic lead compounds, IARC classification group 2B (10).
Target organs of carcinogenicity: rats kidneys/ureter (11).
The carcinogenic potential of lead in humans is not well established, however a number of cases of renal adenocarcinoma in lead workers have been reported (12).
The level of human exposure equivalent to the level of lead acetate producing renal tumours in rats is 810 mg day^{-1}. This level exceeds the maximum tolerated dose in humans (13).

Teratogenicity and reproductive effects

Injection of lead acetate into yolk sac of chick embryos caused malformations at a rate of 50% at the 50-75 μg egg^{-1} level (14).
Survival rate of 100 μg egg^{-1} dosed group reduced from 100% (untreated control) to 62.5% (15).
Lead salts are reported to cause morphological sperm abnormalities in mice (16).
Female mice received 0, 500, 750 and 1000 ppm lead as lead acetate in their drinking water from day-12 of pregnancy to 4 wk after they had delivered their young. Proliferative lesions in the kidney (atypical hyperplasia or tumour) were increased in a dose-related manner in the ♂ offspring, with the tumour incidence being significantly increased at the top dose level. In the ♀ offspring, a significant dose-related trend in renal proliferative lesions was observed. There was no significant chronic lead-induced nephrotoxicity suggesting that lead-induced renal cellular proliferation as a chronic toxic response was not responsible or absolutely required for tumour formation (17).
Ninety-day-old Sprague-Dawley rats were intoxicated for 70 days with 0.3% lead acetate in drinking water. No adverse effects on the reproductive system or fertility were observed (18).

♂ Rabbits (15 per group) were exposed for 15 wk to lead acetate to produce 0, 200, 400 and 800 μg l^{-1} blood lead. At the conclusion of the exposure, ♂ rabbits were mated with unexposed ♀ rabbits. These ♀ rabbits carried their litters to term, delivered, and reared their own offspring. Of the 60 rabbits mated, 57 produced litters, and 2 rabbits died giving birth. Significant postnatal deaths were observed in all groups, with ~½ of the offspring dying before testing was initiated at day-15. There were no treatment-related effects of offspring weight gain during weaning. Data from a similar investigation (7 ♂ rabbits per group exposed to 0, 500, and 1100 μg l^{-1} for 15 wk) suggested that paternal lead exposure of rabbits may reduce exploratory activity in a standard figure-eight aversive conditioning test on day-25, the time of peak activity in the offspring (19).
In men, concentrations of lead (unspecified dose) were associated with a high frequency of altered spermatogenesis. Relatively low levels of lead absorption have a direct toxic action on the male gonads (20).

Metabolism and toxicokinetics
Lead is readily absorbed from gastro-intestinal tract and accumulates in various tissues, in particular the bone (20).

Genotoxicity

Escherichia coli SOS chromotest negative (21).
Lead acetate significantly induced sister chromatid exchange in a dose-dependent manner in Chinese hamster ovary cells (22).
Lead acetate caused dose-related transformation of cultured Syrian hamster embryo cells. Isolated cells from the transformed colonies produced fibrosarcomas when injected subcutaneously into either Syrian hamster or nude mice. Results suggest that lead acetate-induced transformation may be a result of decreased accuracy of DNA synthesis (23).

Other effects

Other adverse effects (human)
Clinical studies have found increased chromosomal defects in workers with blood lead levels above 600 μg l^{-1} (24).
Lead acetate was formerly applied in aqueous solution to the eye for astringent effect, but induced opacities and lead encrustation of the cornea and conjuctiva. Opacities occurred in patients when the cornea epithelium had been injured allowing the lead solution to penetrate. The epithelium normally acts as a barrier to lead salts penetrating the cornea (25).
Symptoms of lead poisoning include thirst, persistent metallic taste, nausea, abdominal pain, vomiting, diarrhoea, and constipation. Central nervous system symptoms include paresthesia, pain and muscle weakness; other symptoms include anaemia, haemoglobinaemia, oliguria and urinary changes. Severe exposure can cause death in 1-2 days. Degenerative changes in motorneurons and axons have been reported. Can cause visage and ocular disturbances (12).
Organic lead poisoning produces mainly central nervous system symptoms, but can have gastro-intestinal and cardiovascular effects, and cause renal and hepatic damage (20).
Recent clinical research has focused on neuropsychiatric, reproductive and renal effects of chronic low dose lead exposure (26).
Increased serum arginase activity may indicate liver damage, while decreased kallikrein activity may indicate kidney damage in workers exposed to lead (27).

Legislation

Control limits for lead are set out in the Health & Safety Commission approved code of practice supporting the Control of Lead at Work Regulations 1980 (28).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 μg l^{-1} (in running water) (29).

Other comments

Lead acetate intoxication, epidemiology studies and genotoxicity testing are reported (21,30-34).

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L13 lead arsenate

$PbHAsO_4$

$AsHO_4Pb$ **Mol. Wt.** 347.13 **CAS Registry No.** 7784-40-9

Synonyms arsenic acid (H_3AsO_4), lead(2+) salt; acid lead arsenate; lead hydrogen arsenate; arsenic acid, lead salt

EINECS No. 232-064-2 **RTECS No.** CG 0980000

Uses Constituent of various insecticides.

Occurrence In the mineral schultenite.

Physical properties

M. Pt. above 280°C with decomposition **Specific gravity** 5.79

Occupational exposure

FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.03 mg m^{-3} (as As)
UK-LTEL MEL 0.1 mg m^{-3} (as As)
US-TWA 0.15 mg m^{-3} (as $Pb_3(AsO_4)_2$)

UN No. 1617 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – May cause harm to the unborn child – Possible risk of impaired fertility – Toxic by inhalation and if swallowed – Danger of cumulative effects (R45, R61, R62, R23/25, R33)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Fish toxicity
LC_{50} (24, 96 hr) channel catfish >100 mg l^{-1} static bioassay, 18°C, hardness 44 mg l^{-1} ($CaCO_3$) and pH 7.1 (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken 450 mg kg^{-1} (2).
LD_{50} oral rat 100 mg kg^{-1} (2).

Sub-acute and sub-chronic data
LC_{50} (5 day) oral Japanese quail 2760 mg kg^{-1} (3).

Carcinogenicity and chronic effects
Oral (2 yr) ♂ rat 0.1%. Enlargement of cells, vesiculation of nuclei and accumulation of brown granules but no tumours were reported (4).

Other effects

Any other adverse effects
Acute and sub-acute testing in animals (species unspecified) showed lead arsenate was moderately toxic. Skin resorption effects were observed. The safe exposure reference level was calculated at 0.01 mg m^{-3} (As) (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 μg l^{-1}; lead: maximum admissible concentration 50 μg l^{-1} (6).
Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Reviews on experimental toxicology and human health effects listed (8).
The risk of developing non-Hodgkins lymphoma in farmworkers using lead arsenates in combination with phenoxy herbicides had an odds ratio of 1.89 and a 95% confidence interval of 1.1-3.3 (9).

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L14 lead arsenite

$$Pb(AsO_2)_2$$

As_2O_4Pb **Mol. Wt.** 421.04 **CAS Registry No.** 10031-13-7

Synonyms arsenious acid, lead(2+) salt

EINECS No. 233-083-9 **RTECS No.** OF 8600000

Uses Insecticide.

Physical properties

Specific gravity 5.85

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
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. 1618 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestrial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$; lead: maximum admissible concentration 50 $\mu g\ l^{-1}$ (3).
Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

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

L15 lead chloride

$PbCl_2$

Cl_2Pb **Mol. Wt.** 278.11 **CAS Registry No.** 7758-95-4

Synonyms lead chloride ($PbCl_2$); lead dichloride; plumbous chloride

EINECS No. 231-845-5 **RTECS No.** OF 9450000

Uses Catalyst. Solder. Flux for steel galvanising. Cathode in magnesium-lead chloride seawater batteries. Chemical scrubber. Flame retardant. Pigment and organolead manufacture.

Physical properties

M. Pt. 501°C **B. Pt.** 950°C **Specific gravity** 5.85 **Volatility** v.p. 1 mmHg at 547°C
Solubility Water: 9.9 $g\ l^{-1}$ at 20°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 2291 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Preliminary static acute toxicity tests using fathead minnows show lead salts are less toxic in hard alkaline waters. 3000 mg l^{-1} as the Cl^- ion did not cause mortality of the newly-hatched fathead minnows. Mortality increased at 3500-4000 mg Pb l^{-1} and appears to be partly due to the removal of protective carbonates initially present in the hard water (1).

LC_{50} (24, 48, 96 hr) fathead minnow, bluegill sunfish, goldfish and guppy 8-6 mg l^{-1}, 26-24 mg l^{-1}, 45-31 mg l^{-1}, 24-20 mg l^{-1}, respectively. Static bioassay, alkalinity 18 mg l^{-1} ($CaCO_3$), hardness 20 mg l^{-1} ($CaCO_3$), 25°C and pH 7.5. Increasing alkalinity and hardness increased lethal concentration to 470-480 mg l^{-1} (2).

Invertebrate toxicity

EC_{50} (4 hr) *Scenedesmus quadricauda* 2.7 mg kg^{-1} (3).

EC_{50} (48 hr) *Daphnia magna* 0.45 mg l^{-1} static bioassay at pH 7.4, alkalinity 41-50 mg l^{-1} ($CaCO_3$), and hardness 44-53 mg l^{-1} ($CaCO_3$) (4).

LC_{50} (96 hr, 30 day) crayfish 2.6, 1.5 mg l^{-1} flow-through bioassay, temperature 15-17°C and pH 7 (5).

EC_{50} (3 wk) *Daphnia magna* 100 µg l^{-1} (lead), reproductive impairment more sensitive measure for toxicity than survival (4).

Soil bacteria, 2500 ppm lead as lead chloride depressed bacterial growth at pH 4 and 6, but not in alkaline soil pH 8 (6).

Environmental fate

Adsorption and retention

Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestrial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (7).

Mammalian & avian toxicity

Acute data

TD_{Lo} oral rat 570 mg kg^{-1} (8).

TD_{Lo} intravenous mouse 20 mg kg^{-1} (9).

LD_{Lo} oral guinea pig 1500 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Oral dog (24 day) 5 mg kg^{-1} day^{-1} lead salt mixture containing unspecified concentrations of lead chloride, lead bromide and lead sulfate caused histopathological lesions consisting of acid fast lead inclusions seen in osteoclasts and renal tubular epithelial cells. Tissue lead concentrations (liver, kidney and bones) were greatly elevated (11).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (12).

Teratogenicity and reproductive effects

Intravenous mice 40 mg kg^{-1} on day 3, 4 or 6 of pregnancy. Attachment of the blastocyst was observed on day-5, invasion of the trophoblast was seen on day-6 and formation of the primitive streak was seen on day-6; all three developmental stages studied were affected by the action of lead (13). Embryotoxic and teratogenic to trout and chick embryos (14).

Intravenous mouse 75 ppm on day-4 of pregnancy was found to interfere in embryo implantation (15).

Caused anophthalmia, fused ribs, spina bifida and exencephaly in golden hamster embryos (16).

Irritancy

Oral guinea pig 1.5-2.0 g kg^{-1} caused mild irritation (17).

Genotoxicity

Allium cepa 1.0 mg l^{-1} slight but significant clastogenic effects without disturbing the mitotic activity (18).
The fidelity and rate of synthesis of avian myloblastosis virus DNA polymerase mediated DNA synthesis was decreased by 1.11 g kg^{-1} of lead chloride (19).
In systems containing *Escherichia coli* RNA polymerase and either calf-thymus DNA or T4 DNA, stimulation of chain initiation of RNA synthesis at a concentrations of 28 mg kg^{-1} inhibited overall RNA synthesis (20).

Other effects

Other adverse effects (human)

Symptoms of poisoning include fatigue, headache, sleep disturbance, constipation, aching bones and muscles, gastro-intestinal tract disturbances and reduced appetite (21).
Symptoms often precipitated by alcohol or exercise (22).

Any other adverse effects

Intravenous rat 5 mg kg^{-1} decreased hepatic cytochrome P_{450} levels, with associated decreases in microsomal oxidative demethylation and hydroxylation enzyme activities (23).
In vitro chick neurons and freshwater snail neurons incubated for 3-4 days with lead chloride reduced the percentage of cells that grew neurites; however, the mechanism of action for both species was different (24).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Guide level 25 mg chloride l^{-1}; approximate chloride concentration above which effects might occur, 200 mg l^{-1} and maximum admissible concentration 50 µg lead l^{-1} (25).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (26).

Other comments

Causes algicidal and herbicidal effects (27).

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L16 lead chromate

$PbCrO_4$

CrO_4Pb **Mol. Wt.** 323.19 **CAS Registry No.** 7758-97-6

Synonyms chromic acid (H_2CrO_4), lead(2+) salt(1:1); lead chromium oxide; plumbous chromate; chrome yellow

EINECS No. 231-846-0 **RTECS No.** GB 2975000

Uses Pigment in oil and water colours. Chemical analysis of organic substances. In traffic paints.
Occurrence In the minerals (crocite, phoenicochroite) (1).

Physical properties

M. Pt. 844°C **B. Pt.** decomposes **Specific gravity** 6.30
Solubility Water: 0.58 mg l^{-1} at 25°C

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 Pb); 0.012 mg m^{-3} (as Cr) **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic, dangerous for the environment
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Danger of cumulative effects – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R61, R62, R33, R40, R50/53)
Safety phrases Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet – Restricted to professional users (S53, S45, S60, S61)

Environmental fate

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestrial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 12 g kg^{-1} (3).

LD_{Lo} oral guinea pig 2000 mg kg^{-1} (4).

LD_{50} intraperitoneal guinea pig 156 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Subcutaneous (117-150 wk) 40 ♂ and ♀ Sprague Dawley rats 30 mg in water. Sarcomas developed at the injection site in 26/40 and 27/40 animals, respectively (5).

Intramuscular (16 month) 25 ♀ NIH-Swiss weaning mice 3 mg injection every 4 month incidence of carcinomas was 2/22 (6).

Intramuscular (9 month) 25 ♂ and ♀ weaning Fischer 344 rat 8 mg $month^{-1}$ induced 14 fibrosarcomas and 17 rhabydosarcomas at the site of injection in 31/47 rats. Renal carcinomas were observed in 3/23 ♂ rats in 24 months (6).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation was positive in the presence of nitrilotriacetic acid (7).

Escherichia coli PQ37 without metabolic activation negative (8).

In vitro Vicia faba root tips lead chromate significantly enhances the frequency of micronucleated cells only in the presence of nitrilotriacetic acid (9).

Chinese hamster V79 cells, with and without metabolic activation negative due to the slow uptake by the cells. When nitrilotriacetic acid was present, positive dose-dependent mutagenicity was observed (10).

Chinese hamster ovary cells and mouse embryo cells, non-mutagenic in either system. Induced a dose-dependent, low frequency of focus formation, and transformation (11).

Cultured Chinese hamster cells, frequency of sister chromatid exchanges significantly increased (12).

In vitro Syrian hamster embryo cells morphological transformations positive (13).

In vivo Drosophila melanogaster no significant increase of the mutation frequency. The addition of nitrilotriacetic acid caused significant increases of the frequency of sex linked lethal mutations, with a significant dose-effect relationship with respect to lead chromate, as a result of the interaction of the compounds and subsequent release of the genotoxic heavy metal chromium(IV) ions (14).

It increased the frequency of micronuclei in polychromatic erythrocyte ratio in bone marrow cells of intraperitoneally treated 57B1/6N mice (15).

Other effects

Other adverse effects (human)

Irritating to eyes, may cause conjunctivitis and lachrymation (4).

May cause ulceration and eczematous dermatitis on skin (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chromium: maximum admissible concentration 50 μg l^{-1} (16).

Included in Schedule 4 (Release into Air: Prescribed Substances) of Statutory Instrument No. 472, 1991 (17).

Other comments

Toxicity reviewed (18).

Acute toxicity is greater than other inorganic lead compounds due to the contributory toxicity of the chromate portion (4).

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

Lead chromate chemistry reviewed (20).

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L17 lead cyanide

$Pb(CN)_2$

C_2N_2Pb **Mol. Wt.** 259.24 **CAS Registry No.** 592-05-2

Synonyms C.I. 77610; C.I. Pigment Yellow 48

EINECS No. 209-742-1 **RTECS No.** OG 0175000

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 1620 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention

Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal rat 100 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).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 μg l^{-1}; cyanides maximum admissible concentration 50 μg l^{-1} (3).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

Other comments

Lead and its compounds have been comprehensively reviewed (1,5).

References

1. *IPCS Environmental Health Criteria 85: Lead-Environmental Aspects* 1989, WHO, Geneva, Switzerland.
2. *IARC Monograph* 1987, **Suppl. 7**, Lyon, France.
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.
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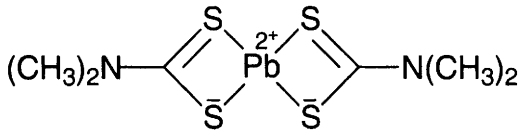
L18 lead dimethyldithiocarbamate



$C_6H_{12}N_2PbS_4$ **Mol. Wt.** 447.64 **CAS Registry No.** 19010-66-3

Synonyms lead, bis(dimethylcarbamodithioato-*S,S'*)-, (T-4)-; bis(dimethyldithiocarbamato)lead; Ledate

EINECS No. 242-748-2 **RTECS No.** OF 8850000

Uses Accelerator for vulcanisation. Compounding natural, styrene-butadiene, isobutylene-isopropene, isoprene and butadiene rubbers.

Physical properties

M. Pt. 258°C **Specific gravity** 2.50

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
UK-LTEL 0.15 mg m^{-3} (as Pb)
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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
TD_{Lo} subcutaneous mouse 1000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Oral (104 or 105 wk) ♂, ♀ Fisher 344 rats and B6C3F1 mice 25 or 50 ppm in feed. No tumours occurred in rats or mice of either sex at incidences that were significantly higher than the control groups (2,3).
Oral (76 wk) ♂, ♀ mice, 46.4 mg kg^{-1} body weight for first 4 wk then 130 mg kg^{-1} diet. Incidence of reticulum cell sarcomas in ♂ was significantly different from that in controls (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1536, TA1537 with and without metabolic activation positive (3).

Legislation

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

References

1. *NTIS Report No. PB223-1561* Natl. Tech. Info. Ser., Springfield, VA, USA.
2. *National Toxicology Program Research and Testing Division* 1992, Report No. TR151, NIEHS, Research Triangle Park, NC 27709, USA.
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4. Innes, J. R. M. et al *J. Natl. Cancer Inst.* 1969, **42**, 1101-1114.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

L19 lead dioxide

$$PbO_2$$

O_2Pb **Mol. Wt.** 239.20 **CAS Registry No.** 1309-60-0

Synonyms lead oxide brown; lead peroxide; lead superoxide; plumbic oxide; C.I.77580

EINECS No. 215-174-5 **RTECS No.** OG 0700000

Uses Electrodes in lead-acid batteries. Paint, rubber and ceramics industry. Manufacture of chemicals, dyes, pyrotechnics and liquid polysulfide polymers.
Occurrence Mineral plattnerite (1).

Physical properties

M. Pt. decomp. at 290°C **Specific gravity** 9.375

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 1872 **HAZCHEM Code** 2Z **Conveyance classification** oxidising substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg Pb kg^{-1} soil (2).

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal guinea pig 220 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).

Metabolism and toxicokinetics
Oral mice (30 day) ~100-1000 ppm in drinking water. Blood lead levels at the end of the period were dose-dependent. Lead dioxide provided the lowest level of blood level concentrations when compared with a series of lead salts (4).

Other effects

Other adverse effects (human)
Symptoms of poisoning include fatigue, headache, sleep disturbances, constipation, aching bones and muscles, gastro-intestinal tract disturbances and reduced appetite. Later anaemia, lead-line on the gums and lead colic may occur. Large doses affect the central nervous system, causing severe headaches, convulsions, coma and possibly death; kidney damage may result from chronic exposure (5).
Causes irritation to eyes and skin (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 µg l^{-1} (6).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Lead and its compounds have been comprehensively reviewed (2,8).

References

1. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
2. *Environmental Quality and Safety, Supplement*, 1975, **1**, 1.
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7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *IPCS Environmental Health Criteria 85: Lead-Environmental Aspects* 1989, WHO, Geneva, Switzerland

L20 lead distearate

$$Pb(C_{18}H_{35}O_2)_2$$

$C_{36}H_{70}O_4Pb$ **Mol. Wt.** 774.15 **CAS Registry No.** 1072-35-1

Synonyms octadecanoic acid, lead salt; normal lead stearate; lead stearate; Stabinex NC_{18}

EINECS No. 214-005-2

Uses In extreme pressure lubricants. As a drier in varnishes.

Physical properties

M. Pt. 125°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
UK-LTEL 0.15 mg m^{-3} (as Pb)
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (1).

Metabolism and toxicokinetics
In workers occupationally exposed to lead stearate, plasma (Pb) concentrations were significantly higher (1.0±5.7 μg l^{-1}) than those workers exposed to inorganic lead (0.42±3 μg l^{-1}) (2,3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC.
Lead: maximum admissible concentration 50 μg l^{-1} (4).

Other comments

Lead and its compounds have been comprehensively reviewed (5).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 65.
2. Ong, C. N. et al *J. Appl. Toxicol.* 1990, **10**(1), 65-68.
3. Cavalleri, A. et al *Scand. J. Work, Environ. Health* 1987, **13**(3), 218-220.
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. *IPCS Environmental Health Criteria 85: Lead – Environmental Aspects* 1989, WHO, Geneva, Switzerland

L21 lead fluoborate

$$Pb(BF_4)_2$$

B_2F_8Pb **Mol. Wt.** 380.81 **CAS Registry No.** 13814-96-5

Synonyms lead tetrafluoroborate; borate(1–), tetrafluro-, lead(II); lead boron fluoride

EINECS No. 237-486-0 **RTECS No.** ED 2700000

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 50 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).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

Other comments

Lead and its compounds have been comprehensively reviewed (1).

References

1. *IPCS Environmental Health Criteria 85: Lead-Environmental Aspects* 1989, WHO, Geneva, Switzerland.
2. *IARC Monograph* 1987, **Suppl. 7**, Lyon, France.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London

L22 lead fluoride

PbF_2

F_2Pb **Mol. Wt.** 245.20 **CAS Registry No.** 7783-46-2

Synonyms lead difluoride; plumbous fluoride

EINECS No. 231-998-8 **RTECS No.** OG 1225000

Physical properties

M. Pt. 824°C **B. Pt.** 1293°C **Specific gravity** 7.750 (cubic); 8.445 (orthorhombic)
Solubility Water: 0.57 g l^{-1} at 0°C, 0.65 g l^{-1} at 20°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 2291 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soils, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} subcutaneous guinea pig 2800 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).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 $\mu g\ l^{-1}$ (4).

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Other comments

Lead and its compounds have been comprehensively reviewed (1).

References

1. *IPCS Environmental Health Criteria 85: Lead-Environmental Aspects* 1989, WHO, Geneva, Switzerland.
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3. *IARC Monograph* 1987, **Suppl. 7**, 230-232.
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

L23 lead hexafluorosilicate

$PbSiF_6$

F_6SiPb **Mol. Wt.** 349.28 **CAS Registry No.** 25808-74-6

Synonyms silicate(2–), hexafluoro-, lead(2+)(1:1); lead fluorosilicate; lead silicon fluoride

EINECS No. 247-278-1 **RTECS No.** VV 8450000

Uses In refining lead by electrolytic methods.

Physical properties

M. Pt. (decomp.)

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)

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

Adsorption and retention

Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effect on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 250 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 for inorganic lead compounds (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 $\mu g\ l^{-1}$ (4).

References

1. *IPCS Environmental Health Criteria 85: Lead - Environmental Aspects* 1989, WHO, Geneva, Switzerland.
2. *Nat. Acad. Sci., Nat. Res. Coun., Chem. Biol. Coord. Cent.* 1953, **5**, 27.
3. *IARC Monograph* 1987, **Suppl. 7**, 65.
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

L24 lead iodide

PbI_2

I_2Pb **Mol. Wt.** 461.01 **CAS Registry No.** 10101-63-0

Synonyms C.I. 77613; lead diiodide; plumbous iodide

EINECS No. 233-256-9 **RTECS No.** OG 1515000

Uses Bronzing, gold pencils, mosaic gold, printing, photography.

Physical properties

M. Pt. 402°C **B. Pt.** 954°C **Specific gravity** 6.16

Solubility Water: 0.74 g l^{-1} cold; 4.34 g l^{-1} hot

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)

FR-VME 0.15 mg m^{-3} (as Pb)

JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 2291 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestrial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B for inorganic lead compounds (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 $\mu g\ l^{-1}$ (3).

Other comments

Lead and its compounds have been comprehensively reviewed (1).

References

1. *IPCS Environmental Health Criteria 85: Lead – Environmental Aspects* 1989, WHO, Geneva, Switzerland.
2. *IARC Monograph* 1987, **Suppl. 7**, 65.
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

L25 lead nitrate

$$Pb(NO_3)_2$$

N_2O_6Pb **Mol. Wt.** 331.21 **CAS Registry No.** 10099-74-8
Synonyms nitric acid, lead(2+) salt; lead dinitrate; plumbous nitrate
EINECS No. 233-245-9 **RTECS No.** OG 2100000

Uses Manufacture of matches and explosives. As mordant in dyeing and printing on textiles. Oxidiser in dye industry. Sensitiser in photography. Has been used as a caustic in equine canker.

Physical properties

M. Pt. 470°C (decomp.) **Specific gravity** 4.53 at 20°C
Solubility Water: 500 g l^{-1} (cold), 1333 g l^{-1} (boiling). Organic solvents: ethanol, methanol

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 1469 **HAZCHEM Code** 2Y **Conveyance classification** oxidising substance, toxic
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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) snakehead fish 13.2 mg l^{-1} (1).
LC_{50} (96 hr) airsac catfish 12.0 mg l^{-1} (1).
LC_{50} (7 day) goldfish 6.6 mg l^{-1} (2).
Red barb (30 day) 0.0474 mg l^{-1} caused changes in physiochemical processes including glycogen uptake, cholesterol levels and lipid analysis (3).
Giant gourami (4 day) 9.5 mg l^{-1} caused physical damage to tissue (4).

Invertebrate toxicity
Chara vulgaris (7 day) 2.5 mg l^{-1}, 100% mortality (5).
LC_{Lo} (exposure unspecified) *Peranema gracilis, Euglena gracilis* 1000 mg lead l^{-1}; *Blepharisma* 42 mg l^{-1}; *Tetrahymena, Paramecium multimicronucleatum* 24 mg l^{-1}; *Chilomanas* 5.6 mg l^{-1} (6).
EC_{50} (2 day) *Asellus aquaticus* (mobility) 120 mg l^{-1} (7).
EC_{50} (2 day) *Crangonyx pseudogracilis* (mobility) 43.8 mg l^{-1} (7).
LC_{50} (96 hr) *Barytelphues guerini* 25 ppm, haemolymph pH, CO_2 and lactate levels increased and haemolymph oxygen levels decreased (8).

Toxicity to other species
Clawed toad continuously exposed for 72 and 48 hr from the blastula and gastrula stage, respectively, to the larval stage. Lethality and abnormality in embryos and larvae; dose dependency was noted. The main abnormality observed was neural tube defects (9)

Bioaccumulation
Accumulation in earthworms 4.3-756 ppm. Accumulation of lead from soil with added lead nitrate was faster in soils with low (3%) organic carbon than in soils with high (17-42%) organic carbon. Earthworms accumulated 1000 ppm without any ill-effects (10).
Procambarus clarkii (96 hr) exposure to 10, 50 or 100 μg l^{-1}. Concentrations of lead accumulated in gills >midgut glands >muscle (11).
Selenastrum capricornutum whole plant bioconcentration factor after exposure to 4.5 μg l^{-1} was 70,000 (7 day) and 102,000 (28 day) and after exposure to 40.1 μg l^{-1} was 27,000 (7 day) and 32,000 (28 day), at temperatures 21-24°C and pH 7.2-7.8 (12).
Mytilus edulis (13 day) 100 μg l^{-1} at 15°C, bioconcentration factor 3000 accumulation in kidney (13).
Daphnia magna (7, 28 day) 4.5 μg l^{-1} bioconcentration factors 2900 and 5140, respectively (12).
Carp exposed to 10,000 μg l^{-1} for 2 day had bioconcentration factors of 4200 for the viscera and 304 for the gills (14).

Guppys exposed to 4.6 μg l^{-1} for 7 or 28 day had whole body bioconcentration factors of 654 and 3459, respectively (12).

Environmental fate

Adsorption and retention

Podzolic soil spiked with lead nitrate, content of water solute lead 0.5-2.22 mg kg^{-1}. Nitrates acidified the 3-40 cm soil layer by adsorption and displacement of H^+ and Al^{3+} (15).

Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (16).

Mammalian & avian toxicity

Acute data

LD_{50} injection (4 day) chicken egg 0.10 mg egg^{-1} (21).

LD_{Lo} oral guinea pig 500 mg kg^{-1} (17).

LD_{Lo} intraperitoneal rat 270 mg kg^{-1} (18).

LD_{50} intraperitoneal mouse 74 mg kg^{-1} (19).

LD_{50} intravenous rat 93 mg kg^{-1} (20).

Sub-acute and sub-chronic data

LC_{50} (>100 day) mallard duck >50 mg kg^{-1} diet (22).

LC_{50} (5 day) Japanese quail >5000 mg kg^{-1} diet (23).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B for inorganic lead (24).

Teratogenicity and reproductive effects

Maternal exposure to 12.5, 25, 50 mg kg^{-1} on day-9 of gestation did not cause embryonic resorption or foetal lethality, it induced chromosomal aberrations in foetal liver and maternal bone marrow cells (25).

Intravenous golden hamster 25 or 50 mg kg^{-1} body weight on days 8 or 9 of pregnancy. Malformations of the sacral and tail region and a few cases of rib fusion were observed, suggesting lead interferes with a specific enzymic event during pregnancy (26).

Intravenous golden hamster 50 mg kg^{-1} body weight on day-8 of pregnancy produced hyperplasia. Disorientation of neuroepithelial cells of the dorsal region of the caudal neural tube were observed in embryos on day-9. Haematomas and extensive necrosis occurred throughout the dorsal region of the compressed neural tube on day-10 of gestation (27).

Intravenous Simonsen Sprague-Dawley rats single dose 25-70 mg kg^{-1} body weight on days 8-17 of pregnancy. With 50 and 70 mg kg^{-1} body weight, malformations of the urogenital and intestinal tracts and abnormalities of the posterior extremities were produced when doses were given on day-9 of pregnancy. Lead was increasingly lethal to foetuses when given on days 10-15 of pregnancy. Hydrocephalus and haemorrhage of the central nervous system occurred with treatment on day-16 of pregnancy (28).

Genotoxicity

In vivo mice bone marrow increased aneuploidy and chromosomal aberrations (29).

In vivo mouse bone marrow did not induce micronuclei (30).

Drosophila melanogaster induced sex linked recessive lethal mutations (31).

Other effects

Any other adverse effects

Single concentration (unspecified) to ♂ Wistar rats caused increased activity of liver enzyme, inhibited ATPase and adenylate cyclase activity at 48-72 hr and 24 hr, respectively (32).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 $\mu g\ l^{-1}$ (33).

Other comments

The aquatic toxicity of lead is dependent on the free ionic concentration, which affects the bioavailability of lead to organisms. Inorganic lead toxicity is strongly dependent on environmental conditions such as water hardness, pH and salinity. The presence of other salts reduces the bioavailability of lead to organisms because of precipitation (16).

Scenedesmus obliquus showed tolerance/resistance to concentrations of ≤300 ppm Pb^{2+}. Nitrate reductase activity was inhibited (34).

References

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2. Kemp, H. T. et al *Water Quality Data Book Vol. 5. Effects of Chemicals on Aquatic Life* 1973, EPA, Water Pollution Control Series 09/73.
3. Teusari, H. et al *Bull. Environ. Contam. Toxicol.* 1987, **38**, 778.
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L26 lead perchlorate

$$Pb(ClO_4)_2$$

Cl_2O_8Pb **Mol. Wt.** 406.10 **CAS Registry No.** 13637-76-8

Synonyms perchloric acid, lead salt; lead diperchlorate

EINECS No. 237-125-7 **RTECS No.** SC 8100000

Physical properties

M. Pt. (decomp.)

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 1470 **HAZCHEM Code** 2Y **Conveyance classification** oxidising substance, toxic
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 µg l^{-1} (3).

Other comments

Lead and its compounds have been comprehensively reviewed (1).

References

1. *IPCS Environmental Health Criteria 85: Lead – Environmental Aspects* 1989, WHO, Geneva, Switzerland.
2. *IARC Monograph* 1987, **Suppl. 7**, 65.
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

L27 lead phosphate

$$Pb_3(PO_4)_2$$

$O_8P_2Pb_3$ **Mol. Wt.** 811.54 **CAS Registry No.** 7446-27-7

Synonyms phosphoric acid, lead(2+) salt (2:3); C.I. 77622; lead orthophosphate; lead diphosphate; Perlex Paste 500; trilead phosphate

EINECS No. 231-205-5 **RTECS No.** OG 3675000

Uses Stabiliser for plastics.

Physical properties

M. Pt. 1014°C **Specific gravity** 6.9-7.3
Solubility Water: 0.14 mg l^{-1} at 20°C

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
In lead adsorption studies on meadow brown soil, lead phosphate was the dominant species. Desorption of lead occurred at pH <5 and at pHs >12.5. Distribution coefficient in soil-water system was 0.5-6.0 × 10^3 (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).
Subcutaneous 270 albino rats (strain and sex unspecified) (16 month) 40-760 mg kg^{-1} body weight 19/29 rats that survived for 10 or more months developed renal tumours. The tumours included adenomas, papillomas, cystadenomas and 3 carcinomas of the renal cortex (3).
Subcutaneous (18 month) 80 albino rats wkly/fortnightly injections of 20 mg kg^{-1}. Renal adenomas developed in 29 rats, no malignant tumours were found (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 μg l^{-1} (4).

Other comments

Lead and its compounds have been comprehensively reviewed (5).

References

1. Li, S. et al *Huanjing Kexue Xuebao* 1987, **7**(4), 493-497 (Ch.) (*Chem. Abstr.* **109**, 210254y).
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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. *IPCS Environmental Health Criteria 85: Lead – Environmental Aspects* 1989, WHO, Geneva, Switzerland

L28 lead phosphite dibasic

$H_4O_{11}P_2Pb_6$ **Mol. Wt.** 733.58 **CAS Registry No.** 12141-20-7

Synonyms lead oxide phosphonate; dibasic lead phosphite

EINECS No. 235-252-2

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 2989 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 μg l^{-1} (3).

Other comments

Lead and its compounds have been comprehensively reviewed (3).

References

1. *IPCS Environmental Health Criteria 85: Lead – Environmental Aspects* 1989, WHO, Geneva, Switzerland.
2. *IARC Monograph* 1987, **Suppl. 7**, 65.
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

L29 lead subacetate

$$Pb(CH_3CO_2)_2{\cdot}2Pb(OH)_2$$

$C_4H_{10}O_8Pb_3$ **Mol. Wt.** 807.72 **CAS Registry No.** 1335-32-6

Synonyms lead, bis(acetato-*O*)tetrahydroxytri-; lead acetate, basic; monobasic lead acetate; bis(acetato)dihydroxytrilead

EINECS No. 215-630-3 **RTECS No.** OF 8750000

Uses In sugar analysis to remove colouring matters, for clarifying and decolorising other solutions of organic substances.

Physical properties

Solubility Water: 62.5 g l^{-1} cold, 250 g l^{-1} hot

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
UK-LTEL 0.15 mg m^{-3} (as Pb)

UN No. 2291 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Danger of cumulative effects – Possible risk of irreversible effects – Harmful: danger of serious damage to health by prolonged exposure if swallowed (R61, R62, R33, R40, R48/22)
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

Sub-acute and sub-chronic data
LC_{50} (5 day) oral Japanese quail >5000 mg kg^{-1} (diet) (1).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, insufficient evidence for carcinogenicity to animals, IARC classification group 3 (2).
Oral 50 ♂, ♀ Swiss mice (2 yr) 0.1% or 1.0%/0.5% in diet induced 3 adenomas and 4 carcinomas in 0.1% dose. Most of the mice receiving 1.0%/0.5% dose died and only 1 carcinoma was found (3).
Oral, 40 Wistar rats (29 or 24 month) 0.1% or 1.0%. Incidence of renal tumours occurred in 11/32 animals

administered 0.1% dose, including 3 carcinomas; for 1.0% dose renal tumours were induced in 13/24 animals, including 6 carcinomas (4).
Oral 10 ♂ Wistar rats (48 wk) 1.5%. All rats developed renal tumours, 6 adenomas and 4 carcinomas, no extrarenal tumours were found (5).

Teratogenicity and reproductive effects
TD_{Lo} oral mouse (28 day) 258 g kg^{-1} caused reproductive effects (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 μg l^{-1} (7).

Other comments

Lead and its compounds have been comprehensively reviewed (8).

References

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L30 lead sulfate

$PbSO_4$

O_4SPb **Mol. Wt.** 303.26 **CAS Registry No.** 7446-14-2

Synonyms sulfuric acid, lead(2+) salt (1:1); Anglislite; C.I. 77630; C.I. Pigment White 3; Freemans white lead; Lead Bottoms; Limstab

EINECS No. 231-198-9 **RTECS No.** OG 4375000

Uses Replaces white lead as pigment. Used with zinc in galvanic batteries. In lithography. Preparing rapidly drying oil varnishes. Weighting fabrics.

Physical properties

M. Pt. 1170°C (decomp.) **Specific gravity** 6.2

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 1794 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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
Preliminary static, acute toxicity tests using fathead minnows, >3000 mg (Pb) l^{-1} introduced as sulfate did not cause morbidity to newly hatched minnows (1).

Environmental fate

Adsorption and retention
Increased pH and humic acid concentration favoured complexation. At low pH values particulate lead compounds adsorbed humic acid inhibiting lead dissolution (2).
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (3).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral dog 2 g kg^{-1} (4).
LD_{Lo} oral guinea pig 30 g kg^{-1} (5).
LD_{Lo} intraperitoneal guinea pig 290 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).

Genotoxicity

Salmonella typhimurium TA100 with and without and metabolic activation in presence and absence of nitrilotriacetic acid. No mutagenic activity observed with nitrilotriacetic acid to solubilise. Encapsulation of lead pigments with amorphous silica rendered compounds non-mutagenic and not-toxic indicating active moieties were biologically unavailable (8).
In vitro human lymphocytes incidence of sister chromatid exchanges increased (9).
In vitro Chinese hamster cells significant increased frequency of sister chromatid exchanges (10).

Other effects

Other adverse effects (human)
It is highly irritating and destructive to the eyes and skin (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50μg l^{-1} (12).

Other comments

Occupational exposure to pottery workers and toxicity discussed (13).
Soluble in cold water, hot water or ammonium salts; nitric acid, sodium hydroxide and concentrated hydriodic acid.

References

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L31 lead sulfide

PbS

PbS **Mol. Wt.** 239.27 **CAS Registry No.** 1314-87-0

Synonyms C.I. 77640; natural lead sulfide; P37; P128; plumbous sulfide

EINECS No. 215-246-6 **RTECS No.** OG 4550000

Uses Glazing earthenware.

Occurrence In the mineral galena.

Physical properties

M. Pt. 1114°C **B. Pt.** 1281°C **Specific gravity** 7.50

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)

UN No. 2291 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Preliminary static, acute toxicity test using fathead minnow, >3000 mg (Pb) l^{-1} introduced as sulfide did not cause mortality to newly hatched minnows (1).

Environmental fate

Adsorption and retention

Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (2).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral guinea pig 10 g kg^{-1} (3).

LD_{Lo} intraperitoneal rat 1847 mg kg^{-1} (4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (5).

Oral Fischer 344 rat prechronic feeding experiments, technical reports were not prepared (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 μg l^{-1} (7).

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L32 lead tetraacetate

$$(CH_3CO_2)_4Pb$$

$C_8H_{12}O_8Pb$ **Mol. Wt.** 443.38 **CAS Registry No.** 546-67-8

Synonyms acetic acid, lead(IV) salt; lead(IV) acetate; plumbic acetate

EINECS No. 208-908-0 **RTECS No.** AI 5300000

Physical properties

M. Pt. 175-180°C **Specific gravity** 2.23 at 17°C with respect to water at 4°C

Solubility Organic solvents: hot glacial acetic acid, benzene, chloroform, nitrobenzene

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
UK-LTEL 0.15 mg m^{-3} (as Pb)

UN No. 1616 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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
Cell multiplication inhibition test *Uronema parduczi Chatton-Lwoff* 0.07 mg l^{-1} (threshold concentration) (1).
Pseudomonas putida, cell multiplication inhibition starts at 1.8 mg l^{-1} (2).
Microcystis aeruginosa, cell multiplication inhibition starts at 0.45 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
TD_{Lo} oral rat 18.9 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).

Genotoxicity

In vitro Chinese hamster ovary cells sister chromatid exchange (metabolic activation unspecified) positive (5).
Tradescantia micronucleus assay, repeated tests for clastogenicity with lead acetate yielded the minimum ED for clastogenicity of 0.44 ppm (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 µg l^{-1} (7).
Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Lead and its compounds have been comprehensively reviewed (9).

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L33 lead thiocyanate

$$Pb(SCN)_2$$

$C_2N_2S_2Pb$ **Mol. Wt.** 323.37 **CAS Registry No.** 592-87-0

Synonyms thiocyanic acid, lead salt; lead bis(thiocyanate); lead dithiocyanate; lead sulfocyanate

EINECS No. 209-774-6 **RTECS No.** XL 1538000

Uses Reverse dyeing with aniline black. Manufacture of safety matches and cartridges.

Physical properties

M. Pt. 190°C (decomp.) **Specific gravity** 3.82

Occupational exposure

DE-MAK 0.1 mg m^{-3} (inhalable dust fraction)
FR-VME 0.15 mg m^{-3} (as Pb)
JP-OEL 0.1 mg m^{-3} (as Pb)
SE-LEVL 0.1 mg m^{-3} (as Pb) (total dust); 0.05 mg m^{-3} (as Pb) (respirable dust)
UK-LTEL 0.15 mg m^{-3} (as Pb)
US-TWA 0.05 mg m^{-3} (as Pb)
Supply classification toxic
Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility – Harmful by inhalation and if swallowed – Danger of cumulative effects (R61, R62, R20/22, R33)
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

Adsorption and retention
Inorganic lead tends to form highly insoluble salts and complexes with various anions and is tightly bound to soil, therefore availability to terrestial plants is drastically reduced and effects on plants are normally only observed at very high environmental concentrations 100-1000 mg kg^{-1} soil (1).

Mammalian & avian toxicity

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Lead: maximum admissible concentration 50 µg l^{-1} (3).

Other comments

Lead and its compounds have been comprehensively reviewed (1).

References

1. *IPCS Environmental Health Criteria 85: Lead – Environmental Aspects* 1989, WHO, Geneva, Switzerland.
2. *IARC Monograph* 1987, **Suppl. 7**, 65.
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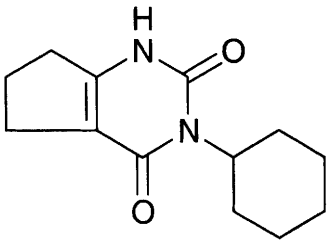
L34 lenacil



$C_{13}H_{18}N_2O_2$ **Mol. Wt.** 234.30 **CAS Registry No.** 2164-08-1

Synonyms 1*H*-cyclopentapyrimidine-2,4(3*H*,5*H*)-dione, 3-cyclohexyl-6,7-dihydro-; Adol; Borderclear; Buracyl; Hexilur; Lenamon; Vigor

EINECS No. 218-499-0 **RTECS No.** GY 5875000

Uses Herbicide.

Physical properties

M. Pt. solid 290°C, commercial product 316-317°C **Specific gravity** 1.32 **Partition coefficient** log P_{ow} 2.31
Solubility Water: 6 mg l^{-1} 25°C. Organic solvents: acetone, benzene, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) carp 10 mg l^{-1} (1).
LC_{50} (96 hr) minnow, trout >2.0 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* >8.4 mg l^{-1} (2).
LC_{50} earthworms >10,000 mg kg^{-1} (2).

Environmental fate

Degradation studies
Under laboratory conditions microbial activity in clay loam soil stimulated heterotrophic N_2 fixation and production of carbon dioxide. Effects on heterotrophic N_2 fixation and soil respiration were only exhibited at high rates of application 100 μg g^{-1} soil (3).
In soil, 100% microbial degradation occurred within 5-6 months (4).

Adsorption and retention
Adsorption on montmorillonite and soil 0.028 g l^{-1} per mol kg^{-1} soil. At a concentration <0.14 g l^{-1} sorption linearly increased with concentration and was complete, ≥0.14 g l^{-1} sorption was non-linear and decreased to 16% (5).

Mammalian & avian toxicity

Acute data
LD_{50} rat >11 g kg^{-1} (6,4).
LD_{50} dermal rabbit >5000 mg kg^{-1} (4).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail 2300 mg kg^{-1} (diet) (2).
Oral rats (22 wk) 200 mg kg^{-1} day^{-1} diet caused increased glycolysis in rat liver, while phosphofructokinase and glucose-6-phosphatase enzyme activities were slightly inhibited (7).

Carcinogenicity and chronic effects
Oral rats (lifetime study) 130 or 200 mg kg^{-1} day^{-1}. In rats which died a natural death hyperplastic changes of flat multilayer gastric epithelium were larger and more frequent than in controls. Symptoms of carcinogenic activity were not found (7).

Teratogenicity and reproductive effects
Oral rats (three generations) 500 ppm, no adverse-effects were found on reproductive indices or lactation and there was no pathology in the F_3 generation (8).
Oral (2 yr) dogs 10,000 ppm. Two ♀ dogs produced healthy offspring (8).

Irritancy
Caused mild irritation to eyes of rabbits (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 (metabolic activation unspecified) negative (9).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (11).

Other comments

Adsorption, decomposition dynamics and environmental fate studied (12).
Metabolic pathways reviewed (13).

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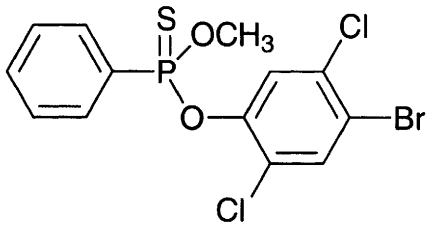
L35 leptophos



$C_{13}H_{10}BrCl_2O_2PS$ **Mol. Wt.** 412.07 **CAS Registry No.** 21609-90-5

Synonyms *O*-(4-bromo-2,5-dichlororophenyl) *O,O*-methyl phenylphosphonothioate; Phosvel; MBCP; NK 711; *O*-(2,5-dichloro-4-bromophenyl) *O*-methyl phenylthiophosphonate

EINECS No. 244-472-8 **RTECS No.** TB 1720000

Uses Insecticide (superseded).

Physical properties

M. Pt. 70°C **Specific gravity** 1.53 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 5.881
Solubility Water: 4.7 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, cyclohexane, heptane, isopropyl alcohol, xylene

Occupational exposure

Supply classification toxic, dangerous for the environment
Risk phrases Harmful in contact with skin – Toxic if swallowed – Toxic: danger of very serious irreversible effects if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21, R25, R39/25, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the eyes – Wear 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, S25, S36/37/39, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) *Leiostomus xanthurus*, rainbow trout 4-10 μg l^{-1} (1,2).
LC_{50} (48 hr) carp >40 mg l^{-1} (2).
LC_{50} (96 hr) *Saccobranchus fossilis* 22.6 mg l^{-1} at 18°C (3).

Invertebrate toxicity
LC_{50} (96 hr) mysid shrimp, marine shrimp 1.88-3.16 μg l^{-1} (1).
LC_{50} (3 hr) *Daphnia* sp. 2 μg l^{-1} (2).

Bioaccumulation
Bioconcentration factor (4 day) *Leiostomus xanthurus* 68 (1).
Bioconcentration factor (14 day) *Pseudorasbora parva* 0.019 (4).

Environmental fate

Anaerobic effects
Nitrogen fixing cyanophytes growing on rice plants showed tolerance limits *Aulosira fertilissima* 300 ppm; *Anabaena doliulum* 175 ppm; and *Nostoc* sp. 200 ppm. Reduced nitrogen content of the algae (20 day): *Aulosira fertilissima* by ~30%; *Anabaena doliulum* by ~4%; and *Nostoc* sp. by ~28% of initial (control) nitrogen value (5).

Abiotic removal

Photodegradation of thin dry film by UV irradiation after 24 hr and by sunlight after 65 days, 47 and 37% of initial concentration, respectively (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 30-65 mg kg^{-1} (7-11).
LD_{50} oral rat 19 mg kg^{-1} (12).
LD_{50} oral rabbit 124 mg kg^{-1} (13).
LD_{50} dermal ♂ rat 103 mg kg^{-1} (10).
LD_{50} dermal rat 44 mg kg^{-1} (12).
LD_{50} dermal rabbit 800 mg kg^{-1} (13).
LD_{50} intraperitoneal ♂ rat 175 mg kg^{-1} (11).
LD_{50} subcutaneous mouse 120 mg kg^{-1} (11).

Sub-acute and sub-chronic data

Oral (30 day) domestic chicken 1200 ppm (diet), fatal to 64% of birds (14).
Oral dog (30 day) 40 mg kg^{-1} day^{-1} caused cholinergic poisoning in 100% of animals treated (15).
Peking duck (30 day) 100 mg kg^{-1} day^{-1} caused delayed neuropathy in 100% of treated birds (16).
Oral mallard duck (30, 60, 90 day) 60 or 270 mg kg^{-1} day^{-1} caused neuropathy and ataxia, while 10 mg kg^{-1} failed to produce ataxia (17-19).
Intravenous (3 day) hens 5 mg kg^{-1} day^{-1} delayed ataxia was observed in 44% of test population. Transfer from blood to affinitive tissues such as sciatic nerve or leg muscles occurred. Accumulated in nerves and muscles at initial stages and caused enhancement of neuropathy (20).

Teratogenicity and reproductive effects

Pregnant rats (8-20 days gestation) were fed 125, 50 or 12.5 ppm. Two cases of gross foetal malformation were found in 50 ppm group, wavy rib and abnormal construction of nasal cavity. Survival rate of neonates was decreased (11).

Metabolism and toxicokinetics

Following oral administration to domestic chicken 250 mg kg^{-1} as a single dose, levels in adipose tissue were 25, 9, 1.5 and 0 ppm after 1, 3, 7 and 38 days, respectively. Blood plasma levels peaked 3 hr after dose (21).
Oral administration to domestic chicken 400 mg kg^{-1}. After 24 hr levels in the brain and blood plasma were 0.66 and 0.15 ppm, respectively. After 72 hr these decreased to 0.06 ppm in the brain and 0.11 ppm in the spinal cord. Complete metabolism occurred after 8 days (brain) and 15 days (spinal cord) (22).
The disappearance rate in hens was 70% at 6 hr and 93% at 96 hr. The $t_{1/2}$ was 1.37 hr for the early phase and 45 hr for the late phase. Only 0.1% of the administered dose was detected in excreta, its disappearance from the hen's body was due to its metabolism (23).
In mammals, monooxygenase system enzymes in the liver metabolically converted leptophos into more active substances, i.e. oxonium leptophos, desmethyl leptophos, desbromoleptophos. It is rapidly metabolised in non-sensitive species, e.g. mice and rats. Eliminated in the urine in the form of polar degradation products with an elimination $t_{1/2}$ of 9 hr (24).
A single intragastric dose of ^{14}C-leptophos was given to rats as a 15 mg kg^{-1} dose, the ^{14}C in the liver, kidneys and fatty tissues did not exceed 2-5% of the ^{14}C dose. In 9 days 46-75% of the dose was eliminated in the urine, 12-29% in the faeces and 1.35-5.38% in exhaled air. The following metabolic products of leptophos were detected in the urine: oxonium leptophos, *O*-methylphenylthiophosphoric acid, phenylphosphoric acid and 4-bromo-2,5-dichlorophenol (25).
Cholinesterase activity in pregnant rats following leptophos treatment decreased as follows: maternal brain, liver, placenta, foetus and maternal serum (7).
The uncoupling action on liver mitochondrial oxidative phosphorylation was not marked (7).

Genotoxicity

In vitro Chinese hamster ovary cells without metabolic activation induced a significant increase in sister chromatid exchanges (26).

Other effects

Other adverse effects (human)

Oral, inhalation and/or dermal, exposure at conditions of local agriculture usage (4 day). Epigastric pain, diarrhoea, nausea, coughing, bradycardia, insomnia, headaches and weariness were observed in subjects. Erythrocyte cholinesterase activity was moderately inhibited (27).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (28).

Other comments

No neuropathy detected in Japanese quails (29).
Denied registration as pesticide in USA (30).
Residues detected in foods (0.12 ppm), fruits (0.005 ppm), potatoes (0.1 ppm) and water in USA (31-33).
Highly toxic to sporulation in *Metarhizium anisopliae* var. *anisopliae* isolate E_9 (34).
Toxicology and environmental fate reviewed (35).

References

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L36 DL-leucine

$$CH_3CH(CH_3)CH_2CH(NH_2)CO_2H$$

$C_6H_{13}NO_2$ **Mol. Wt.** 131.17 **CAS Registry No.** 328-39-2

Synonyms leucine

EINECS No. 206-328-2 **RTECS No.** OH 2840000

Physical properties

M. Pt. 322°C (decomp.) **Specific gravity** 1.293 at 18°C
Solubility Water: 7.97 g l^{-1} 0°C

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal rat 6430 mg kg^{-1} (1).

Other comments

Leucine is very susceptible to peroxidation. Hydroxyl radical attack on L-leucine gives rise to five major oxidation products: (2*S*)-γ-hydroxyleucine, (2*S*,4*S*)-δ-hydroxyleucine, (2*S*,4*R*)-δ-hydroxyleucine, (2*S*,4*R*)-4-methylproline and (2*S*,4*S*)-4-methylproline. The presence of hydroxyleucines in proteins in physiological and pathological samples has been demonstrated (2).
Halobacterium halobium can utilise D-leucine for growth (3,4).

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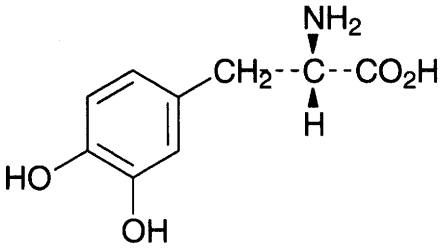
L37 levodopa



$C_9H_{11}NO_4$ **Mol. Wt.** 197.19 **CAS Registry No.** 59-92-7

Synonyms 3-hydroxy-L-tyrosine; dihydroxy-L-phenylalanine; 3,4-dihydroxyphenylalanine; L-DOPA; DOPA; eldopal; pardopa; Dopaflex; Dopaston; Insulamina; Bendopa; Dopar

EINECS No. 200-445-2 **RTECS No.** AY 5600000

Uses Antiparkinsonian drug, anticholinergic agent.

Physical properties

M. Pt. 276-278°C

Solubility Water: 1.65 g l^{-1}. Organic solvents: formic acid

Environmental fate

Anaerobic effects

IC_{50} methanogenic bacterial culture ~330 mg l^{-1} (exposure not specified) (1).

Degradation studies

Metabolised in wastewater by methanogenic bacteria. Both *p*- and *m*-cresol were identified as intermediate degradation products (1).

Decarboxylation to dopamine by a *Pseudomonas* species was reported (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1780, 2360 mg kg^{-1}, respectively (3).

LD_{50} oral rabbit 610 mg kg^{-1} (3).

LD_{50} intravenous mouse 450 mg kg^{-1} (3).

LD_{50} intraperitoneal rat, mouse 590, 620 mg kg^{-1}, respectively (3).

LD_{50} subcutaneous mouse 4450 mg kg^{-1} (4).

Teratogenicity and reproductive effects

In vitro mouse limb bud micromass assay, ratio of IC_{50} for thymidine and sulfate incorporation (T/S ratio) of 1.27 indicates a low potential for developmental hazard (5).

Metabolism and toxicokinetics

Following oral administration in the treatment of Parkinsons disease, rapidly converted into dopamine (6).

Genotoxicity

Salmonella typhimurium TA92, TA97, TA104 with and without metabolic activation positive (7).

In vitro mouse lymphoma L5178Y tk^+/tk^- assay without metabolic activation positive (8).

In vitro human melanoma cells without metabolic activation, DNA damage positive, DNA repair and interstrand cross-links negative (9).

Other effects

Other adverse effects (human)

Adverse effects associated with therapeutic use include nausea, vomiting and anorexia. Cases of haemolytic anaemia, orthostatic hypotension, cardiac arrhythmias and dyskinesia have been reported (6).

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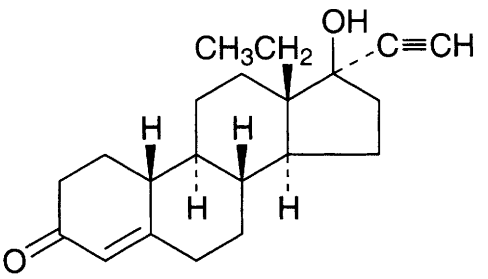
L38 levonorgestrel



$C_{21}H_{28}O_2$ **Mol. Wt.** 312.45 **CAS Registry No.** 797-63-7

Synonyms 18,19-dinorpregn-4-en-20-yn-3-one, 13-ethyl-17-hydroxy-, (17α)-; Norplant

EINECS No. 212-349-8 **RTECS No.** JF 8225000

Uses Inhibitor of ovulation, oral contraceptive.

Physical properties

M. Pt. 239-241°C

Solubility Organic solvents: acetone, chloroform, diethyl ether, dioxane, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂, ♀ rat, mouse 1140-2130 mg kg^{-1} (50:30 ratio levonorgesterol/ethinylestradiol mix) (1).
LD_{50} intraperitoneal ♂, ♀ mouse 700-800 mg kg^{-1} (1).

Sub-acute and sub-chronic data

TD_{Lo} implant woman (52 wk pregnant) 1600 μg kg^{-1} caused reproductive effects (2).
Oral ♀ rat (3 month) 0.0025, 0.025, 0.25, 2.5 and 25 mg kg^{-1}. Highest dose increased liver weight, blood α1-globulin, decreased blood cholesterol. No histological changes observed as all changes were reversible (3).
Rabbits administered 500 μg day^{-1} 6 day wk^{-1} for 3 months, no influence on growth or body weight, enzyme activity, cholesterol levels and no organ damage (4).

Carcinogenicity and chronic effects

TD_{Lo} oral mouse (69 wk) 29 mg kg^{-1} caused neoplastic effects (5).

Metabolism and toxicokinetics

Intravenous rabbits (unspecified dose) absorbed bioavailability was 40%. Oral rabbit 0.3 mg (initial dose) blood concentration peaked after 30 min. Rapid absorption followed with blood concentration of <0.2 ng ml^{-1} detected (6).

Other effects

Other adverse effects (human)

A 3-yr study of users of Norplant-2 rods for contraception indicated a possible increased predisposition to thrombosis, evidenced by significant increase in platelet count and aggregability (7).

Legislation

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

Other comments

Norplant is approved for use in 39 countries (9).

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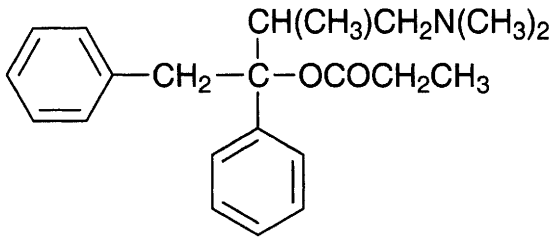
L39 levopropoxyphene



$C_{22}H_{29}NO_2$ **Mol. Wt.** 339.48 **CAS Registry No.** 2338-37-6

Synonyms benzeneethanol, α-[2-(dimethylamino)-1-methylethyl]-α-phenyl-, propanoate (ester),[*R*-(*R*'S']; 2-butanol, 4-(dimethylethylamino)-3-methyl-1,2-diphenyl-, propionate (ester), (–)-; Leropropoxyphene; *l*-propoxyphene

Uses Antitussive.

Physical properties

M. Pt. 75-76°C

Mammalian & avian toxicity

Acute data

LD_{50} oral ♀ rat 1455 mg kg^{-1} (1).

References

1. Goldenthal, E. I. *Toxicol. Appl. Pharmacol.* 1971, **18**, 185

L40 levulinic acid

$$CH_3C(O)CH_2CH_2CO_2H$$

$C_5H_8O_3$ **Mol. Wt.** 116.12 **CAS Registry No.** 123-76-2

Synonyms 4-oxo-pentanoic acid; β-acetylpropionic acid; 4-ketovaleric acid; levulic acid; 4-oxovaleric acid

EINECS No. 204-649-2 **RTECS No.** OI 1575000

Uses In organic synthesis; in the manufacture of nylon, synthetic rubber, plastics and medicinals.

Physical properties

M. Pt. 33-35°C **B. Pt.** 245-246°C **Flash point** 137°C **Specific gravity** 1.144

Solubility Water: freely soluble. Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1850 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 450 mg kg^{-1} (2).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *Food Cosmet. Toxicol.* 1979, **17**, 695.
2. *NTIS Report AD 607-952* Natl. Tech. Info. Ser., Springfield, VA, USA.
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L41 Lewisite

$$ClCH{=}CHAsCl_2$$

$C_2H_2AsCl_3$ **Mol. Wt.** 207.32 **CAS Registry No.** 541-25-3

Synonyms arsonous dichloride, (2-chloroethenyl)-; chlorovinylarsine dichloride; dichloro(2-chlorovinyl)arsine

RTECS No. CH 2975000

Uses Formerly used in chemical warfare.

Physical properties

M. Pt. 0.1°C (solidifies at –13°C) **B. Pt.** 190°C (decomp.) **Flash point** –13°C **Specific gravity** 1.88 at 20°C with respect to water at 4°C **Volatility** v.den. 7.15

Mammalian & avian toxicity

Acute data

LD_{Lo} dermal human 38 mg kg^{-1} (1).
LD_{50} dermal rat, mouse, dog 15 mg kg^{-1} (2,3).
LD_{50} subcutaneous rat, dog 1-2 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Gavage rats (13 wk) 0, 0.01, 0.5, 1.0 or 2.0 mg kg^{-1} in sesame oil 5 day wk^{-1}. A treatment-related lesion was detected in the forestomach of both sexes at 2.0 mg kg^{-1}. Lesions were characterised by necrosis of the stratified squamous epithelium accompanied by infiltration of neutrophils and macrophages, proliferation of neocapillaries, haemorrhage, oedema and fibroblast proliferation. Mild acute inflammation of glandular stomach also observed with 1.0 and 2.0 mg kg^{-1} (4).

Teratogenicity and reproductive effects

Gavage ♂, ♀ rats (42 wk) two-generation study 0, 0.10, 0.25 or 0.60 mg kg^{-1} day^{-1} 5 day wk^{-1}. No adverse-effect on reproduction performance, fertility or reproductive organ weights through two consecutive generations. Severe inflammation of the lung was observed at necropsy (5).
Rats (unspecified route) 1.5 mg kg^{-1} did not cause toxic or teratogenic effects in maternal animals or foetuses, however 10% maternal mortality occurred at 2 mg kg^{-1}. In rabbits 13 and 100% mortality were observed after doses of 0.07 and 1.5 mg kg^{-1}, respectively (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 with and without metabolic activation negative (7).

Other effects

Other adverse effects (human)

0.5 ml may give rise to sufficient absorption to produce severe systemic effects, 2 ml may cause death (8).

Any other adverse effects

Dermal pig (high dose) caused blistering of skin. Exposure to vapour produced diffuse lesions of less severity (9).
In vitro isolated perfused porcine skin flap topical exposure to 6 concentrations ranging from 0.07-5.0 mg ml^{-1}. Lesions were characterised 1, 3, 5 and 8 hr after exposure, increased activation of lactate dehydrogenase and vascular resistance, and mild increases in glucose utilisation were observed (10).

Legislation

Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Antidote: British Anti Lewisite (dimercaptopropanol) (8).
Neutralised and inactivated by sodium hypochlorite (8).
Toxicity amd physical and chemical properties reviewed (12).

References

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L42 lignin alkali

CAS Registry No. 8068-05-1

Synonyms alkali lignin; Indulin A; Kraft lignin; Meadol MRM; sulfate lignin; Tomlinite

Environmental fate

Anaerobic effects

Desulfovibrio desulfuricans, lignin alkali could not substitute for lactate or sulfate when added to the culture medium, though it did enhance the viability of the cells. After biological treatment it bound larger quantities of heavy metals (1).

Degradation studies

During a study of metabolism of various lignins, lignin alkali was found to be most refractory (2).
Heterobasidion annosum, *Pleurotus ostreatus* and *Stereum purpureum* caused the degradation of lignin alkali, shown by spectophotometric studies at 280 nm. *Stereum purpureum* had the highest lignolytic activity (3).

Other comments

Physico-chemical properties and uses reviewed (4).

References

1. Ziomek, E. et al *Appl. Environ. Microbiol.* 1989, **55**(9), 2262-2266.
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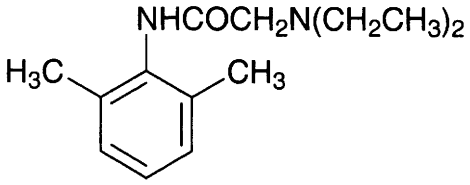
L43 lignocaine



$C_{14}H_{22}N_2O$ **Mol. Wt.** 234.34 **CAS Registry No.** 137-58-6

Synonyms acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl)-; Anestacon; Duncaine; Xyline; Lidocaine; Xylocitin

EINECS No. 205-302-8 **RTECS No.** AN 7525000

Uses Local anaesthetic. Antiarrhythmic.

Physical properties

M. Pt. 68-69°C **B. Pt.** 180-182°C at 4 mmHg

Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

Scaphechinus mirabilis exposed for 10 min to 234-2343 mg kg^{-1} increased intracellular pH in unfertilised egg and decreased the pH rise associated with fertilisation (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 220, 317 mg kg^{-1}, respectively (2,3).

LD_{50} subcutaneous mouse, rat 238, 335 mg kg^{-1}, respectively (4,5).

LD_{Lo} intravenous rat 25 mg kg^{-1} (6).

LD_{50} intraperitoneal mouse 102 mg kg^{-1} (4).

LD_{100} intravenous sheep 1450 mg. Death occurred from respiratory depression with bradycardia and hypotension without arrhythmias (7).

TD_{Lo} intravenous human 23 mg kg^{-1} (8).

Irritancy

Eye rabbit 100 mg in 0.1 ml caused moderate irritation, persisting for more than 24 hr but recovery occurred within 21 days after treatment (9).

Genotoxicity

In vitro Syrian hamster embryo cells induced sister chromatid exchanges but not chromosomal aberrations at 30-300 μg l^{-1} for 18-20 hr (10).

Other effects

Any other adverse effects

Extraneural injection rat (concentration unspecified) produced concentration-dependent direct cellular toxicity including oedema, lipid inclusions and fibre injury (11).

Intravenous dog 8 mg kg^{-1} min^{-1}, seizure occurred at dose level of 20.8 mg kg^{-1} and arterial plasma concentration of 47.2 μg ml^{-1}. Two animals died of progressive hypotension, respiratory arrest and cardiovascular collapse (12).

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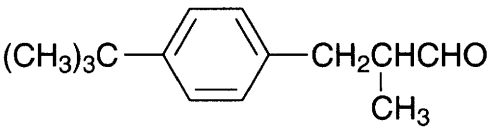
L44 lilial



$C_{14}H_{20}O$ **Mol. Wt.** 204.31 **CAS Registry No.** 80-54-6

Synonyms 2-methyl-3-(4-*tert*-butylphenyl)propionaldehyde; benzenepropanal, 4-(1,1-dimethylethyl)-α-methyl-; hydrocinnamaldehyde, *p*-*tert*-butyl-α-methyl-; Lilyal

EINECS No. 201-289-8 **RTECS No.** MW 4895000

Physical properties

B. Pt. 150°C at 10 mmHg **Specific gravity** 0.939 at 25°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3700 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (1).

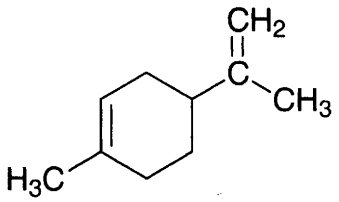
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. *Food Cosmet. Toxicol.* 1978, **16**, 637.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

L45 limonene



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 138-86-3

Synonyms 1-methyl-4-(1-methylethenyl)cyclohexene; *p*-mentha-1,8-diene; α-limonene; Dipanol

EINECS No. 205-341-0 **RTECS No.** OS 8100000

Uses In air-fresheners and perfumes. In the manufacture of cleaning compounds. Flavouring agent. Lubricating oil additive. Solvent.

Occurrence In the essential oil of many plants. In the defensive secretions of termite species.

Physical properties

M. Pt. -96.9°C **B. Pt.** 170-180°C **Flash point** 48°C (open cup) **Specific gravity** 0.8402 at 21°C with respect to water at 4°C **Volatility** v.den. 4.7

Solubility Organic solvents: diethyl ether, dimethylformamide, dimethyl sulfoxide, ethanol

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

UN No. 2052 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Supply classification irritant, dangerous for the environment

Risk phrases Flammable – Irritating to the skin – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R10, R38, R43, R50/53)

Safety phrases Avoid contact with the skin – Wear suitable gloves – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S24, S37, S60, S61)

Ecotoxicity

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia pulex* 70 mg l^{-1} (1).

Environmental fate

Degradation studies

Removed from water to below the limit of detection in activated sludge system and by air stripping (2).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

A CASE study predicted marginal carcinogenicity (3).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (4).

Other effects

Any other adverse effects

Inhibited oxidative phosphorylation in mitochondria *in vitro* through depletion of the transmembrane potential and inhibition of oxygen consumption (species and concentration not specified) (5).

Legislation

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

Other comments

Toxicity reviews cited (7).
Autoignition temperature 237°C.

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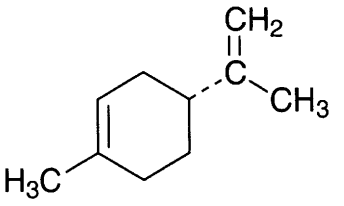
L46 (*R*)-(+)-limonene



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 5989-27-5

Synonyms 1-methyl-4-(1-methylethenyl)cyclohexene, (*R*)-; Carvene; (+)-limonene; D-limonene; (*R*)-limonene

EINECS No. 227-813-5 **RTECS No.** GW 6360000

Uses Flavour and fragrance additive for food and domestic products. Industrial solvent. Naturally occurring insecticide.

Occurrence Volatile oils, especially citrus oils.

Physical properties

B. Pt. 175.5-176°C **Flash point** 48°C **Specific gravity** 0.8402 at 25°C with respect to water at 4°C
Solubility Organic solvents: ethanol

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})
UN No. 2052 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity
LC_{50} earthworm 6 ppm. Chronic and acute intoxication involved a rapid and predictable cascade of behavioural and morphological symptoms, including increased mucous secretion, writhing, clitellar swelling and elongation of the body (1).

Environmental fate

Nitrification inhibition
Limits nitrogen mineralisation and nitrification, enhances immobilisation of NO_3^--N relative to NH_4^+-N and stimulates overall net immobilisation of nitrogen during breakdown of high carbon-content material (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >111 mg kg^{-1} (3).
LD_{50} oral rat 4400 mg kg^{-1} (4).
LD_{50} oral mouse 5600 mg kg^{-1} (4).
LD_{50} intravenous rat 110 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 600 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Gavage ♂, ♀ dog (6 month) 100 or 1000 mg kg^{-1} day^{-1} induced no histopathological changes in kidney (6).
Gavage ♂ rat (1, 4 wk) 75, 150, 300 mg kg^{-1} single daily dose 5 day wk^{-1} kidney damage observed (7).

Carcinogenicity and chronic effects
Gavage ♂, ♀ rat (103 wk) 0, 75, 150 mg kg^{-1} and 0, 300, 600 mg kg^{-1} in corn oil, respectively; ♂, ♀ mouse 0, 250, 500 mg kg^{-1} and 0, 500, 1000 mg kg^{-1} in corn oil, respectively. No evidence for carcinogenicity in ♀ rats, ♂, ♀ mice. Clear evidence for carcinogenicity, kidney tubular cell adenoma and adenocarcinoma in ♂ rats (8-12).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (11-13).
Mouse L5178Y/tk^+/tk^- assay, did not significantly increase the number of trifluorothymidine (Tft)-resistant cells (11).
In vitro Chinese hamster ovary cells, did not induce chromosomal aberrations or sister chromatid exchanges (11).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (15).

Other comments

Insect repellency, fumigant activity, acute toxicity (LD_{50}: ♀ house fly, ♂ German cockroach 90 and 700 µg $insect^{-1}$, respectively), reproductive toxicity and neurotoxicity investigated. The study concluded the substance has considerable potential as a naturally occurring insecticide (16).
Nephrotoxicity and nephrocarcinogenicity reviewed (17).

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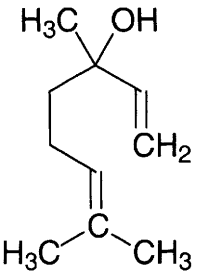
L47 linalool



$C_{10}H_{18}O$ **Mol. Wt.** 154.25 **CAS Registry No.** 78-70-6

Synonyms 3,7-dimethyl-1,6-octadien-3-ol; 2,6-dimethyl-2,7-octadien-6-ol; linalyl alcohol; linalol

EINECS No. 201-134-4 **RTECS No.** RG 5775000

Uses In perfumery instead of bergamot or French lavender oil. Synthetic flavouring substance and adjuvant.
Occurrence Chief constituent of linaloe oil. Occurs in oils of Ceylon cinnamon, sassafras, orange flower, bergamot.

Physical properties

B. Pt. *l*-form 198°C, *d*-form 198-200°C, *dl*-form 194-197°C at 720 mmHg **Flash point** 76°C
Specific gravity 0.87 at 20°C **Partition coefficient** P_{ow} 2.97 **Volatility** v.p. 21 Pa at 25°C
Solubility Water: practically insoluble in water. Organic solvents: miscible with alcohol, diethyl ether

Ecotoxicity

Invertebrate toxicity

The major route from linalool to CO_2 in *Pseudomonas incognita* adapted to grow on linalool as sole carbon source involved oxidation of the 10-methyl group to a carboxyl function. Oxidation of linalool at position-8 was a minor process and linalool-8-carboxylic acid was not significantly metabolised (1).

A *Pseudomonas* bacterium, isolated from soil, growing in a mineral salt medium with linalool as sole carbon source formed 10-hydroxylinalool, 10-carboxylinalool, oleuropeic acid, 2-vinyl-2-methyl-5-hydroxyisopropyl-tetrahydrofuran (linalool oxide), 2-vinyl-2-methyl-tetrahydrofuran-5-one, and a few unidentified minor metabolites (2).

The predominant product (>90%) of linalool biotransformation by *Botrytis cinerea* was (*E*)-2,6-dimethyl-2,7-octadiene-1,6-diol. The corresponding (*Z*)-isomer and 2-vinyl-2-methyl-tetrahydrofuran-5-one, the four isomeric linalool oxides in their furanoid and pyranoid forms, the isomeric acetate of pyranoid linalool oxides and 3,9-epoxy-*p*-menth-1-ene were produced in minor amounts (3).
High doses of linalool applied to oothecae of gravid ♀ cockroaches had no effect on ♀ mortality but significantly decreased the probability of the emergence of live young (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2790 mg kg^{-1} (5).
LD_{50} dermal rabbit 5610 mg kg^{-1} (6).
LD_{50} intramuscular mouse 8000 mg kg^{-1} (7).

Irritancy
Skin and eye irritant in humans (8).
Mildly irritating in the human patch test at 32% concentration (9).

Genotoxicity

In vitro Chinese hamster fibroblast cells (48 hr) 0.0625-0.25 mg ml^{-1}, chromosomal aberrations negative (10).

Other effects

Other adverse effects (human)
Long-term or repeated exposure may have effects on the liver (8).

Any other adverse effects
Gastric intubation of 1.5 g kg^{-1} for 5 days to ♂ Wistar rats caused induction of peroxisomal enzymes but not of cytochrome P_{450} IVA1 (11).
Cats sprayed with an insecticidal preparation containing 1% linalool, 1% D-limonene and 0.50% piperonyl butoxide showed mild salivation. Controls also showed mild salivation. Cats sprayed with a 20× stronger concentration of the insecticide suffered severe muscle tremor after 1 day, but eventually recovered without treatment (12).

Other comments

Toxicity of linalool, disposition in animals, and clinical signs and physiological effects reviewed (13).
Natural occurrence and isolation, cosmetic and perfumery uses, legal status of use in food, and metabolism, toxicology, carcinogenicity, biological activity and pharmacology of linalool reviewed (14).

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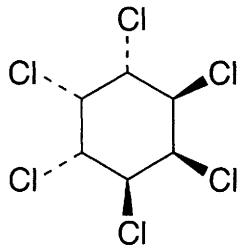
L48 ε-lindane



$C_6H_6Cl_6$ **Mol. Wt.** 290.83 **CAS Registry No.** 6108-10-7

Synonyms (1α,2α,3α,4β,5β,6β)-1,2,3,4,5,6-hexachlorocyclohexane; ε-benzene hexachloride; ε-BHC; ε-HCH; ε-hexachlorocyclohexane; ε-1,2,3,4,5,6-hexachlorocyclohexane

EINECS No. 228-068-9

Uses Pesticide.

Physical properties

M. Pt. 219.3°C **Partition coefficient** log P_{ow} 3.76
Solubility Water: 7 mg l^{-1}

Occupational exposure

Supply classification toxic
Supply classification dangerous for the environment
Risk phrases Harmful in contact with skin – Toxic if swallowed – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21, R25, 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) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S22, S36/37, S45, S60, S61)

Ecotoxicity

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* 522 μg l^{-1} (1).
EC_{50} (48 hr) *Daphnia* 107 μg l^{-1} (adsorbed to algae) (1).
EC_{50} (72 hr) *Tubifex tubifex* for autotomy 172 mg kg^{-1} dry wt. sediment, and for sediment avoidance 217 mg kg^{-1}. LC_{50} >1000 mg kg^{-1}. No-observed-effect concentration for reworking activity 8 mg kg^{-1} (2).

Bioaccumulation
The bioaccumulation factor for tubificid sludgeworms *Tubifex tubifex* and *Limnodrilus hoffmeisteri* from sediment is 4 (3).

Environmental fate

Degradation studies
Lindane is degraded by the white rot fungus *Pleurotus sajor-caju* (4).

Abiotic removal
40-80% removal from contaminated groundwater by biological trickling filter and rotating biocontactor (5).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Oral rats (90 days) 2, 3 or 5 mg kg^{-1} daily exhibited increased geotaxis and decreased spontaneous drug-induced locomotor activity. High voltage slow-wave EEG activity patterns with occasional spindles were seen. A significant increase in the cerebellum GABA levels and a significant increase in cerebellar membrane benzodiazepine receptors occurred in the 3 and 5 mg dosed rats (6).

Teratogenicity and reproductive effects

The effect on the sexual behaviour of ♂ rats following prenatal exposure was studied. ♀ rats were given a single dose (30 mg kg^{-1} body weight) on day-15 of gestation. The ♂ offspring demonstrated a changed libido and reduced testosterone levels without a reduction in fertility (7).

♀ Mink were fed 1 mg kg^{-1} day^{-1} in diet from before mating until weaning. Minks were mated twice at 7-8 day intervals. No effect on the numbers of mink accepting the first mating but reduced percentage accepting the second. Whelping rate but not implantation rate was decreased (8).

Other effects

Any other adverse effects

Rats administered high doses in chronic exposures suffer hyperexcitability and convulsions and impaired motor activity involving GABA-ergic mechanisms (6).

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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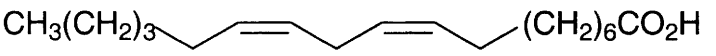
L49 linoleic acid



$C_{18}H_{32}O_2$ **Mol. Wt.** 280.45 **CAS Registry No.** 60-33-3

Synonyms 9,12-octadecadienoic acid, (Z,Z)-; linolic acid; Polylin 515; Telfairic acid; Uifac 6550; Crossential L99; Pamolyn

EINECS No. 200-470-9 **RTECS No.** RF 9990000

Uses Manufacture of paints, coatings, emulsifiers, vitamins. Aluminium salt used to manufacture lacquers. Nutrient.

Occurrence Major constituent of many vegetable oils (1).

Physical properties

M. Pt. –12°C **B. Pt.** 230°C at 16 mmHg **Flash point** > 110°C (closed cup) **Specific gravity** 0.9038 at 18°C with respect to water at 4°C **Partition coefficient** log P_{ow} 7.05 (2)

Solubility Organic solvents: diethyl ether, ethanol, light petroleum; miscible with dimethylformamide

Ecotoxicity

Invertebrate toxicity

EC_{50} (duration unspecified) purple sea urchin 0.28-1.07 mg kg^{-1} inhibited fertilisation (3).

Environmental fate

Degradation studies

Readily biodegradable in batch bioassay innoculated with anaerobic granular sludge at 30°C and 35-200 mg l^{-1} linoleic acid (4).

The correlation between BOD and COD for fatty acids was studied. COD values were 1.2-29.6% ThOD averaging 8.38%. BOD values were 12.7-98.8% of ThOD averaging 71% BOD/COD ratio 2.76-52.9% (5).

Mammalian & avian toxicity

Metabolism and toxicokinetics

Oral rat (unspecified concentration) as cream accumulates in triacylglycerols of the small intestine and plasma (6).

Intraduodenal infusion rats radiolabelled linoleic acid, after 1 hr 64% of radiolabel disappearing from mucosa was recovered in blood (7).

Oral hamster, mouse, rat, rabbit, dog studied for 3 months after lactation, accumulates in adipose tissue (8).

Irritancy

Dermal human (3 day) 75 mg caused moderate irritation (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (10).

Other effects

Any other adverse effects

Administration to dogs of 10 mg kg^{-1} (route unspecified) causes no haemodynamic changes, while 50 mg kg^{-1} caused cardiotoxic effects (11).

The log P_{ow} exceeds the European Community recommended level 3.0 (6th and 7th amendments) (12).

Other comments

The role of fatty acids in the development of cancers discussed (13).
Hazards, metabolism reviewed (14-16).

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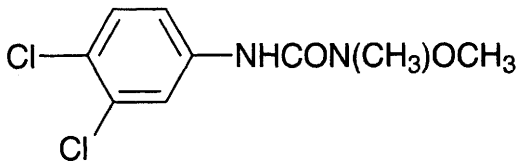
L50 linuron



$C_9H_{10}Cl_2N_2O_2$ **Mol. Wt.** 249.10 **CAS Registry No.** 330-55-2

Synonyms 3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea; *N'*-(3,4-dichlorophenyl)-*N*-methoxy-*N*-methylurea; methoxydiuron; Linex 4L; Afalon; Algrol; Arbax; Boliron; Calin; Herlin

EINECS No. 206-356-5 **RTECS No.** YS 9100000

Uses Herbicide.

Physical properties

M. Pt. 93-95°C **Specific gravity** 1.49 at 20°C **Partition coefficient** log P_{ow} 3.18 (1) **Volatility** v.p. 1.5×10^{-5} mmHg at 24°C

Solubility Water: 81 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, toluene, xylene

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

LD_{50} (96 hr) rainbow trout, bluegill sunfish and channel catfish 3-16 mg l^{-1} (1,2).

Invertebrate toxicity

EC_{50} (24 hr) *Daphnia magna* 310 μg l^{-1} (3).

Environmental fate

Nitrification inhibition

Application rates of 2.5-5.0 μg g^{-1} soil had no measurable effect on nitrification. 100 μg g^{-1} soil resulted in a lag of ~3 days in nitrate formation (4).

Degradation studies

$t_{1/2}$ for microbial degradation in soil 2-5 months (5).

Degraded anaerobically in pond sediment in 74 days. Metabolites included 3-chlorophenyl-1-methoxyl-methylurea and 3,4-dichlorophenyl-1-methylurea (6).

Abiotic removal

Complete photolysis was reported in water at 75 mg l^{-1} by UV light and natural sunlight (7).

Jar tests using 30 mg l^{-1} alum at pH 6 showed that coagulation was ineffective in removing 52 μg l^{-1} linuron in water.

Full scale plant data also showed that coagulation was ineffective at 0.57 μg l^{-1} (8).

Coagulation with 200 mg l^{-1} ferric sulfate at pH 7.4-7.8 reduced concentrations of ~ 10 mg l^{-1} by 30% (9).

Adsorption by powdered activated carbon: 55.3 mg g^{-1} carbon at a concentration of 100 μg l^{-1} (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit 1500, 4000 mg kg^{-1}, respectively (2,11,12).

LC_{50} (4 hr) inhalation rat 48 mg m^{-3} (12).

LD_{50} dermal rabbit >5000 mg kg^{-1} (2).

Sub-acute and sub-chronic data

LD_{50} (8 day) oral ring-necked pheasant, mallard duck, chicken 3080-3440 mg kg^{-1} (13,14).

LD_{50} (8 day) oral Japanese quail >5,000 mg kg^{-1} (13).

Rats were dosed daily with 0, 10, 20 or 40 mg kg^{-1} day^{-1} for 10 wk (route unspecified). Effects on bone morphometry included a significant reduction in medullary cross-sectional area at the two high doses and decreased total femur cross-sectional area at the high-dose level in the absence of effects on calcium excretion. Femur diameter and strength were also significantly reduced at the highest dose level. Serum concentrations of parathyroid hormone or 1,25-dihydroxyvitamin D-3 were not affected. Serum cholesterol was increased and serum triglyceride concentrations decreased (15).

Rats were administered 0.5-5.0 mg kg^{-1} day^{-1} for 7 months (route unspecified).

It was reported that 4 mg kg^{-1} caused decreased weight gain, hypochromic anaemia, decreased the activities of cholinesterase and peroxidase in the blood and caused ultrastructural changes in the liver (16).

Carcinogenicity and chronic effects

Oral rat and dog (2 yr) no-adverse-effect level for dogs was 125 mg kg^{-1} diet, but rats receiving 125 mg kg^{-1} diet showed significant increases in testicular tumours (2).

Teratogenicity and reproductive effects

Oral rat, 100 or 200 mg on days 6-15 of gestation, the high dose was reported to be teratogenic (17).

Genotoxicity

Escherichia coli SOS chromotest positive (18).
Rats were administered 150, 300, or 450 mg kg^{-1} linuron by gavage. No increase in the frequency of micronucleated polychromatic erythrocytes was observed in bone marrow. The viability of hepatocytes isolated from animals treated with the higher doses was decreased and this was accompanied by the induction of DNA single-strand breaks in the liver cells (as determined by the alkaline elution assay). The ability of linuron to cause DNA damage *in vivo* was confirmed with the "comet assay". Cytotoxicity was seen in rat testes cells but no indication of DNA damage was visible (19).

Other effects

Any other adverse effects
In vitro mouse inhibition of testicular DNA synthesis positive (20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (21).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (22).
WHO Toxicity Class Table 5 (23).
EPA Toxicity Class III (formulation) (2).
ADI 0.008 mg kg^{-1} body weight (24).
Advisory value for drinking water in UK 10 μg l^{-1} (25).

Other comments

In plants, metabolism involves demethylation and demethoxylation (2).
Odour threshold 3.3 mg l^{-1}, taste threshold 4.3 mg l^{-1} (16).
Metabolic pathways reviewed (26).

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L51 lipase

CAS Registry No. 9001-62-1

Synonyms glycerol ester hydrolase; butyrinase; triacylglycerol hydrolase; triglyceridase; triolein hydrolase; tweenase; Lipozyme; Palatase; Resinase

EINECS No. 232-619-9 **RTECS No.** TO 9776500

Uses In detergent formulations.

Occurrence Digestive enzyme, widely distributed in plants, moulds, bacteria and mammalian tissues.

Mammalian & avian toxicity

Metabolism and toxicokinetics

Undergoes renal filtration and reabsorption followed by intrarenal degradation to amino acids. Rats were injected intravenously with a single dose of ^{125}I-labelled homologous lipase. <1% of the lipase activity and >10% of the radioactivity was found in the urine after 120 min (1).

Other effects

Any other adverse effects

Elevated serum lipase levels in an acute pancreatitis episode may potentiate the autodigestion of the pancreas (2).

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L52 lithium

Li

Li **Mol. Wt.** 6.94 **CAS Registry No.** 7439-93-2

EINECS No. 231-102-5 **RTECS No.** OJ 5540000

Uses Used in alloys, catalysts, aircraft fuels.

Occurrence

Occurs in minerals spodumene, lepidolite, petalite, amblyganite and triphylite. Found naturally in food, air and drinking water. Occurrence in Earth's crust: 0.005% by wt.

Physical properties

M. Pt. 180.54°C **B. Pt.** 1336±5°C **Specific gravity** 0.584 **Volatility** v.p. 1 mmHg at 723°C
Solubility Water: reacts with water forming hydroxide and releasing hydrogen

Occupational exposure

UN No. 1415 **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 container dry – In case of fire, use dry powder or sand never use water – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S8, S43, S45)

Ecotoxicity

Fish toxicity
LC_{50} (28, 35 day) rainbow trout 9.28, 1.4 mg l^{-1} (salt), respectively (1,2).
LC_{50} (96 hr) fathead minnows 42 mg l^{-1}, NOEC 13 mg l^{-1} (3).

Invertebrate toxicity
Microinjection of lithium chloride into prospective ventral blastomeres of the 32-cell *Xenopus laevis* embryo gives rise to duplication of dorsanterior structures such as the notochord, neural tube and eyes (4).
EC_{50} (48 hr) for immobility of *Daphnia magna* 24 mg l^{-1}, NOEC 11 mg l^{-1} (5).
Lithium chloride flow-through embryo-larval toxicity test (26 day) with fathead minnow. LC_{50} 8.7 mg l^{-1} (1.4 mg l^{-1} Li), EC_{50} 6.4 mg l^{-1} (1.0 mg l^{-1} Li), NOEC 1.2 mg l^{-1} (0.20 mg l^{-1} Li), LOEC 1.9 mg l^{-1} (0.31 mg l^{-1} Li) (6).

Bioaccumulation
Accumulates in several species of fish, molluscs and crustaceans. Stored in the digestive tract and exoskeleton (7).

Environmental fate

Anaerobic effects
Methanogenesis of granular anaerobic sludge at 35°C with initial COD of 5750 mg l^{-1} O_2 at pH 7.2 was stimulated at lithium ion concentration 10-20 mg l^{-1}, slightly inhibited at lithium ion concentration 350 mg l^{-1} and seriously inhibited at lithium ion concentration ≥500 mg l^{-1} (8).

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Adult ♂ rat, 2.4 mg lithium chloride 100 g^{-1} day^{-1} for 21 days reduced red blood cell count, haemoglobin concentration, haematocrit and mean corpuscular Hb on the 22nd day. Chronic Li^+ treatment can cause anaemia (9).
Newborn rats administered with lithium salts orally for 8-16 wk had chronic renal failure (10).
Lungs of rabbits exposed to 0.6 and 1.9 mg m^{-3} lithium chloride for 4-8 wk, 5 day wk^{-1}, 6 hr day^{-1} showed no significant effects (11).
2 mg m^{-3} combustion products of metallic lithium via inhalation in rats caused damage of nervous and cardiovascular systems, liver and kidney (12).

Teratogenicity and reproductive effects
♀ F_1 rats were treated with elemental lithium for 3 wk before mating and throughout pregnancy. Treatment-related effects were detected in the endocrine system of ♀ and their pups. Reproductive parameters of the ♀ offspring were not greatly affected (13).
Inhibits human sperm motility *in vitro* at concentrations comparable with those found in semen after oral administration of the compound (14).

≥100 μM administered to rats had no adverse effect on cell viability or hormone induced steroidogenesis in adrenal and Leydig cells of the testis (15).
Reduced litter weights, increased numbers of resorption, wavy ribs, short or deformed limb bones or increased incidence of incomplete ossification of sternebrae and wide bone separation in the skull observed in ♀ pregnant Wistar rats administered orally with 100 mg kg^{-1} lithium carbonate (16).

Metabolism and toxicokinetics

Lithium is absorbed rapidly from the gastro-intestinal tract and excreted unchanged, primarily by the kidneys (17).
30-67% of a single oral dose is excreted within 6-8 hr (18).
Rat plasma clearance of Li^+ was 169 ml hr kg^{-1} with a terminal $t_{1/2}$ 5.0 hr (19).
Lithium absorption from guinea pig jejunum is unaffected by metabolic inhibition and appears to be a passive process occurring primarily through the paracellular pathway (20).
The distribution of lithium in the embryo of pregnant mice subjected to chronic or acute lithium treatment was investigated by neutron capture radiography. The lithium image in the various organs of the embryo decreased in intensity between days 10-19 of pregnancy, with a minimum close to day-16, and then increased. The time course of lithium accumulation in the embryo paralleled the lithium concentration in the mother's blood. The lithium image was intense in the bones, heart, eyes, hypophysis and thyroid. Tissues of endodermal origin such as the liver, stomach and lungs were less strongly labelled. The distribution of lithium in the nervous tissues of the embryos was almost homogeneous whereas in the adult brain it is regionalised (21).

Genotoxicity

Trilithium citrate was the only compound tested in the following study. *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (22).
Escherichia coli K12/343/113 with and without metabolic activation negative (22).
Drosophila melanogaster sex linked recessives negative (22).
In vivo intraperitoneal mice, two injections of 27 mg kg^{-1} did not induce micronuclei (22).

Other effects

Other adverse effects (human)

Compared with an age-matched control group the conduction velocity of the sural nerve was reduced in patients receiving long-term lithium therapy (60.8 and 57.8 m sec^{-1}, respectively) (23).
20-30% of patients receiving lithium therapy experienced gastro-intestinal symptoms including anorexia, nausea, vomiting, diarrhoea and abdominal pain (24).
Absorption of lithium from workplace exposure is usually insufficient to alter lithium body burden or cause systemic toxicity although some upper respiratory symptoms are associated with high levels of dusts containing lithium carbonate and hydride. The 8-hour time-weighted average workplace exposure limit of 0.025 mg m^{-3} for lithium hydride is based on nasal irritation (25).
A retrospective study of patients treated for 1 month-15 yr with lithium chromate ($LiCrO_3$) indicated no correlation between lithium treatment and chronic nephrotoxicity (26).

Legislation

Included in Schedules 4 and 6 (Release into Air and Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (27).

Other comments

Reproductive effects reviewed (28).
Reviews on human health effects, experimental toxicity, environmental effects and physico-chemical properties listed (29).

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L53 lithium aluminium hydride

AlH_4Li

AlH_4Li **Mol. Wt.** 37.95 **CAS Registry No.** 16853-85-3

Synonyms lithium alanate; lithium aluminohydride; aluminium lithium hydride

EINECS No. 240-877-9 **RTECS No.** BD 0100000

Uses Reducing agent in preparation of ether hydrides. Used to identify structure of drugs.

Physical properties

M. Pt. 125°C (decomp.) **Specific gravity** 0.92 at 25°C (1)

Solubility Organic solvents: dibutyl ether, 1,4-dioxane, diethyl ether, tetrahydrofuran

Occupational exposure

UN No. 1410 **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 specially manufactured dry powder extinguishers (S2, S7/8, S24/25, S43)

Ecotoxicity

Fish toxicity

Aluminium lithium hydride would release ionic lithium on contact with water. Lithium is lethal to rainbow trout in 35 days at a concentration of 1.4 mg l^{-1} (2).

Other effects

Any other adverse effects

Inhibits adenylate cyclase activity and therefore hormone function in human cells (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Aluminium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.2 mg l^{-1} (4).

Other comments

The main hazards associated with lithium aluminium hydride relate to its highly caustic reaction on inhalation, injection or contact with skin, and the formation of lithium hydroxide on contact with moisture (5).
Aluminium and its compounds have been implicated in Alzheimer's disease (6-9).
Reviews on human health effects, experimental toxicology, ecotoxicology, physico-chemical properties and environmental effects listed (10).

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L54 lithium hydride

LiH

LiH **Mol. Wt.** 7.95 **CAS Registry No.** 7580-67-8

Synonyms lithium monohydride

EINECS No. 231-484-3 **RTECS No.** OJ 6300000

Uses Reducing agent. Desiccant. Hydrogen generator. Condensing agent with ketones and acid esters.

Physical properties

M. Pt. 680°C **Specific gravity** 0.76-0.77

Occupational exposure

FR-VME 0.025 mg m^{-3}
UK-LTEL 0.025 mg m^{-3}
US-TWA 0.025 mg m^{-3}

UN No. 1414

UN No. 2805 (fused solid) **HAZCHEM Code** 4W (fused solid) **Conveyance classification** substance which in contact with water emits flammable gas

Mammalian & avian toxicity

Acute data
LC_{Lo} (4 hr) inhalation rat 10 mg m^{-3} (1).

Irritancy
Rabbit eye exposed to 5 mg m^{-3} (72 hr) caused irritation (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 toxicity, workplace experience, environmental effects and epidemiology listed (3).

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L55 lithium hypochlorite

LiOCl

ClLiO **Mol. Wt.** 58.39 **CAS Registry No.** 13840-33-0

Synonyms hypochlorous acid, lithium salt; lithium chloride oxide; lithium oxychloride; HyPure L

EINECS No. 237-558-1 **RTECS No.** NH 3486000

Uses Swimming pool sanitiser.

Occupational exposure

UN No. 1471 **HAZCHEM Code** 2WE **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Maternal and developmental no-observable-adverse-effect level for lithium hypochlorite in rats 100 mg kg^{-1}. Effects are consistent with chlorine toxicity (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (2).
In vitro Chinese hamster ovary cells chromosomal aberrations positive at 12 and 18 hr without metabolic activation, at 22 hr with metabolic activation (2).
In vivo rat bone marrow cells showed no increased incidence in chromosomal aberrations 6, 24, 48 hr after a single oral dose of 100, 500, 1000 mg kg^{-1} to ♂ and 50, 250, 500 mg kg^{-1} to ♀ (2).

Other effects

Other adverse effects (human)

Ionic lithium (up to 40 mg Li l^{-1}) did not affect serum levels of bathers in hot spas (101°F) under repetitive exposure, 20 min day^{-1}, 4 days wk^{-1} for 2 wk (3).

Legislation

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

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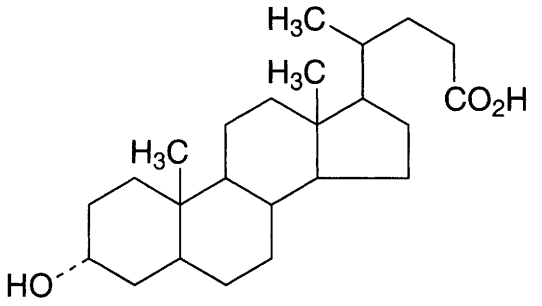
L56 lithocholic acid



$C_{24}H_{40}O_3$ **Mol. Wt.** 376.58 **CAS Registry No.** 434-13-9

Synonyms 3-hydroxy-cholan-24-oic acid, (3α,5β)-; 3α-hydroxycholanic acid; 3α-hydroxy-5β-cholan-24-oic acid

EINECS No. 207-099-1 **RTECS No.** FZ 2275000

Occurrence In ox, rabbit and human bile and in ox and pig gallstones.

Physical properties

M. Pt. 184-186°C
Solubility Organic solvents: benzene, diethyl ether, ethanol, glacial acetic acid

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 3900 mg kg^{-1} (1).

Carcinogenicity and chronic effects
National Toxicology Program tested mice and rats via gavage. No evidence of carcinogenicity in ♂ or ♀ rats or mice (2).

Teratogenicity and reproductive effects
Addition of 36 mg l^{-1} lithocholic acid to *in vitro* 10.5-day-old rat embryos resulted in 9% growth-retarded and 12% malformed embryos. Abnormalities in the development of the neural tube and exencephaly were the most common malformations (3).

Metabolism and toxicokinetics
Four hydroxylation reactions of lithocholic acid occur in rat liver microsomes resulting in 5 major metabolites: 3α,6β-dihydroxy-5β-cholanic acid (80%); 3α,6α-dihydroxy-5β-cholanic acid; 3α,7α-dihydroxy-5β-cholanic acid; 3α,6β,7β-trihydroxy-5-cholanic acid; and 3α-hydroxy-6(3)-oxo-5β-cholanic acid (4).
Organs of rats sacrificed hrly for 8 hr after intrarectal instillation of 0.5 ml of a peanut oil solution containing 183.7 μg showed ~45% of the instilled acid was absorbed (5).

Genotoxicity

Salmonella typhimurium TA97, TA98 with and without metabolic activation negative (6).
Saccharomyces cerevisiae chromosome loss induced but no mitotic recombination or mutation (7).

Other effects

Any other adverse effects
50% cytotoxic concentration to isolated rat hepatocytes was 18.37 mg l^{-1} (8).

Other comments

The additive effects of lithocholic acid in oxygen radical generation may overcome the antioxidant defense mechanism of the stem cell leading ultimately to semiquinone and hydroxyl radical mediated DNA damage and tumour induction (9).

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L57 locust bean gum

CAS Registry No. 9000-40-2

Synonyms carob gum; algaroba; fructoline; Indalca PR90; lupogum; tragacol; Ceragum; Seagel L

EINECS No. 232-541-5 **RTECS No.** OJ 8690000

Uses Stabiliser and thickener in foods and cosmetics. Sizing and finishing agent in textiles, and bonding agent in paper manufacture.

Occurrence Ground kernal endosperms of tree pods of *Ceratonia siliqua*

Environmental fate

Degradation studies

Degraded to reducing sugars by *Pseudomonas* sp. (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, hamster, rat, mouse 9, 10, 10, 13 g kg^{-1}, respectively (2).

Carcinogenicity and chronic effects

National Toxicology Program investigated locust bean gum carcinogenicity in rat and mouse. Designated non-carcinogen in rat and mouse (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA97/TA1537 with and without metabolic activation negative (4).

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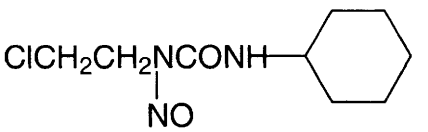
L58 lomustine



$C_9H_{16}ClN_3O_2$ **Mol. Wt.** 233.70 **CAS Registry No.** 13010-47-4

Synonyms chloroethylcyclohexylnitrosourea; *N*-(2-chloroethyl)-*N'*-cyclohexyl-*N*-nitrosourea; 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea; Belustine; CCNU; CeeNu

EINECS No. 235-859-2 **RTECS No.** YS 4900000

Uses Antineoplastic agent. Direct acting bifunctional alkylating agent.

Physical properties

M. Pt. 90°C
Solubility Water: <0.05 mg ml^{-1}. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 70 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 54 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Sufficient evidence of carcinogenicity to humans and animals, IARC classification group 2A (2).
Produces lung tumours in rats after intraperitoneal/intravenous injection, slight increase in incidence of lymphomas in mice by intraperitoneal injection (3,4).
Intravenous rats (life study) 1.5, 4, 8 or 20 mg kg^{-1} every 6 wk; treatment was discontinued when severe lethal toxicity became apparent (7 applications highest dose or 10 applications of other doses). Tumours induced included lung adenomas and papillomas of the forestomach (5).
Intravenous rats exerted a weak tumorigenic response to nervous system, lung and forestomach (6).

Teratogenicity and reproductive effects
Intraperitoneal rats (days 6-9 pregnancy) 2, 4 or 8 mg kg^{-1} day^{-1} caused omphalocell, ectopia cordis and aortic arch anomalies, syndactyly and anophthalmia occurred most frequently (7).
Intravenous/intraperitoneal rabbits (days 6-18 gestation) 1.5 or 3 mg kg^{-1} day^{-1} caused no teratogenic effect, but a high incidence of abortion was observed with the highest dose (8).

Metabolism and toxicokinetics
Decomposition in physiological conditions to yield alkylating species and organic isocyanates is discussed. Its antitumour activity has been attributed to the alkylation of DNA and the carbamoylation of intracellular proteins by isocyanates having pharmacological and toxicological relevance (9).
Undergoes spontaneous decomposition under physiological conditions to release alkylating and carbamoylating entities (10).
Disappears from plasma within 5 min of administration but the antitumour effects of its metabolites may persist for 15 min (11).
Oral mouse (24 hr), 80% excreted in urine (12).
May be converted by microsomal metabolism into six isomeric hydroxylated derivatives (13).
Intraperitoneal ♂ Fischer rats 50 mg kg^{-1} caused a peak plasma concentration of 3 μg ml^{-1}. Lomustine was eliminated with biphasic kinetics with terminal $t_{1/2}$ 47 min (14).
Binds to proteins and nucleic acids in cells (15).
Sensitive to oxidation and hydrolysis; forms alkylating and carbamoylating intermediates, $t_{1/2}$ 117 min 25°C at neutral pH (16).

Genotoxicity

Salmonella typhimurium TA100 (metabolic activation unspecified) positive (17).
Escherichia coli indused *alkA* gene expression (18).
In vitro Chinese hamster lung V79 cells induced DNA single strand breaks (19).
In vitro Chinese hamster cells without metabolic activation, positive sister chromatid exchanges (20).
Neurospora crassa slim mutant *in vitro* DNA synthesis caused increased strand separation. *Neurospora crassa* had excessive and unscheduled replication, indicating a destabilised nature of its DNA (21).
Human peripheral lymphocytes induced dose-dependent increases in sister chromatid exchanges through DNA interstrand cross-links (22).
Rat liver microsomes catalysed biotransformation to alkylating metabolites that bound covalently to microsomal protein and to DNA (23).
In vivo rats with metabolic activation induced dominant lethal mutations and DNA damage (8).

Other effects

Other adverse effects (human)

Human systemic effects by ingestion include anorexia, nausea, vomiting, thrombocytopenia, leucopenia and nephrotoxicity. A characteristic feature of the antitumour nitro- sources is their delayed bone marrow toxicity (24).

Any other adverse effects

In rats caused lesions of cerebral blood vessels with accompanying disfunction to the blood-brain barrier and changes in brain function (25).

Single dose rats 20 or 50 mg kg^{-1} caused irreversible liver lesions which were histologically detectable after 1 month. At the lower dose, they remained stable for 3 months, but at 50 mg kg^{-1} the lesions continued to develop, with progression toward cholangiolitic adenomatous transformation of the parenchyma or binary cirrhosis (26).

Morphological alterations were studied in the common bile duct and interlobular bile duct in rats given a single oral dose of 50 mg kg^{-1}. The results indicate that early injury appears to be localised in the large bile duct and reflects inflammatory oedema, bile stasis and degeneration of epithelial cells (27).

In dog and monkey, a single intravenous infusion caused toxic changes in bone marrow and lymphoid tissue with neutropenia and lymphopenia, also causes cardiopulmonary and gastro-intestinal toxicity in dogs (28).

Other comments

Toxicity and hazards reviewed (29-31).

References

1. *Toxicol. Appl. Pharmacol.*, 1972, **21**, 405.
2. *IARC Monograph* 1987, **Suppl. 7**, 150-152.
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4. Cantor, K. P. et al *Environ. Health Perspect.* 1982, **46**, 187-195.
5. Habs, M. *Experimental Studies on the Carcinogenic Effect of Cytostatic Drugs* 1980, Thesis Medical Faculty, Heidelberg University, Germany.
6. Eisenbrand, G. et al *Dev. Toxicol. Environ. Sci.* 1980, **8**, 273-278.
7. Thompson, D. J. et al *Teratology* 1975, **11**, 36A.
8. Thompson, D. J. et al *Toxicol. Appl. Pharmacol.* 1975, **34**, 456-466.
9. Dive, C. et al *Biochem. Pharmacol.* 1988, **37**(20), 3987-3993.
10. Read, D. J. et al *Life Sci.* 1975, **16**, 1263-1270.
11. Oliverio, V.T. et al *Cancer Treat. Rep.* 1976, **60**, 703-707.
12. Oliverio, V. T. et al *Cancer Res.* 1970, **30**, 1330-1377.
13. Wheeler, G. P. et al *Biochem. Pharmacol.* 1977, **26**, 2331-2336.
14. Wong, K. H. et al *Int. J. Radiat. Oncol., Biol., Phys.* 1990, **18**(5) 1043-1050.
15. Connors, T. A. *Br. J. Cancer* 1974, **30**, 477-480.
16. Schein, P. S. et al *Fundam. Cancer Chemother. Antibiot. Chemother.* 1978, **23**, 64-75.
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21. Beljanski, H. et al *Oncology* 1987, **44**(5), 327-330.
22. Best, R. G. et al *Teratog., Carcinog., Mutagen.* 1988, **8**(6), 339-346.
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24. Young, R. C. et al *New Engl. J. Med.* 1971, **285**, 475-479.
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26. Viotte, G. et al *Pathol. Biol.* 1987, **35**(2), 139-144 (*Chem. Abstr.* **106**, 2073380).
27. Kretschmer, N. W. et al *Cancer Chemother. Pharmacol.* 1987, **19**(2), 109-117.
28. Oliverio, V. T. et al *Cancer Chemother.* 1973, **4**(3), 13-20.
29. *IARC Monograph* 1981, **26**, 79-95, 137-149.
30. Katz, M. E. et al *Cancer Clin. Treat.* 1979, **2**, 297-316.
31. *Dangerous Prop. Ind. Mater. Rep.* 1993, **13**(1), 63-66

L59 LPG

CAS Registry No. 68476-85-7

Synonyms petroleum gases, liquefied; liquefied petroleum gas; Burstane; Pyrofax

EINECS No. 270-704-2 **RTECS No.** SE 7547000

Occupational exposure

UK-LTEL 1000 ppm (1750 mg m^{-3}) **UK-STEL** 1250 ppm (2180 mg m^{-3})
US-TWA 1000 ppm (1800 mg m^{-3})

UN No. 1075 **Conveyance classification** flammable gas

Other effects

Other adverse effects (human)
LPG containing mixed C_3 and C_4 compounds (TLV 1000 mg m^{-3}) caused necrosis (sites unspecified) (1).

Other comments

Reviews on human health effects, experimental toxicity and workplace experience listed (2).

References

1. Sunshine, I. *Handbook of Analytical Toxicology* 1969, The Chemical Rubber Co., Cleveland, OH, USA.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

L60 lutetium

Lu

Lu **Mol. Wt.** 174.97 **CAS Registry No.** 7439-94-3

Synonyms lutecium

EINECS No. 231-103-0

Occurrence 0.8-1.7 ppm in Earth's crust, occurs in xenotime, gadolinite and other rare earth minerals.

Physical properties

M. Pt. 1652°C **Specific gravity** 9.842

Ecotoxicity

Bioaccumulation
370 ng g^{-1} dry weight found in *Euglena* sp. in tailings drainage at a Canadian mining camp (1).

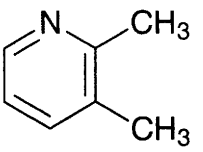
Genotoxicity

Lu^{3+} weakly inhibited the proliferative response of human lymphocytes to various polyclonal mitogens and the purified protein derivative of the tuberculin antigen (2).

References

1. Mann, H. et al *Toxic. Assess.* 1988, **3**(1), 1-16.
2. Yamage, M. et al *Experientia* 1989, **45**(11-12), 1129-1131

L61 2,3-lutidine



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 583-61-9

Synonyms 2,3-dimethylpyridine

EINECS No. 209-514-1

Physical properties

M. Pt. -15°C **B. Pt.** 162-164°C **Flash point** 50°C **Specific gravity** 0.945

Mammalian & avian toxicity

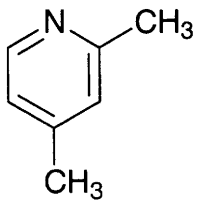
Carcinogenicity and chronic effects

No reports of carcinogenicity; predicted to be non-carcinogenic (1).

References

1. Sakamoto, Y. et al *Bull. Chem. Soc. Jpn.* 1989, **62**, 330-332

L62 2,4-lutidine



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 108-47-4

Synonyms pyridine, 2,4-dimethyl-; α,γ-dimethylpyridine; 2,4-dimethylpyridine

EINECS No. 203-586-8 **RTECS No.** OK 9400000

Physical properties

M. Pt. –60°C **B. Pt.** 159°C **Flash point** 37°C **Specific gravity** 0.9309 at 20°C with respect to water at 4°C
Solubility Organic solvents: acetone, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
Pyridine bases (unspecified) at concentrations of 1000 mg l^{-1} kill fish in 1 hr (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 18.6 ppm Microtox test (2).
Pyridine bases (unspecified) at concentrations of 1000 mg l^{-1} kill *Tubifex tubifex* in 24 hr (1).

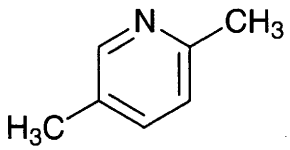
Mammalian & avian toxicity

Carcinogenicity and chronic effects
Predicted non-carcinogenic (3).

References

1. Roubickova, J. *Vodni Hospod.: B* 1986, **36**(10), 271-277 (Czech.) (*Chem. Abstr.* **106**, 55222m)
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Sakamoto, Y. et al *Bull. Chem. Soc. Jpn.* 1989, **62**(1), 330-332.

L63 2,5-lutidine



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 589-93-5
Synonyms 2,5-dimethylpyridine
EINECS No. 209-666-9 **RTECS No.** OK 9625000

Physical properties

M. Pt. –15°C **B. Pt.** 157°C **Flash point** 46°C **Specific gravity** 0.926

Mammalian & avian toxicity

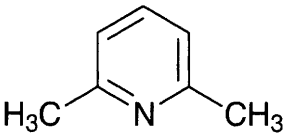
Acute data
LD_{50} oral mouse, rat, guinea pig 670, 800, 827 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects
No studies of carcinogenicity reported; predicted to be non-carcinogenic (2).

References

1. *Hyg. Sanit. (USSR)* 1968, **33**, 341.
2. Sakamato, Y. et al *Bull. Chem. Soc. Jpn.* 1989, **62**, 333-335

L64 2,6-lutidine



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 108-48-5

Synonyms 2,6-dimethylpyridine; α,α'-lutidine; α,α-dimethylpyridine

EINECS No. 203-587-3 **RTECS No.** OK 9700000

Uses Stabiliser for percarboxylic acids. Carbonation catalyst.

Occurrence Isolated from the basic fraction of coal tar. In bone oil.

Physical properties

M. Pt. -5.8°C **B. Pt.** 144°C **Flash point** 38°C **Specific gravity** 0.9252 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 1.68

Solubility Organic solvents: diethyl ether, ethanol; miscible with dimethylformamide and tetrahydrofuran

Ecotoxicity

Invertebrate toxicity

LC_{100} (24 hr) *Tetrahymena pyriformis* 3.50 g l^{-1} (1).

EC_{50} (5-30 min) *Photobacterium phosphoreum* 117 mg l^{-1} Microtox test (2).

Not significantly toxic to *Nitzschia closterium* in oil shale wastewater (3).

Environmental fate

Degradation studies

Wastewater containing 2,6-lutidine was biodegraded by adapted or fresh sludge to an unspecified extent (4).

References

1. Schultz, T. W. et al *Arch. Environ. Contam. Toxicol.* 1978, **7**, 457-463.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Mann, K. et al *Fuel* 1987, **66**(3), 404-407.
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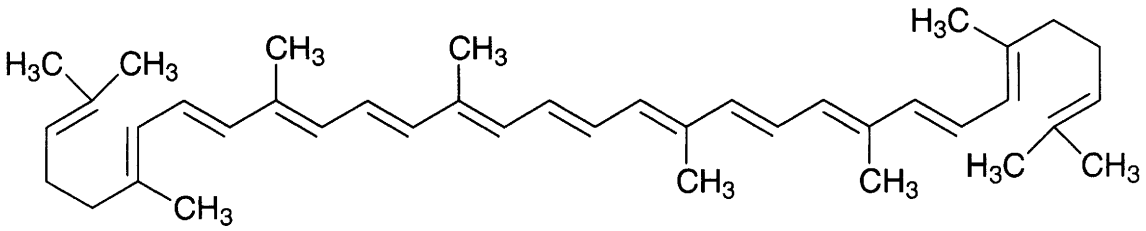
L65 lycopene



$C_{40}H_{56}$ **Mol. Wt.** 536.88 **CAS Registry No.** 502-65-8

Synonyms φ,φ-carotene; lycopene, *all-trans-*; *trans*-lycopene; C.I. 75125; lycopene 7; C.I. Natural Yellow 27

EINECS No. 207-949-1

Occurrence In ripe fruit, especially tomatoes.

Physical properties

M. Pt. 172-173°C

Solubility Organic solvents: benzene, chloroform

Mammalian & avian toxicity

Metabolism and toxicokinetics

Oral administration to rats and rhesus monkeys of [^{14}C]lycopene in olive oil resulted in a peak accumulation of radioactivity in plasma at 4-8 hr in rats and 8-48 hr in monkeys. The liver contained the largest amount of radioactive pigment in rats and monkeys compared with other organs tested (1).

Other comments

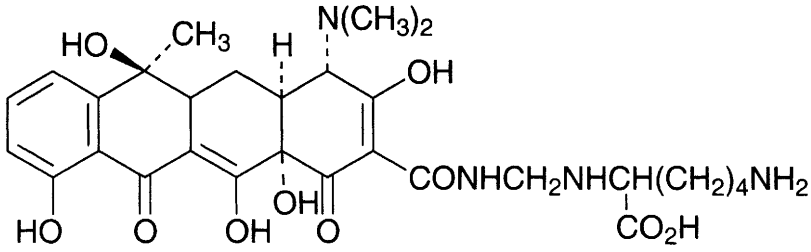
B6C3F1 mice receiving 25 or 50 ppm in drinking water from wk-11 to wk-32 following combined treatment with diethylnitrosamine, *N*-methyl-*N*-nitrosourea and 1,2-dimethylhydrazine exerted a chemopreventive effect on lung carcinogenesis (2).

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

References

1. Mathews-Roth, M. M. et al *J. Nutr.* 1990, **120**(10), 1205-1213.
2. Kim, D. J. et al *Cancer Lett. (Shannon, Irel.)* 1997, **120**(1), 15-22.
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

L66 lymecycline



$C_{29}H_{38}N_4O_{10}$ **Mol. Wt.** 602.64 **CAS Registry No.** 992-21-2

Synonyms L-lysine, N^6-[[[[4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenyl]carbonyl]amino]methyl]-, [4*S*-(4α,4aα,5aα,6β,12aα)]-; Armyl; Ciclisin; cidolysal; tetracycline methylenelysine

EINECS No. 213-592-2 **RTECS No.** OL 5615000

Uses Antibacterial.

Physical properties

Solubility Organic solvents: ethanol

Mammalian & avian toxicity

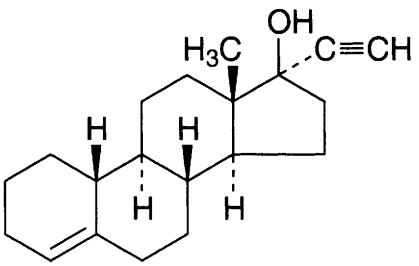
Acute data

LD_{50} intravenous mouse 181 mg kg^{-1} (1).

References

1. *Kalikasan* 1970, **2**, 333

L67 lynestrenol



$C_{20}H_{28}O$ **Mol. Wt.** 284.44 **CAS Registry No.** 52-76-6

Synonyms 19-norpregn-4-en-20-yn-17-ol, (17α)-; 19-nor-17α-pregn-4-en-20-yn-17-ol; 3-deoxynorlutin; ethynylestrenol; exluton; orgametril

EINECS No. 200-151-4 **RTECS No.** RC 8964300

Uses Progestogen. Used in combination with oestrogen as oral contraceptive.

Physical properties

M. Pt. 158-160°C

Solubility Organic solvents: acetone, chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Oral ♂ ♀ rats, mice received 2-5, 50-150 and 200-400 × the human contraceptive dose of lynestrenol or lynestrenol and mestranol (33:1) in diet for 80 wk (dose unspecified). Benign liver tumours occurred in 7% ♂ mice fed lynestrenol only, compared with 2% in controls. Malignant mammary tumours occurred in 4% ♀ mice fed lynestrenol only, 6% fed the combination (0% in controls), and 3% in rats fed lynstrenol alone (0% in controls) (1).

Teratogenicity and reproductive effects

No effects observed on rat embryos on day-7 after subcutaneous injection of 0.1 mg lynestrenol on days 2, 3, 4, 5 gestation. 1 mg dose terminated pregnancy (2).

No effects on fertility, sexual behaviour or fecundity of offspring of next two generations of female golden hamsters receiving 0.6 mg lynestrenol and 18.7 μg mestranol daily for 4.5-8 months (route unspecified) (3).

Metabolism and toxicokinetics

Metabolised in rabbits via ethynodiol to norethisterone (4,5).

Genotoxicity

Dominant lethal mutations observed in ♀ mice dosed 3 days prior to mating with 420 μg lynestrenol and 12 μg kg^{-1} mestranol (6).

Other effects

Other adverse effects (human)

No significant difference in sex ratio or frequency of abnormal karyotypes in 124 abortuses of women who had taken oral contraceptives, including lynestrenol, compared with 122 controls (7).

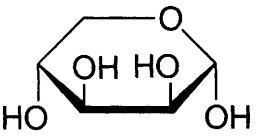
Other comments

Predicted riverine concentration 0.09 μg l^{-1} (8).

References

1. Committee on Safety of Medicines *Carcinogenicity Tests of Oral Contraceptives* 1972, HMSO, London, UK.
2. Castro-Vazquez, A. et al *Fert. Steril.* 1971, **22**, 741-744.
3. Cottinet, D. et al C. *R. Seances Soc. Biol. Ses Fil.* 1974, **168**, 517-520 (Fr.).
4. Okada, H. et al *Nippon Naibunpi Gakkai Zasshi* 1964, **40**, 1095-1098.
5. Mazaheri, A. et al *J. Endocrinol.* 1970, **47**, 251-252.
6. Badr, F. M. et al *Mutat. Res.* 1974, **26**, 529-534.
7. Launtsen, J. A. *Acta Obstet. Gynecol. Scand.* 1975, **54**, 261-264.
8. Richardson, M. L. et al *J. Pharm. Pharmacol.* 1985, **37**, 1-12

L68 D-lyxose



$C_5H_{10}O_5$ **Mol. Wt.** 150.13 **CAS Registry No.** 1114-34-7

Synonyms lyxose, D-; α-D-lyxose

EINECS No. 214-212-8

Physical properties

M. Pt. 106-107°C **Specific gravity** 1.545 at 20°C

Solubility Water: freely soluble. Organic solvents: ethanol

Environmental fate

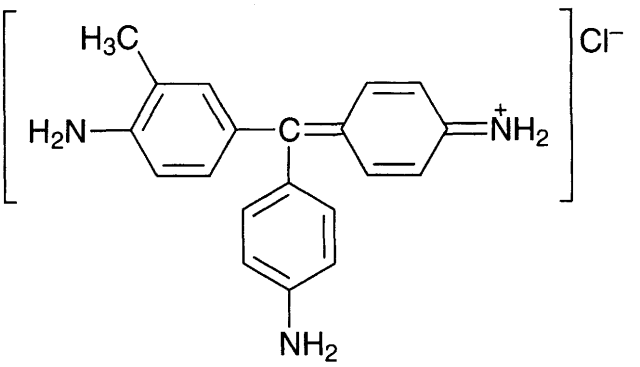
Degradation studies

Degraded by soil microbes more slowly than natural pentoses (1).

References

1. Izumori, K. et al *Kagawa Daigaku Nogakubu Gakujutsu Hokoku* 1987, **39**(1), 83-86 (Japan.) (*Chem. Abstr.* **111**, 170854j)

M1 Magenta I



$C_{20}H_{20}N_3Cl$ **Mol. Wt.** 337.85 **CAS Registry No.** 632-99-5

Synonyms benzenamine, 4-[(4-aminophenyl) (4-imino-2,5-cyclohexadien-1-ylidene)methyl]-2-methyl-, monohydrochloride; C.I. Basic Violet 14 monohydrochloride; Aizen Magenta; Calcozine Fuchsine HO; Fuchsine; Rosaniline; Basic Fuchsin

EINECS No. 211-189-6 **RTECS No.** CX 9850000

Uses Antifungal. Used as a dye or in dye manufacture.

Physical properties

M. Pt. 250°C (decomp.)
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Magenta: No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3. Magenta manufacturing process, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (1).
12 mg wk^{-1} in arachis oil administered orally to mice for 52 wk by gavage caused stained tissues at autopsy. Four lymphomas and one hepatoma were seen in the 21 test mice compared with five lymphomas in controls (2).
10 mg *p*-magenta, a component of commercial magenta, subcutaneously or intramuscularly injected into rats as a 1% aqueous solution 1 × wk^{-1}. One sarcoma appeared after 300 days at a dose of 370 mg. 7 sarcomas were seen in 12 rats surviving after the appearance of the first tumour (3).

Genotoxicity

Salmonella typhimurium TA98, TA1538 with metabolic activation positive (4).

Other effects

Other adverse effects (human)
5/85 men manufacturing magenta but not exposed to 1- or 2-naphthylamine or benzidine had bladder cancer, showing a higher risk than expected. Modern manufacturing replaces aniline with *o*-toluidine and it is possible the *o*-toluidine is implicated in the aetiology of the magenta tumours (5).

Legislation

Listed as a controlled substance in the UK Carcinogenic Substances Regulations 1967 (6).

Other comments

Technical grade magenta consists of a mixture of magenta-I, *p*-magenta and related compounds (1).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 65.
2. Bonser, G. M. et al *Br. J. Cancer* 1956, **10**, 653.
3. Druckrey, H. et al *Naturwissenschaften* 1956, **43**, 543.
4. Bonin, A. M. et al *Mutat. Res.* 1981, **89**, 21-34.
5. Case, R. A. M. et al *Br. J. Ind. Med.* 1954, **11**, 213.
6. *S. I. 1967 No. 879 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1967, HMSO, London, UK

M2 magnesium arsenate

$$Mg_x{\cdot}AsH_3O_4$$

$AsH_3O_4Mg_x$ **CAS Registry No.** 10103-50-1
Synonyms arsenic acid, magnesium salt
EINECS No. 233-285-7 **RTECS No.** CG 1050000

Physical properties

Specific gravity 2.60-2.61

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. 1622 **HAZCHEM Code** 2Z **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

Acute data
LD_{50} oral mouse 315 mg kg^{-1} (1).

References

1. *Int. Arch. Gewerbepathol. Gewerbehyg.* 1963, **20**, 21

M3 magnesium chlorate

$$Mg(ClO_3)_2$$

Cl_2MgO_6 **Mol. Wt.** 191.21 **CAS Registry No.** 10326-21-3
Synonyms chloric acid, magnesium salt; magnesium dichlorate; magron; Defoal
EINECS No. 233-711-1 **RTECS No.** FO 0175000

Physical properties

M. Pt. ~35°C **B. Pt.** 120°C (decomp.) **Specific gravity** 1.80 at 25°C
Solubility Water: soluble in 0.01 parts water. Organic solvents: slightly soluble ethanol

Occupational exposure

UN No. 2723 **HAZCHEM Code** 1YE **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat, rabbit 5.2, 6.3, 8.7 g kg^{-1}, respectively (1,2).
LD_{Lo} intraperitoneal rat 1100 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Oral (156 day) rat 24.7 mg kg^{-1} day^{-1} increased incidence of lung, stomach, skin, liver tumours (3).

Teratogenicity and reproductive effects
Oral administration of 127 mg kg^{-1} day^{-1} to pregnant rats increased preimplantation mortality of embryos, decreased number of progeny dam^{-1}, and decreased body weight of progeny. No teratogenic effects were observed (4).

Genotoxicity

In vivo intraperitoneal mice 1500 mg kg^{-1} caused a fivefold increase in chromosomal aberration frequency (5).

Other effects

Any other adverse effects

Increased levels of methaemoglobin and sulfhaemoglobin reported in rats following oral administration of up to 10 mg kg^{-1} (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Magnesium: guide level and maximum admissible concentration 50 mg l^{-1}, chloride guide level 25 mg l^{-1} (7).

Other comments

Health hazards evaluated (8).

References

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M4 magnesium fluorosilicate

$$MgSiF_6$$

F_6MgSi **Mol. Wt.** 166.38 **CAS Registry No.** 16949-65-8

Synonyms hexafluorosilicate(2–) magnesium(1:1); magnesium hexafluorosilicate; magnesium silicofluoride; silicon fluoride magnesium salt

EINECS No. 241-022-2 **RTECS No.** VV 8470000

Uses Mothproofing of textiles.

Physical properties

Specific gravity 1.788 (hexahydrate)

Solubility Water: 650 g l^{-1}

Occupational exposure

SE-LEVL 2 mg m^{-3} (as F)

UN No. 2853 **HAZCHEM Code** 1Z **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig 200 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Magnesium: guide level and maximum admissible concentration 50 mg l^{-1} (2).

References

1. Spector, W. S. (Ed.) *Handbook of Toxicology* 1956, **1**, 180-81, Saunders, Philadelphia, USA.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg

M5 magnesium nitrate

$$Mg(NO_3)_2$$

MgN_2O_6 **Mol. Wt.** 148.31 **CAS Registry No.** 10377-60-3

Synonyms nitric acid, magnesium salt; magnesium dinitrate; magniosan

EINECS No. 233-826-7 **RTECS No.** OM 3750000

Uses In pyrotechnics. In the concentration of nitric acid.

Occurrence Hydrated form occurs in the mineral nitromagnesite.

Physical properties

M. Pt. 89°C (hexahydrate) **Specific gravity** 1.636

Solubility Water: 1 in 0.8 parts water. Organic solvents: ethanol

Occupational exposure

UN No. 1474 **HAZCHEM Code** 1Z **Conveyance classification** oxidising substance

Other effects

Other adverse effects (human)

Increases human amniotic membrane stability on maternal side but decreases it on foetal side (1).

References

1. Bara, U. et al *Magnesium Res.* 1988, **1**(2), 23-27

M6 magnesium oxide

MgO

MgO **Mol. Wt.** 40.30 **CAS Registry No.** 1309-48-4

Synonyms magnesa preprata; magnesium monoxide; Animag; Maglite; Magox; Rhenomag; Luvomag; Dynamag

EINECS No. 215-171-9 **RTECS No.** OM 3850000

Uses Manufacture of fire bricks, magnesia cements. Reflector in optical instruments. Antacid. Food additive. White colour standard.

Occurrence Occurs as the mineral periclase.

Physical properties

M. Pt. 2500-2800°C **B. Pt.** 3600°C **Specific gravity** 3.65-3.75

Solubility Water: slightly soluble in pure water, solubility increased by carbon dioxide

Occupational exposure

DE-MAK 1.5 mg m^{-3} (respirable fraction or aerosol)

FR-VME 10 mg m^{-3}(fume)

UK-LTEL 10 mg m^{-3} (as Mg) (total inhalable dust); 4 mg m^{-3} (as Mg) (fume and respirable dust)

UK-STEL 10 mg m^{-3} (as Mg) (fume and respirable dust)

US-TWA 10 mg m^{-3} (fume)

Mammalian & avian toxicity

Acute data

TC_{Lo} (duration unspecified) inhalation human 400 mg m^{-3} (1).

Inhalation human (5-9 min) 15-29 mg of freshly generated magnesium oxide. 2/4 experienced mild body temperature rise followed by fever and a rise in white blood cell count from 7000 to 15500 after 6 hr. Recovery was complete by the next day (2).

Carcinogenicity and chronic effects

In a cohort study of 2391 ♂ workers producing magnesium metal (work experience >1 yr) 152 cases of cancer were recorded (20 more than expected); cancers included cancer of lip, stomach and lung (3).

Other effects

Other adverse effects (human)

95 men exposed to magnesium oxide dust had slight irritation of eyes and nose. The magnesium level in the serum was above the normal level of 3.5 mg percent (4).

Can cause diarrhoea (5).

Occupational exposure causes higher than normal incidence of digestive disorders and gastric or duodenal ulcers (6).

References

1. *Documentation of Threshold Limit Values for Substances in Workroom Air* 1971, **3**, 147.
2. Drinker, D. et al *J. Ind. Hyg.* 1927, **9**, 187.
3. Heldaas, S. S. et al *Br. J. Ind. Med.* 1989, **46**(9), 617-623.
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5. *Martindale. The Extra Pharmacopoeia* 30th ed., 1993, The Pharmaceutical Press, London, UK.
6. Gwizdelz, E. et al *Arch. Mal. Prof., Med. Trav. Secur. Soc.* 1967, **28**(6), 531-534

M7 magnesium perchlorate

$$Mg(ClO_4)_2$$

Cl_2MgO_8 **Mol. Wt.** 223.21 **CAS Registry No.** 10034-81-8

Synonyms perchloric acid, magnesium salt; anhydrous magnesium perchlorate; anhydrone; dehydrite; magnesium diperchlorate

EINECS No. 233-108-3 **RTECS No.** SC 8925000

Uses Drying agent for gases. Growth stimulant in animal feed.

Physical properties

B. Pt. >250°C (decomp.) **Specific gravity** 2.6 at 25°C
Solubility Water: 993 g l^{-1} at 25°C. Organic solvents: ethanol

Occupational exposure

UN No. 1475 **HAZCHEM Code** 1Y **Conveyance classification** oxidising substance

Mammalian & avian toxicity

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Magnesium: guide level 50 mg l^{-1}; maximum admissible concentration 50 mg l^{-1}; chloride: guide level 25 mg l^{-1} (2).

References

1. *J. Agric. Food. Chem.* 1966, **14**, 512.
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

M8 magnesium phosphide

Mg_3P_2

Mg_3P_2 **Mol. Wt.** 134.86 **CAS Registry No.** 12057-74-8

EINECS No. 235-023-7 **RTECS No.** OM 4200000

Uses Fumigant. Insecticide.

Physical properties

Specific gravity 2.055
Solubility Water: decomposes

Occupational exposure

UN No. 2011 **Conveyance classification** substance which in contact with water emits flammable gas, toxic
Supply classification highly flammable, very toxic
Risk phrases Contact with water liberates toxic, extremely flammable gas – Very toxic if swallowed (R15/29, R28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – In case of fire, use dry powder extinguisher – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S43, S45)

Mammalian & avian toxicity

Acute data
LC_{Lo} inhalation rat (1 hr) 580 ppm; cat, guinea pig (2 hr) 173, 288 ppm, respectively (1).
LC_{50} inhalation (1 hr) rat 580 ppm (2).

Other effects

Any other adverse effects
A potent acute mammalian poison, but feeding trials with fumigated feedstuffs have shown no chronic effects in rats (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (4).

Other comments

Stable when dry. Reacts with atmosphere moisture, and reacts violently with acids producing phosphine.

References

1. *Z. Gesundheitstech. Staedtehyg.* 1933, **25**, 279.
2. *Chemical Safety Data Sheets* 1991, The Royal Society of Chemistry, London, UK.
3. Hackenberg, U. *Appl. Pharmacol.* 1972, **23**, 147.
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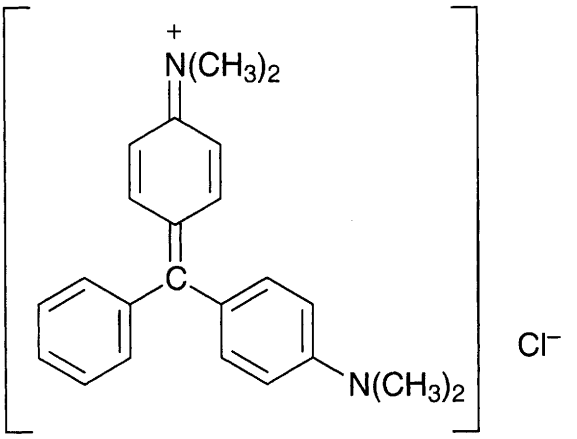
M9 Malachite Green



$C_{23}H_{25}ClN_2$ **Mol. Wt.** 364.92 **CAS Registry No.** 569-64-2

Synonyms bis[*p*-(dimethylamino)-phenyl]phenylmethylium chloride; [[4-(*p*-(dimethylamino)-α-phenylbenzylidene]-2,5-cyclohexadien-1-ylidene]dimethylammonium chloride; Acryl Brilliant Green B; Malachite Green chloride; Light Green N; C.I. Basic Green 4; C.I. 42000

EINECS No. 209-322-8

Uses Biological stain. Indicator. Disinfectant. Fungicide/algicide in fish farming. For directly dyeing silk, wool, jute and leather. Dyeing cotton after mordanting.

Physical properties

Solubility Water: very soluble in water. Organic solvents: amyl alcohol, ethanol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) Gunther's walking catfish (*Claris macrocephalus*), Nile tilapia (*Tilapia nilotica*) 0.066 – 0.425 mg l^{-1} (1).
LC_{50} (24, 48, 96 hr) rainbow trout 1.05, 0.6 and 0.49 ppm, respectively (2).
Juvenile rainbow trout can be bathed in 1.25×10^{-4} g l^{-1} Malachite Green for up to 24 hr without mortalities (3).
Rainbow trout were exposed to 1.6 ppm Malachite Green for 40 min at wkly intervals. After three exposures sinusoidal congestion and focal necrosis were evident in the livers. Mitochondrial damage with swelling and disruption of the cristae, together with dilation of the rough endoplasmic reticulum occurred. Nuclear alterations increased in severity with increasing exposure. The hepatic changes were not severe enough to be reflected in serum protein changes. Separation of the epithelial lining from both lamellar and interlamellar regions of the gills occurred and lamellar cell necrosis and leukocyte infiltration became more frequent with increased exposure (4).

Invertebrate toxicity

Selenastrum capricornutum (7, 14 day) incubated at 24°C, dyes tested at 1 mg l^{-1} and 10 mg l^{-1}. Concentrations of 1 mg l^{-1} inhibited algal growth by >80% after 7 days of incubation (5).
Penaeus stylirostris nauplii 12 and 24 hr static bioassay. Metamorphosis inhibited at 80 μg l^{-1}; no observed toxic effects at 16 μg l^{-1} (6).
Alexandrium minutum, a toxic dinoflagellate that causes paralytic shellfish poisoning, is destroyed by 0.2 ppm Malachite Green (7).

Bioaccumulation

Rainbow trout eggs were exposed to Malachite Green chloride on day-0 and on every third day thereafter to day-24, with a final treatment given to fry on day-31. Total Malachite Green residues increased throughout the

exposure period to 0.271 μg g^{-1} on day-31. Residues declined to 0.055 μg g^{-1} on day-59. The depuration phase declined monoexponentially with $t_{1/2}$ 9.7 days for the concentration of Malachite Green residues (8).

Environmental fate

Anaerobic effects

Gradual feeding of Malachite Green to an active sludge digester, resulting in a final concentration of 140 mg dye l^{-1} in the digester after 45 days, had no significant effect upon the anaerobic digestion of added sludge over this period. During the course of the experiment some decolorisation was observed. It is suggested that some physical adsorption accompanied by biodegradation and chemical reduction could account for this (5).

Degradation studies

Degraded by the lignin-degrading system of white rot fungus *Phanerochaete chrysosporium* (9).

Degradation in a natural aquatic environment estimated as 80 days; hydrolysis plays an important part in degradation (10).

A dye solution was added to provide a concentration of 25 mg l^{-1} of organic carbon to an activated sludge 1500 mg l^{-1} in settled domestic sewage. Oxygen uptake of the system was followed for 7 hr. Oxygen uptake at least 10% lower than control. Acclimated sludge (14 day) 25 mg l^{-1} (organic carbon) before acclimatisation 49.4%, after acclimatisation 77.4% oxygen consumed. However, it should be kept in mind that the dye concentration of 25 mg l^{-1} (organic carbon) is significantly higher than the concentrations likely to be encountered in real life biological oxidation treatments.

To study the effect on stream oxidative process, dye-sewage sludge systems (dye concentration to yield 25 mg l^{-1} organic carbon) diluted to 1:10 and 1:100 in river water. Inhibition was observed at dilution 1:10 50% oxygen consumed, 1:100 90% oxygen consumed (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 80 mg kg^{-1} (9).

LD_{50} intraperitoneal mouse 4.2 mg kg^{-1} (11).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 with and without verapamil (a cardiac drug and co-mutagen) negative (12).

Chinese hamster ovary cell chromosomal aberration without metabolic activation negative (13).

Other effects

Any other adverse effects

Malachite Green 0.025-0.4 μg l^{-1} inhibited the rate of DNA synthesis in both untreated and rat hepatocytes treated with epidermal growth factor. The author suggested that the cytotoxic and mito-inhibitory properties of Malachite Green play an important role during tumour promotion (14).

Metabolism of Malachite Green by Syrian hamster embryo (SHE) cells leads to the generation of free radicals; catalase and glutathione peroxidase decrease the lipid peroxidation and DNA damage induced by Malachite Green. The authors suggest that there is a possible relationship between the genotoxicity of Malachite Green to SHE cells and the involvement of reactive free radical formation (15).

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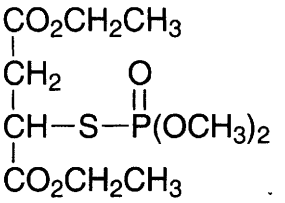
M10 malaoxon



$C_{10}H_{19}O_7PS$ **Mol. Wt.** 314.30 **CAS Registry No.** 1634-78-2

Synonyms butanedioic acid, [(dimethoxyphosphinyl)thio]-, diethyl ester; succinic acid, mercapto-, diethyl ester, *S*-ester with *O,O*-dimethyl phosphorothioate; Liromat; malathion-*O*-analog; oxycarbophos

RTECS No. WM 8410000

Ecotoxicity

Invertebrate toxicity

LC_{50} (24 hr) *Chironomus riparius* larva 5.4 mg l^{-1} (1).

Toxicity to other species

Clawed frog embryos, dose-dependent severe developmental effects, reduced growth, notochordal defects, abnormal pigmentation (2).

Reduced NAD^+ levels in clawed frog (2).

Mammalian & avian toxicity

Acute data

LD_{50} *oral rat* 158 mg kg^{-1} (3).

LD_{50} intraperitoneal rat 17.5 mg kg^{-1} (4).

Carcinogenicity and chronic effects

National Toxicology Program tested (103 wk) rats and mice orally 500 or 1000 ppm via feed. No evidence for carcinogenicity in rats or mice (5).

Oral rat, mice 1000 ppm in diet (duration unspecified) no increased incidence of tumours compared with controls (6).

Genotoxicity

Salmonella typhimurium TA97, TA98 with and without metabolic activation negative (7).

In vitro Chinese hamster ovary cells with metabolic activation weakly positive, without metabolic activation positive for sister chromatid exchanges, and with and without metabolic activation negative for chromosomal aberrations (8).

In vitro mouse lymphoma tk^+/tk^- with metabolic activation equivocal and without metabolic activation positive (9).

Other effects

Any other adverse effects

Brain acetylcholinesterase activity inactivation: mice and rats were more sensitive than minnows or trout (10).

Other comments

In mammals this compound is the degradation metabolite of the insecticide malathion (11).

References

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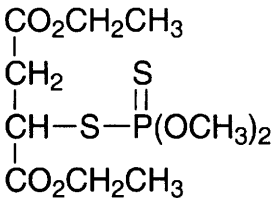
M11 malathion



$C_{10}H_{19}O_6PS_2$ **Mol. Wt.** 330.36 **CAS Registry No.** 121-75-5

Synonyms *S*-[1,2-bis(ethoxycarbonyl)ethyl] *O,O*-dimethyl phosphorodithioate; carbofos; mercaptothion; phosphothion; moldison; sodophos; [(dimethoxyphosphinothioyl)thio]butanedioic acid, diethyl ester; mercaptosuccinic acid diethyl ester, *S*-ester with *O,O*-dimethyl phosphorodithioate; diethyl (dimethoxythiophosphorylthio)succinate; Afrathion; Agrian; Benathion; Callimal; Diamal; Endomozal

EINECS No. 204-497-7 **RTECS No.** WM 8400000

Uses Insecticide. Pediculicide. Veterinary ectoparasiticide.

Physical properties

M. Pt. 2.9°C **B. Pt.** 156-157°C at 0.7 mmHg **Specific gravity** 1.2315 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.75 **Volatility** v.p. 4×10^{-5} mmHg at 30°C
Solubility Water: 145 mg l^{-1} at 20°C. Organic solvents: alcohols, aromatic and alkylated aromatic hydrocarbons, esters, ethers, ketones, vegetable oils

Occupational exposure

DE-MAK 15 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 10 mg m^{-3}
JP-OEL 10 mg m^{-3}

UK-LTEL 10 mg m^{-3}
US-TWA 10 mg m^{-3}
Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin (S2, S24)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, bass, brown trout, rainbow trout 0.1-0.29 mg l^{-1} (1,2).
LC_{50} (48 hr) carp 9.80-10.04 mg l^{-1} (3).
Snakehead fish (6 month resting to spawning phase) 0.20 mg l^{-1}; ♂ inhibition of gonadal development and gonadosomatic index, ♀ immature oocytes exhibited cytoplasmic proteinaceous inclusion bodies which ultimately lead to their degeneration (4).
In vivo spinally transected rainbow trout exposed to toxic aqueous concentrations, caused immediate reduction in oxygen utilisation and heart rate and an increase in ventilation volume (5).
Newly hatched larvae of African catfish (*Clarias gariepinus*) exposed to ≥2.5 mg l^{-1} malathion for five days posthatch suffered a significantly high proportion of deformed notocord and pericardial oedema (6).
LC_{50} (48 hr) killifish 1.8 mg l^{-1} (7).

Invertebrate toxicity

LC_{50} (24, 48, 72, 96 hr) freshwater crab 8.9, 6.5, 5.6, 3.8 ppm, respectively (8).
Anabaena oryzae and *Phormidium fragile* 93.5% and 85.7% of applied dose recovered in respiration; the metabolites identified were mono- and dicarboxylic acid, mercaptoethyl succinate, mono and di-ethylsuccinate (9).
Anabaena survived up to 0.5 mg l^{-1} (10).
EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) >140 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) 74 mg l^{-1} (11).
LC_{50} (48 hr) *Daphnia pulex* 1.8 μg l^{-1} (12).
A refined microcosm technique was used to study the toxicity of malathion to trophic groups of soil nematodes and to the microarthropod community. Microarthropods were far more sensitive to malathion than were nematodes, and total microarthropod abundance was lower than controls at 400 μg g^{-1} (13).
LC_{50} (96 hr) adult unionid mussels *Lampsilis siliquoidea*, *Utterbackia imbecillus* and *Villosa lienosa* > 350 mg l^{-1} (14).
LD_{50} topical application to bees 0.71 μg bee^{-1} (1).

Bioaccumulation

Bioconcentration factor for carp in muscle, liver and kidney 2.7-17.3 (15).
Bioconcentration factor coho salmon 29.3 (16).
Bioconcentration factor for killifish (whole body) 11 (7).
Excretion rate constant for killifish (whole body) 0.27 hr^{-1} (7).

Environmental fate

Nitrification inhibition

Threshold for inhibition of denitrification and nitrification (rotating disc and activated sludge) 10.0 mg l^{-1} (17).

Degradation studies

The time required for complete biodegradation in a model river water were 8, 12 and 18 days for 5, 10 and 15 mg dm^{-3}, respectively (18).
Rate of degradation in 10 days 81-92% in various non-sterile loam soils and 5-19% in various sterile loam soils (19).
Unsterile seawater and sedimented cores under laboratory light at 20°C, pH 8, $t_{1/2}$ 2.6 and 20 days, respectively (20).
Field application, 1 ml in 40 ml distilled water, tropical grassland soil initially adversely affected microfungal and microbial biomass. Statistical analysis over a 15 month period showed no significant difference from controls (21).

Abiotic removal

Removal rates by activated carbon from wastewater; COD 50-55% and organic phosphorous moiety 90% (22).

The adsorption capacity of activated charcoal for malathion in saline water was 117 mg g^{-1} (23).
The rate of removal with aqueous oxidisers was up to 5 times as rapid when exposed to UV irradiation (280-320 nm) (24).
$t_{1/2}$ for thin film of 0.67 μg cm^{-2} irradiated at environmentally important wavelengths 2.1 days (25).
Alkaline hydrolysis is the most important pathway of degradation in the Indian River Estuary, biological and photolytic degradation only play a small role (26).

Adsorption and retention

Of clay minerals, maximum absorption occurred with calcium-saturated Trancos montmorillonite (27).
Model to establish the potential to reach groundwater. The model assumes steady waterflow, equilibrium linear adsorption and depth-dependent first-order biodegradation. K_{oc}, groundwater travel times and residual concentrations are determined (28).
Mobility through Sakit sandy loam and Itwa loam soils and the effect of soil organic matter (including humic and fulvic acids), clay fractions, free aluminium oxide and ferric oxide, soil pH and and exchangeable cations were studied. All parameters decreased mobility except for the addition of humic acid which increased mobility (29).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 190, 290 mg kg^{-1}, respectively (30).
LC_{50} oral redwing blackbird 400 mg kg^{-1} (diet) (31).
LC_{50} (4 hr) inhalation rat 84.6 mg m^{-3} (32).
LD_{50} (24 hr) dermal rabbit 4100 mg kg^{-1} (1).
LD_{50} intraperitoneal rat, mouse 193, 250 mg kg^{-1}, respectively (33,34).
LD_{50} subcutaneous mouse 221 mg kg^{-1} (35).
LD_{50} intravenous rat, mouse 50, 184 mg kg^{-1}, respectively (36,37).
The acute toxicity of malathion is reported to depend on its purity (38).

Sub-acute and sub-chronic data

LC_{50} oral (8 day) Japanese quail, bobwhite quail, ringnecked pheasant, mallard duck 2962->5000 mg kg^{-1} diet (39).
Oral mice (20 day) 14 mg kg^{-1} increased the primary response to sheep erythrocytes (sRBC) indicated by haemolysin titre and suppressed the secondary response to sRBC. The activity of α-naphthyl acetate esterase was also inhibited. These effects occurred with the inhibition of cholinesterase in the whole blood (40).
The uptake of ^{131}I in rats given 44 mg kg^{-1} for 12 wk (route not specified) was reduced by 6.25%. There was also a 37.5% reduction in serum protein-bound iodine. Normal thyroid function was observed in rats whose malathion was discontinued for 2 wk before the animals were examined (41).
In rats given 90% technical malathion in the diet for 4-6 wk, at average daily intakes of 62 and 68 mg kg^{-1} to ♂ and ♀, respectively, cholinesterase activity in the brain, plasma and erythrocytes was inhibited by ~50%. No adverse effect was noted in the animals (42).

Carcinogenicity and chronic effects

In 21-month feeding trials, rats receiving 100 mg kg^{-1} diet showed normal weight gain (1).
In a 2-yr feeding study in ♂ rats, a level of 100 mg kg^{-1} 90% technical grade (6 mg kg^{-1} body weight), the lowest dose tested, resulted in a 10-30% depression in brain, plasma and erythrocyte cholinesterase activity, with no effect on food intake or growth (42).
No adequate data for evaluation of carcinogenicity in humans, inadequate evidence for carcinogenicity in animals, IARC classification group 3 (43).
National Toxicology Program tested rats and mice orally via feed. No evidence for carcinogenicity in rats or mice (44).
There was no significant increase in the incidence of tumours in mice fed diets containing 8000 or 16,000 mg kg^{-1} for 80 wk (45).
There was no significant increase in the incidence of tumours in rats fed diets containing 2000 or 4000 mg kg^{-1} for 103 wk when compared with controls (46).
There was no significant increase in the incidence of tumours in rats and mice fed diets containing metabolites of malathion when compared with controls (38).

Teratogenicity and reproductive effects

Malathion (technical grade, 95% pure) was fed to rats at a dietary concentration of 4000 mg kg^{-1} (~ daily intake 240 mg kg^{-1} body weight) for two generations. ♂ and ♀ of 70-100 days of age were bred after 10 wk of test; survival of the progeny on days 7 and 21 after birth was found to be reduced, and the surviving offspring showed growth retardation and an increased incidence of ring-tail disease (47).

A single intraperitoneal injection of 600 or 900 mg kg^{-1} on day-11 of pregnancy to rats produced maternal toxicity; foetal weight reduction but no malformations were induced with the high dose only (48).

Technical grade malathion (purity unspecified) administered daily at maternally tolerated doses of 50-300 mg kg^{-1} via gavage to rats on days 6-15 of pregnancy induced no embryotoxicity (49).

Oral rabbit (days 7-12 of gestation) 100 mg kg^{-1} no detectable difference in the number of resorptions, foetal size or abnormalities compared with controls (50).

Pregnant women exposed to malathion whilst their town was fumigated (over 23 days) showed no increase in congenital malformations or stillbirths when compared with the previous year (51).

Metabolism and toxicokinetics

Following oral administration to animals, the major part of the dose was excreted in the urine and faeces within 24 hr. Degradation occurs by oxidative desulfurisation by liver microsomal enzymes, leading to the formation of malaoxon. Malathion and malaoxon are hydrolysed and thus detoxified by carboxylesterases. In insects, metabolism involves hydrolysis of the carboxylate and phosphorodithioate esters, and oxidation to malaoxon (1).

Rat intravenous ^{14}C-malathion highest levels detected in liver and kidney which reached a peak 1-3 min after administration. After 24 hr low levels of radioactivity were detected into the liver, kidneys, intestines and the Harderian gland (52).

Genotoxicity

Salmonella typhimurium TA98, TA1535, TA1537 with and without metabolic activation, negative (53).

Escherichia coli with metabolic activation negative (54).

Did not induce sex-linked recessive lethal mutations in *Drosophila melanogaster* (55).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges and chromosomal aberrations positive (56).

Induced an increase in sister chromatid exchanges in human foetal fibroblasts *in vitro* (57).

Induced chromosomal aberrations and sister chromatid exchanges in human lymphocytes *in vitro* (58).

Induced an increase in chromosomal aberrations in primary spermatocytes *in vivo* following oral administration to mice (59).

Threshold dose for cytogenetic toxicity in meristematic cells of *Allium cepa* root tips 25 ppm (60).

Other effects

Other adverse effects (human)

♂ Pesticide applicators had a significant increase in the frequency of sister chromatid exchanges compared with controls. They also showed cell cycle delay and decrease in mitotic index (61).

Causes hprt mutations in treated human T-lymphocytes (62).

Any other adverse effects

Acute toxicity is due to acetylcholinesterase inhibition at nerve endings, leading to an accumulation of endogenous acetylcholine. 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 (63).

Causes dose-related immunological changes (species unspecified) (64).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (65).

Included in Schedules 5 and 6 (Release into Water/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (66).

UK Department of Environment advisory value for drinking water 7 μg l^{-1} (67).
WHO Toxicity Class III (68).
EPA Toxicity Class III (formulation). ADI 0.02 mg kg^{-1} body weight (69).

Other comments

Attributed endocrine disruption effects in wildlife. Fish growth reduced (70).
Residues have been found in water, air, soil, crops and animal and fish tissues.
Xenopus laevis embryos were exposed to malathion or its metabolite malaoxon during the first 4 days of development. The following defects were observed in a dose-dependent manner: reduced size, abnormal pigmentation, abnormal gut, enlargement of the atria and aorta, bent notochord and lowered NAD^+ levels (71).
Organophosphorus hydrolase from *Pseudomonas diminuta* hydrolysed the P-H bond of malathion. This hydrolysis resulted in the complete loss of acetylcholinesterase inhibitory potency (72).
Toxic and carcinogenic potential and hazards reviewed (73-75).
Soil has some stabilising effect on malathion due to adsorption. Addition of humanic material helps in the decay in soil (76).
Occupational exposure from pesticide application assessed (77).

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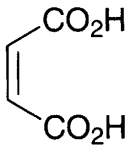
M12 maleic acid



$C_4H_4O_4$ **Mol. Wt.** 116.07 **CAS Registry No.** 110-16-7

Synonyms (*Z*)-butenedioic acid; *cis*-butenedioic acid; *cis*-1,2-ethylenedicarboxylic acid; maleinic acid; malenic acid; toxilic acid

EINECS No. 203-742-5 **RTECS No.** OM 9625000

Uses Manufacture of artificial resins. Retards rancidity of fats and oils. Used in the dyeing of wool, cotton, silk. In manufacture of plasticisers and polymers.

Physical properties

M. Pt. 130.5°C **B. Pt.** 135°C (decomp.) **Specific gravity** 1.590 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} –0.79
Solubility Water: 788 g l^{-1} at 25°C. Organic solvents: acetone, benzene, carbon tetrachloride, chloroform, diethyl ether, ethanol, methanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to eyes, respiratory system and skin (R22, R36/37/38)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water – Wear suitable gloves (S2, S26, S28, S37)

Ecotoxicity

Fish toxicity
LC_{100} (24 hr) carp 130 mg l^{-1} (1).
LC_{50} (24 hr) ide 106 mg l^{-1} (2).
LC_{50} (24-48 hr) mosquito fish 240 ppm (3).
LC_{50} (96 hr) fathead minnow 5 mg l^{-1} (4).

Invertebrate toxicity
EC_{100} (24 hr) *Daphnia magna* 200 mg l^{-1} (2).

Bioaccumulation
Chlorella fenea var. *vacuolata* exposed to 50 μg l^{-1}, bioconcentration factor ranged 10-14 (5-7).
Ide (3 day) exposure to median concentration of 31 μg l^{-1} at 20-25°C bioconcentration factor <10 (6,7).

Environmental fate

Carbonaceous inhibition
EC_{10} (16-18 hr) *Pseudomonas putida* 1190 mg l^{-1} (2).

Degradation studies
ThOD (6, 12, 24 hr) 2.7, 4.5 and 2.7%, respectively, using wastewater bench-activated sludge (8).
Incubation (5 day, 23°C) 1 g l^{-1}, activated sludge and 50 μg l^{-1} maleic acid, volatilisation 26.9%; mineralisation 26.3% (CO_2); 41% sludge metabolite and non-extractable residues 96.8% (6,7).
ED_{50} (4 hr) *Haematococcus pluvialis* (80×10^6 cells l^{-1}) 125 mg l^{-1} (2).

Degraded by five newly isolated types of anaerobic, mesophilic, Gram-negative, sulfur-reducing eubacteria isolated from shallow marine or deep-sea sediments (designated Kyprop, Gyprop, Kysw2, Gylac and Kyval) (9).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 708 mg kg^{-1} (10).
LD_{50} oral mouse 2400 mg kg^{-1} (10).
LD_{50} dermal rabbit 1560 mg kg^{-1} (11).

Metabolism and toxicokinetics

♂ Wistar albino rats (7 day) 1 mg kg^{-1} unspecified route, 17.3% excreted via faeces and 7.7% via urine. Percentage of dose retained liver 0.45%, lungs 0.04% and carcass 6.7% (6,7).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye caused severe irritation (11).

Other effects

Any other adverse effects

Unspecified route rat 200 mg kg^{-1} hr^{-1} caused decrease in renal water clearance. Kidney nephron clearance controls 7.16%, drugged rats 4.03% (12,13).
Unspecified route rat (24 hr) 200 or 400 mg kg^{-1} caused proximal tubular necrosis in 40-90% of kidney (14). ♂ Sprague Dawley rats were studied before and 2 and 24 h after i.v. injection (100 mg kg^{-1}). An early and reversible decline in Na:K pump activity was induced in the proximal convoluted tubule paralleled by a decrease in oxidative metabolism (with recovery to normal 24 h after administration of the dose) (15).

Other comments

Low level air pollutant (16).
Reviews on experimental toxicology and human health effects listed (17).

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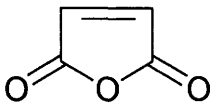
M13 maleic anhydride



$C_4H_2O_3$ **Mol. Wt.** 98.06 **CAS Registry No.** 108-31-6

Synonyms 2,5-furandione; *cis*-butenedioic anhydride; dihydro-2,5-dioxofuran; Toxilic anhydride

EINECS No. 203-571-6 **RTECS No.** ON 3675000

Uses Dye intermediate. Manufacture of copolymers, pharmaceuticals and pesticides. In Diels-Alder synthesis.

Physical properties

M. Pt. 54-56°C **B. Pt.** 200°C **Flash point** 103°C (closed cup) **Specific gravity** 1.48 at 20°C with respect to water at 4°C **Volatility** v.p. 1 mmHg at 44°C ; v.den. 3.4

Solubility Water: miscible. Organic solvents: acetone, benzene, chloroform, 1,4-dioxane, ethanol, ethyl acetate, ligroin, toluene, xylene

Occupational exposure

DE-MAK 0.1 ppm (0.41 mg m^{-3})

FR-VLE 1 mg m^{-3}

SE-LEVL 0.3 ppm (1.2 mg m^{-3}) **SE-STEL** 0.6 ppm (2.5 mg m^{-3})

UK-LTEL MEL 1 mg m^{-3} **UK-STEL** MEL 3 mg m^{-3}

US-TWA 0.25 ppm (1 mg m^{-3})

UN No. 2215 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Supply classification corrosive

Risk phrases Harmful if swallowed – Causes burns– May cause sensitisation by inhalation and skin contact (R22, R34, R42/43)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S2, S22, S26, S36/37/39, S45)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) mosquito fish 240 mg l^{-1} (1).

LC_{50} (24 hr) bluegill sunfish 150 mg l^{-1} (2).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 44 ppm Microtox test (3).

Environmental fate

Degradation studies

99% removal by activated sludge in 4 hr. In view of the rapid hydrolysis, the reported biodegradation probably relates to maleic acid (1,4).

Abiotic removal

Hydrolyses rapidly to form maleic acid in water with a $t_{1/2}$ 0.37 min at 25°C (5).

In the vapour phase undergoes complete hydrolysis in 21 hr at 96% relative humidity; whereas, no hydrolysis occurs at 50% relative humidity (6).

Estimated $t_{1/2}$ 1.7 hr for reaction with photochemically produced hydroxyl radicals and ozone in the atmosphere (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, rat, mouse, rabbit 390, 400, 465, 875 mg kg^{-1}, respectively (8-10).
LD_{50} dermal rabbit 2620 mg kg^{-1} (11).
LD_{50} intraperitoneal rat 97 mg kg^{-1} (8).

Sub-acute and sub-chronic data

Inhalation rat, hamster, monkey (6 month) 0, 1.1, 3.3 or 9.8 mg m^{-3} 6 hr day^{-1} for 5 days wk^{-1} caused dose-related nasal and ocular irritation, and a reduction in body weight gain. No significant treatment-related mortality was observed in any species (12).

Carcinogenicity and chronic effects

Oral rat (2 yr) 0, 10, 32 or 100 mg kg^{-1} day^{-1} caused a significant decrease in red blood cell count in all treated ♂ rats at 6 month and in high-dose ♀ rats after 12 month. Haematocrit decreased in ♂ rat after 6 month, and thyroid clear cell adenomas and hypoplasia was observed in treated ♀ rats. There was no significant effect on body weight, mortality, neurology, ophthalmology or urinalysis (13).

Teratogenicity and reproductive effects

Oral rat, 0, 30, 90 or 140 mg kg^{-1} day^{-1} on day 6-15 of gestation. No teratogenic effects were observed (14).

Irritancy

1% solution instilled into rabbit eye caused severe irritation (exposure unspecified) (15).

Sensitisation

Asthma has been reported among exposed workers and in clinical studies (16,17).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (18).
In vivo rat bone marrow, chromosomal aberrations negative (19).

Other effects

Other adverse effects (human)

Powerful irritant. Inhalation can cause pulmonary oedema (20).

Other comments

Toxicology and environmental fate reviewed (21-24).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (25).
Autoignition temperature 477°C.

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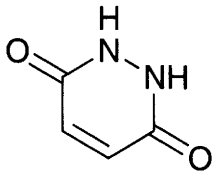
M14 maleic hydrazide



$C_4H_4N_2O_2$ **Mol. Wt.** 112.09 **CAS Registry No.** 123-33-1

Synonyms 1,2-dihydro-3,6-pyridazinedione; 3,6-dihydroxypyridazine; 6-hydroxy-2*H*-pyridazin-3-one; 1,2-dihydropyridazine-3,6-one; 6-hydroxy-3(2*H*)-pyridazinone; MH; malic acid hydrazide; Antergon; Malepin; Malzid; Regulox; Allirem; Burtolin; Fazor; Malehid

EINECS No. 204-619-9 **RTECS No.** UR 5950000

Uses Plant growth inhibitor and herbicide, principal use is in the control of sucker growth on tobacco. Also tested to retard growth of trees, hedges and grass and sprouting of carrots, onions, beets, rutabagas and potatoes.

Physical properties

M. Pt. 310-312°C **B. Pt.** 260°C (decomp.) **Specific gravity** 1.60 at 20°C **Partition coefficient** log P_{ow}-1.959 (1) **Volatility** v.p. 0 mmHg at 50°C

Solubility Water: 6 g l^{-1}. Organic solvents: dimethylformamide, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish 1400-1600 mg l^{-1} (1).

LC_{50} (96 hr) harlequin fish 100 mg l^{-1} (2).

Trout, bluegill sunfish, goldfish 5 ppm caused death in 8-12 hr. Test conditions: pH 7.0; dissolved oxygen content 7.5 ppm; total hardness (soap method) 300 ppm; free carbon dioxide 5 ppm; and temperature 12.8°C (3).

Invertebrate toxicity

LC_{50} (96 hr) *Daphnia* sp. 107 mg l^{-1} (4).

Environmental fate

Degradation studies

In various soils from eastern, southern and midwestern USA, $t_{1/2}$ 14-100 days, may be related to the soils organic content. Microbial degradation appeared to be rapid (5).

Abiotic removal

Stable to hydrolysis at pH 3, 6, 9 (5).
Rapid photochemical degradation occurs in water (1).

Adsorption and retention

Highly mobile in un-aged soils. Aerobic ageing of maleic hydrazide lowered the leaching potential (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck, bobwhite quail >10,000 mg kg^{-1} (1,4).
LD_{50} oral rat 3800-6800 mg kg^{-1} (6).
LC_{50} (1 hr) inhalation rat 20 mg l^{-1} (1,4).
LD_{50} dermal rabbit >4000 mg kg^{-1} (6).

Sub-acute and sub-chronic data

LD_{50} (15 day) oral rat ♂ 6300 kg^{-1}, ♀ 6680 mg kg^{-1} (7).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (8).
Mouse (3 wk) gavage 1000 mg kg^{-1} followed by (18 month) oral in feed *ad libitum* 3000 ppm. No evidence of increased tumour incidence compared with controls (9).
Oral (100 wk) rats 1% in diet, no increase in number of tumours compared with the controls (10).
Oral (2 yr) rat 30 g kg^{-1} diet (technical potassium salt) caused no adverse effects (4).
Subcutaneous (100 wk) mice, rats 500 mg kg^{-1} wkly, no difference in tumour incidence as compared with controls (10,11).

Teratogenicity and reproductive effects

Four-generation reproduction study in rats of feeding 5000, 10,000, 20,000, 50,000 ppm of sodium salt, showed no effects on fertility, lactation or other reproductive parameters (7).
Gavage rats (6-15 day of gestation) 0, 400, 800, 1200, 1600 mg kg^{-1} rats killed on day-22 of gestation. No adverse maternal, foetotoxicity or teratogenic effects were observed (12).
Gavage rabbit (7-27 day of gestation) 0, 100, 300, 1000 mg kg^{-1} day^{-1}. No maternal toxicity. 300 or 1000 mg kg^{-1} caused malformed scapulae in foetuses, indicating a no-observed-effect level of 100 mg kg^{-1} day^{-1} for developmental effects (7).

Metabolism and toxicokinetics

Oral rabbit 100 mg kg^{-1} 43-62% excreted in urine unchanged within 48 hr (10).
Oral rat [^{14}C]-labelled maleic hydrazide, after 6 days only 12% had been excreted in faeces, suggesting the remainder had been absorbed (13).
Pregnant rats, 0.5, 5.0 mg kg^{-1}, mothers killed on day-20 gestation and foetuses examined or mothers allowed to litter and feed pups before pups were killed and stomach contents examined. Maleic hydrazide can cross the placenta and is transmitted to pups via milk (7).
Oral rat (6 day) [^{14}C]-labelled maleic hydrazide 0.2% recovered in expired carbon dioxide. 77% was recovered in urine which contained 92-94% of the unchanged compound and 6-8% in the form of conjugates of maleic hydrazide, and 12% was recovered in faeces. Only trace amounts were detected in the blood and tissues (13).

Irritancy

Dermal rabbit (duration unspecified) 0.5 ml caused mild irritation and 100 mg instilled into the eye caused no irritation (7).

Genotoxicity

Salmonella typhimurium TA98, TA1535, TA1537 with and without metabolic activation negative (14).
Escherichia coli WP2*hcr* and *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (15).
Bacillus subtilis (metabolic activation unspecified) positive (16).
In vitro human lymphocytes and V97 Chinese hamster cells ≥100 ppm, dose-related increases in sister chromatid exchanges (17).
In vivo intraperitoneal 100, 200 mg kg^{-1} no effect on bone marrow erythrocyte micronuclei or the ratio of poly- to normo-chromatic erythrocytes (18).

Other effects

Any other adverse effects
Dermal rabbit (14 day) single dose 20 g kg^{-1}. 2 of 5 ♂ and 1 of 5 ♀ rabbits died on day-1. The rabbits that died were comatose and showed ataxia and shallow respiration (7).

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).
WHO Toxicity Class Table 5 (21).
EPA Toxicity Class III (formulation) (4).
ADI 0.3 mg kg^{-1} body weight (4).

Other comments

Mode of action in plants: inhibited meristemic cell division but had no effect on cell elongation (1).
Metabolic pathways reviewed (22).

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M15 malic acid

$$HO_2CCH_2CH(OH)CO_2H$$

$C_4H_6O_5$ **Mol. Wt.** 134.09 **CAS Registry No.** 6915-15-7

Synonyms hydroxybutanedioic acid; deoxyteraric acid; hydroxysuccinic acid; Pomalus Acid

EINECS No. 230-022-8 **RTECS No.** ON 7175000

Occurrence Trace amounts detected in forest soils of S.E. USA (1). Found in many fruits.

Physical properties

M. Pt. 131-132°C (DL-form) **B. Pt.** decomp. **Specific gravity** 1.595 **Partition coefficient** log P_{ow} –1.26 (2)
Solubility Water: 558 g l^{-1} at 20°C. Organic solvents: acetone, diethyl ether, ethanol, methanol

Environmental fate

Degradation studies
Activated sludge process treatment at 20°C 120 hr, 70-100% was removed (3).
BOD_5 0.468 mg l^{-1} O_2, BOD_5 0.34-0.57 mg l^{-1} O_2 Warburg sewage (2).
COD 0.68; 0.70 mg l^{-1} O_2 (2,4).
Activated sludge 6, 12, 24 hr (L-isomer) 9.6%, 22.9%, 44,8% ThOD, (D-isomer) 6.0%, 4.6%, 20.8% ThOD (5).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 1600 mg kg^{-1} (6).

Irritancy
Dermal rabbit (24 hr) caused moderate irritation and 750 µg instilled into the eye (24 hr) caused severe irritation (7).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA104 with and without metabolic activation negative (8).

Other comments

Toxicity reviewed (9).

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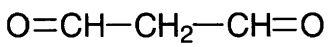
M16 malonaldehyde



$C_3H_4O_2$ **Mol. Wt.** 72.06 **CAS Registry No.** 542-78-9

Synonyms 1,3-propanedialdehyde; 1,3-propanedione; 1,3-propanedial; malonic aldehyde; malonic dialdehyde; malondialdehyde; NCI-C54842

Occurrence

Found in animal tissue as a result of lipid peroxidation and as a by-product of prostaglandin and thromboxane biosynthesis. Occurs in the leaves of pea and cotton plants and is present in many foodstuffs, particularly rancid foods.

Occurs in beef at levels of 2-15 μg g^{-1}; levels in pork, chicken and fish are comparatively low, and various types of fruit and vegetables have either very low levels or no malonaldehyde (1).

Physical properties

M. Pt. 72-74°C

Ecotoxicity

Invertebrate toxicity

Lethal dose in *Saccharomyces cerevisiae* 5 mM. Prior exposure to a non-lethal concentration, 1 mM, confers resistance to the lethal concentration (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 606 mg kg^{-1} (3).

LD_{50} oral rat 632 mg kg^{-1} (given as the sodium enol salt) (4).

Sub-acute and sub-chronic data

Subcutaneous injection to chickens 1 ml 50% malonaldehyde in corn oil kg^{-1} 3 times a wk for 4 wk. Plasma cholesterol and triglyceride levels were not significantly affected by the treatment. Degenerate cells without stainable lipid were frequently observed in the arteries of treated chickens. It is suggested that malonaldehyde is a potent angiotoxin (5).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (6).

Mice tested with 0.1-10.0 μg malonaldehyde sodium enol salt g^{-1} day^{-1} in drinking water for 12 months developed dose-dependent hyperplastic and neoplastic changes in liver nuclei; mortality was increased at the highest dose level, but no gross hepatic tumours were observed (7).

Metabolism and toxicokinetics

In vitro rat liver mitochondria rapidly oxidised radiolabelled malonaldehyde to acetic acid. *In vivo*, it was metabolised to CO_2, and ~10% of the radioactivity was recovered in the urine. A major urinary metabolite was identified as *N*-acetyl-ε-(2-propenal)lysine, primarily derived from *N*-α-(2-propenal)lysine, which is formed by the reaction of malonaldehyde with the ε-amino groups of *N*-terminal lysine residues in food proteins (7).

In *in vitro* tests with rat liver fractions, the cytosolic fraction showed high metabolising activity, and was found to contain two aldehyde dehydrogenase enzymes, with K_m values of 16 μM and 128 μM. The mitochondrial fraction also contained an aldehyde dehydrogenase enzyme, with a lower K_m value of 7.3 mM with NAD+ (8); this enzyme is irreversibly inhibited by malonaldehyde in a two-phase process with concentration-dependent rates (9).

In rats orally administered 158 mg kg^{-1}, the urinary excretion of malonaldehyde increased 192-fold over control

values in the first 12 hr after treatment; that of acetaldehyde increased 70-fold. Increased excretion of formaldehyde occurred 12-24 hr after administration and a decrease in acetone excretion was seen at 12-48 hr. Methyl ethyl ketone was detected in the urine from 0-24 hr after administration (10).

Genotoxicity

Salmonella typhimurium TA102, TA104, TA2638, weakly positive; TA1535, TA1537, TA1538 negative (11).
Chinese hamster ovary cells with and without metabolic activation negative, sister chromatid exchange test positive (sodium malonaldehyde) (12).
Escherichia coli with active DNA-repair system positive, *recA* and *uvrB* derivatives negative, suggesting that malonaldehyde induces interstrand cross-linking (13).
Salmonella typhimurium his D 3052 weakly positive (14).
Drosophila melanogaster mosaic spot test positive, sex-linked recessive lethal mutation assay negative (15).

Other effects

Other adverse effects (human)

Malonaldehyde forms DNA adducts in humans; adducts of deoxyadenosine and deoxyguanosine occur at higher concentrations in normal breast tissues from cancer patients than in those from non-cancer patients (16).
Thiobarbituric acid (TBA)-reactive material found in human serum is due to the presence of malonaldehyde and other aldehydes (17).
These TBA-reactive materials have been found at increased levels in serum following a myocardial infarction (18,19).

Any other adverse effects

Causes major membrane damage at high concentrations in *in vitro* tests (20).
In vitro rat skin fibroblasts developed nuclear abnormalities at 10^{-6} M malonaldehyde, despite an uptake of only 4% (7).
Swiss mice exposed to malonaldehyde in drinking water developed inflammation and fibrosis of the glandular stomach mucosa (21).
In vitro tests with model proteins suggest that malonaldehyde interacts with these to increase their carbonyl contents (22).

Other comments

In a group of 15 men given 1.5 g ethanol kg^{-1} over a 3 hr period, plasma malonaldehyde concentration increased compared with a control group (23).
Effect of antioxidants on the carcinogenicity and mutagenicity of malonaldehyde reviewed (24).
Mutagenicity of malonaldehyde and β-substituted acroleins in *Salmonella typhimurium* reviewed (25).
Recent studies on the metabolism of exogenous and endogenous malonaldehyde reviewed (26).

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M17 malonic acid

$HO_2CCH_2CO_2H$

$C_3H_4O_4$ **Mol. Wt.** 104.06 **CAS Registry No.** 141-82-2

Synonyms propanedioic acid; carboxyacetic acid; dicarboxymethane; methanedicarboxylic acid

EINECS No. 205-503-0 **RTECS No.** OO 0175000

Uses Manufacture of barbiturates.

Physical properties

M. Pt. ~135°C (decomp.) **B. Pt.** sublimes *in vacuo*

Solubility Water: 1538 g l^{-1}. Organic solvents: diethyl ether, ethanol, methanol, propyl alcohol, pyridine

Environmental fate

Degradation studies

BOD_{25} 2, 5, 10, 20 days 0.31, 0.36, 0.52, 0.53 mg l^{-1} O_2, respectively, with a substance concentration of 13.5 mg l^{-1} and an inoculum of soil microorganisms (1).

Wastewater treatment activated sludge 6, 12, 24 hr: 1.2% ThOD, toxic, 0.9% ThOD, respectively (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1310, 4000 mg kg^{-1}, respectively (3,4).

LD_{50} intraperitoneal mouse 300 mg kg^{-1} (5).

Irritancy

Dermal (24 hr) rabbit 500 mg caused mild irritation and 100 mg caused severe eye irritation (duration unspecified) (3).

Other effects

Any other adverse effects

Salamander embryo at blastula stage 15-20 ppm induced abnormal development (6).

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M18 malononitrile

$$CNCH_2CN$$

$C_3H_2N_2$ **Mol. Wt.** 66.06 **CAS Registry No.** 109-77-3

Synonyms propanedinitrile; cyanoacetonitrile; dicyanomethane; malonic acid dinitrile; methylene cyanide; methylenedinitrile

EINECS No. 203-703-2 **RTECS No.** OO 3150000

Uses Used in organic synthesis. Leaching gold from gold ores. Vitamin B_1 synthesis.

Physical properties

M. Pt. 32-34°C **B. Pt.** 220°C **Flash point** 112°C (open cup) **Specific gravity** 1.1910 at 20°C with respect to water at 4°C

Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2647 **HAZCHEM Code** 2X **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) – Do not breathe vapour – 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, S23, S27, S45)

Ecotoxicity

Fish toxicity

LC_{50} (12, 24, 48, 96 hr) rainbow trout 19.4, 6.2, 4.2, 1.6 mg l^{-1}, respectively (hard water) (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 19, 61 mg kg^{-1}, respectively (2,3).

LD_{50} intravenous rabbit, mouse 28, 32 mg kg^{-1}, respectively (4,5).

LD_{50} intraperitoneal mouse 12.9 mg kg^{-1} (6).

LD_{Lo} subcutaneous rabbit, dog, mouse 6-8 mg kg^{-1} (7,8).

Irritancy

Severe eye irritant and causes local skin irritation (species unspecified) (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (10).

Other effects

Other adverse effects (human)
Vapour inhalation can cause methaemoglobinaemia (9).

Other comments

EPA requiring and/or recommending testing for human health effects and for chemical fate to establish levels at which waste is no longer hazardous (11).
May polymerise violently at 130°C. Prolonged exposure to the air and ultra-violet radiation will result in hydrogen cyanide release (9).

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M19 mancozeb

CAS Registry No. 8018-01-7

Synonyms [[1,2-ethanediylbis[carbamodithioacto]] (2–)]manganese mixture with [[1,2-ethanediyl-bis[carbamodithioato]](2–)]zinc; manzeb; dithane; karamate; zimanat

RTECS No. ZB 3200000

Uses Fungicide for fieldcrops, nuts, vegetables, fruits and ornamentals.

Physical properties

M. Pt. 192-194°C (decomp. without melting) **Flash point** 137.8°C (open cup) **Volatility** v.p. negligible at 20°C
Solubility Water: 6-20 mg l^{-1}. Organic solvents: insoluble in most organic solvents

Occupational exposure

UK-LTEL 5 mg m^{-3} (as Mn)
Supply classification irritant
Risk phrases Irritating to the respiratory system – May cause sensitisation by skin contact (R37, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container dry – Avoid contact with skin and eyes – If swallowed seek medical advice immediately and show this container or label (S2, S8, S24/25, S46)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) rainbow trout, guppy, brown bullhead, goldfish 1.9-7.7 mg l^{-1} (1,2).
LC_{50} (48 hr) carp 24 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} honeybee 0.193 mg bee^{-1} (2).

Environmental fate

Anaerobic effects

Methanosarcina barkeri methanogenesis from glucose greatly inhibited by 100 mg l^{-1} (3).

Degradation studies

$t_{1/2}$ 15 days in unsterilised soil, initial concentration 3 ppm, after which the rate of loss slowed. In sterilised soil the rate of loss was slower for the first 15 days, but subsequent rate of loss was similar in both cases. Hence microorganisms play an important role in degradation but long-term persistence is significant, even in the presence of microflora (4).

Abiotic removal

Decomposes on prolonged exposure to air or moisture. Rapidly hydrolysed in acidic media (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5-15 g kg^{-1} (5-7).
LD_{50} dermal rabbit, rat >5000, >10,000 mg kg^{-1}, respectively (2,5).

Sub-acute and sub-chronic data

Oral (10 day) Japanese quail, mallard duck 3200-6400 mg kg^{-1} day^{-1}, no mortalities (2,5).
Rat (17 day) 300 mg kg^{-1} (route unspecified) caused hind limb paralysis indicating motor neuropathy (8).
Oral (12 wk) ♂ Wistar rats 0, 10, 50, 75, 113, 169, 253, 379 mg kg^{-1} with feed. 379 mg kg^{-1} caused the death of a third of the rats. ≥169 mg kg^{-1} decreased growth and nutrient utilisation and the weight of kidneys, adrenals and testes were increased in the two highest dose groups. Liver detoxifying function was also reduced. ≥75 mg kg^{-1} increased liver and thyroid weights. Even very low doses impaired thyroid function (9).

Carcinogenicity and chronic effects

Dermal (60 wk) ♀ mice 100 mg 3 × wk^{-1}. Development of tumours observed after 31 wk, mainly benign squamous cell papillomas and keratoacanthomas. High mortality was observed after 54 wk due to mancozeb toxicity (10).
Dermal ♀ Swiss albino mice initiated with a single sub-carcinogenic dose of 7,12-dimethylbenz[*a*]anthracene (52 μg). 7 days after initiation, mice were treated with mancozeb 100 mg kg^{-1} 3 × wk^{-1}. 100% tumorigenesis was recorded after 17 wk of treatment, examination showed most of these tumours to be benign (11).
Oral rats 500, 1000 and 1500 mg kg^{-1} day^{-1} for 30, 90, 180 and 360 days suffered dose-dependent signs of toxicity and death, significant increase in thyroid/body weight ratio and histopathological changes. Marked structural and functional changes occurred in the thyroid (7).

Teratogenicity and reproductive effects

Intragastric mice 100-1000 mg kg^{-1} increased number of abnormal sperm, testes weight and histology were normal (12).
Gavage ♂, ♀ rats (8 wk) 70, 140, 280, 350, 700 mg kg^{-1} 6 × wk^{-1}. High doses caused reduction in maternal body weight, paralysis of hind legs and dose-dependent mortality. Changes in fertility parameters were minimal. No difference in fertility parameters in F_1 generation (13).
High levels have caused birth defects in test animals (details unspecified) (2).
Vineyard workers (couples) exposed to pesticides including mancozeb showed an increased frequency of miscarriages and still births compared with controls, and an increase in the percentage of chromosomal aberrations (14).

Metabolism and toxicokinetics

The major metabolite (species unspecified) is ethylenethiourea, comprising almost 24% of the bioavailable dose in urine and bile. Ethylenethiourea residues were detected at levels of 1ppm in the thyroid and liver; by 24 hr residues were undetectable (15).

Irritancy

Pesticide patch test 1% (72 hr) on 200 volunteers (50 were agricultural workers) negative (16).

Genotoxicity

Salmonella typhimurium TA92, TA98, TA100, TA102, TA1535, TA1537, TA2637 with and without metabolic activation negative (17,18).

Aspergillus nidulans (activation unspecified) induction of point mutation positive (19).

In vitro human peripheral blood lymphocytes with metabolic activation, unscheduled DNA synthesis and sister chromatid exchanges negative; without activation, unscheduled DNA synthesis positive and there was a dose-dependent inhibition of thymidine uptake (20).

Occupationally exposed workers *in vitro* short term peripheral lymphocyte cultures. Mancozeb exposure was associated with significant increases in the frequencies of structural chromosome aberrations and sister chromatid exchanges (21).

In vivo mouse bone marrow cells chromosomal aberrations and physiological effects, such as end-to-end chromosomal associations, clumping, uneven stretching of chromatin material, were observed (22).

Other effects

Other adverse effects (human)

Cytogenetic analysis of workers exposed during manufacture showed increased chromosomal aberrations, especially in ♀ packers of the final product, and increased immunoglobulins I and G and α-2-microglobulin (23).

Occupational exposure to the ethylenebis(dithiocarbamate) of managanese and zinc (mancozeb) was evaluated in 14 subjects exposed for 5-10 yr during production and in 13 non-exposed controls. The levels of carbon disulfide, a metabolite of dithiocarbamates, was measured in blood and urine and immune system tests were carried out. The exposed subjects had increased T-lymphocyte proliferative responses, and both cytokine production and utilisation were increased. The *in vitro* enhanced T-cell functional activity was associated with an *in vivo* normal immune status. The results indicated that prolonged low-level exposure to mancozeb causes a slight immunomodulatory effect on cellular immunity (24).

Any other adverse effects

Attributed endocrine disruption effects in wildlife. Avian reproduction impaired, delay in egg laying (25).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (26).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (27).

WHO Toxicity Class Table 5 (28).

EPA Toxicity Class IV (formulation) (2).

ADI 0.03 mg kg^{-1} body weight (2).

Other comments

Toxicity and occupational limit values reviewed (29).

Dissolves in powerful chelating agents but cannot be recovered from them (2).

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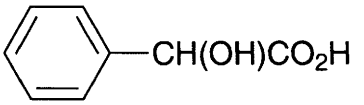
M20 DL-mandelic acid



$C_8H_8O_3$ **Mol. Wt.** 152.15 **CAS Registry No.** 611-72-3

Synonyms (±)-α-hydroxybenzeneacetic acid; (±)-mandelic acid

EINECS No. 210-277-1 **RTECS No.** OO 6300000

Physical properties

M. Pt. 121-123°C **Specific gravity** 1.30 at 20°C

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Metabolism and toxicokinetics

In rats the extent to which mandelic acid is metabolised to phenylglyoxylic acid is dependent on the enantiomeric composition of mandelic acid administered (1).

Other effects

Other adverse effects (human)

Occasional clinical side-effects include giddiness, tinnitus, gastric disturbances, dysuria and haematuria. It should be avoided by patients with renal disfunction (2).

Other comments

Used in the treatment of urinary tract infections, usually as the ammonium or calcium salt (2).

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M21 maneb

$C_4H_6MnN_2S_4$ **Mol. Wt.** 265.31 **CAS Registry No.** 12427-38-2

Synonyms ethylene bis(dithiocarbamato)manganese; manganese ethylenebis(dithiocarbamate); [[1,2-ethanediylbis[carbamodithioato]](2–)]-manganese; Amangan; Manzate; Nespor; Trimangol; MEB

EINECS No. 235-654-8 **RTECS No.** OP 0700000

Uses Fungicide.

Physical properties

M. Pt. 192-204°C (decomp. without melting) **Specific gravity** 1.92 at 20°C **Volatility** v.p. $<7.5 \times 10^{-8}$ mmHg at 20°C

Solubility Water: practically insoluble in water. Organic solvents: practically insoluble in common organic solvents

Occupational exposure

UK-LTEL 5 mg m^{-3} (as Mn)

UN No. 2210 (maneb or maneb preparations with ≥60% maneb)

UN No. 2968 (maneb or maneb preparations, stabilised against self-heating) **HAZCHEM Code** 1W **HAZCHEM Code** 4WE (stabilised) **Conveyance classification** spontaneously combustible substance, danger of emission of flammable gas on contact with water (maneb or maneb preparations with ≥60% maneb) substance which in contact with water emits flammable gas

Supply classification irritant

Risk phrases Irritating to the respiratory system – May cause sensitisation by skin contact (R37, R43)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container dry – Avoid contact with skin and eyes – If swallowed seek medical advice immediately and show this container or label (S2, S8, S24/25, S46)

Ecotoxicity

Fish toxicity

Rainbow trout continuous exposure (dose unspecified) from fertilised egg to early fry state induced embryotoxicity and was teratogenic. Major effects, severe spinal and vertebral abnormalities, mostly associated with retarded yolk sac resorption (1).

LC_{50} (96 hr) harlequin fish 0.53 mg l^{-1} (2).
LC_{50} (96 hr) guppy 3.7 mg l^{-1} (3).
LC_{50} (48 hr) carp 1.8 mg l^{-1} (4).

Invertebrate toxicity
EC_{50} (96 hr) reproduction *Chlorella pyrenoidosa* 3.2 mg l^{-1} (5).
EC_{50} (48 hr) *Daphnia magna*, brown shrimp 1-3.3 mg l^{-1} (5,6).
LC_{50} (21 day) *Daphnia magna* 0.11 mg l^{-1} (5).
EC_{50} (30 min) *Photobacterium phosphoreum* 3.31 ppm Microtox test (7).

Environmental fate

Nitrification inhibition
Minimum inhibitory concentration (3 hr) for *Nitrosomonas* and *Nitrobacter* 56 mg l^{-1} (3).
Nitrosomonas in soil >960 mg l^{-1} caused some inhibition of nitrification (8).

Degradation studies
Rapidly degraded in the environment by metabolism, hydrolysis, photolysis and oxidation (4).
$t_{1/2}$ in soil 6-36 day (9).

Adsorption and retention
Calculated K_{oc} of >2000 indicates that maneb will adsorb to soil and sediments (10).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >100 mg kg^{-1} (11).
LD_{50} oral mouse, rat 2.6-3.0 g kg^{-1} (12).
LD_{50} oral mouse, rat 4-4.5 g kg^{-1} (13).
LC_{50} inhalation (4 hr) rat >3.8 mg l^{-1} (8).
LD_{50} dermal rat, rabbit >5000 mg kg^{-1} (8).

Sub-acute and sub-chronic data
LC_{50} (8 day) mallard duck, bobwhite quail >10,000 mg kg^{-1} diet (4).
Inhalation (4.5 month) rat 2, 12, 135 mg m^{-3} caused toxicity and irritation in the trachea and lungs (14).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (15).
Gavage (78 wk) ♂ ♀ mouse, 46 mg kg^{-1} at 7-days-old and then the same amount not adjusted for body weight for up to 4 wk of age, for the rest of the period they were given 158 mg kg^{-1} diet. No significant increase in tumour incidences recorded (16).
Gavage (9 month) mouse 6 wkly administrations of 500 mg kg^{-1}. 4 lung adenomas occurred compared with 0 in the untreated controls (17).
Gavage (22 month) rat 335 mg kg^{-1} 2 × wk^{-1} for life. 6/60 rats survived at 22 months. One rat developed a subcutaneous rhabdomyosarcoma and 1 developed a mammary carcinoma. 1/46 controls developed a fibrosarcoma (18,19).
Subcutaneous (78 wk) ♂, ♀ mouse 100 mg kg^{-1} in 0.5% gelatine on day-28 of life. 70 mice survived to the end of the experiment (original number 72); no increased incidence of tumours observed (20).
Subcutaneous (22 month) mouse single injection of 12.5 mg kg^{-1} in paraffin. Of 4/46 survivors at 22 months, 3 developed malignant tumours (2 fibrosarcomas and 1 thyroid carcinoma). One fibrosarcoma was seen in 46 controls which survived at 22 months (19).

Teratogenicity and reproductive effects
Doses of 0.002-0.1 LD_{50} reduced fertility in both ♂ and ♀ mice characterised by disturbed spermatozoa maturation, low numbers or lack of differentiated spermatogenesis, autotrophic changes in sertoli cells, suppressed ovopoiesis, and increased numbers of atresic follicles. No effect on thyroid activity was reported (14).

Chick embryos, eggs pre-incubation dipped in 0.2% or 1.2% aqueous dispersions for 30 sec, no evidence of teratogenic or embryotoxic effects (21).
Chick embryos, eggs pre-incubation dipped in 0.5, 1.5, 4.5 or 13.5 g l^{-1} for 30 sec. All concentrations tested were teratogenic, mainly inducing unilateral lower limb deformities (22).
Pregnant rats 40 mg kg^{-1} caused embryo growth retardation. Also decreased activity of liver microsomal *N*-demethylase in nulliparous ♀ (23).
Gavage pregnant mice day 6-15 of gestation 1200 mg kg^{-1} day^{-1}. Offspring examined 60, 65 days post-natally for skeletal variations. Major changes in frequencies of parted frontals, abnormal metopic roots, reduced articular processes of thoractic vertebrae and carpal fusions occurred. Prenatal mortality was higher (20% compared with 7.5%) but litter size and litter weight were not altered (24).
Oral immature ♂, ♀ rat (1 month) 50 mg kg^{-1} day^{-1} after 10 wk control ♂ were mated with treated ♀ and control ♀ with treated ♂. A decline in fertility was observed in both sexes which was reversible after 3.5 months (25).
Gavage mouse, 2000 mg kg^{-1} day^{-1} on days 8-12 of gestation did not reduce the viabilities of foetuses or cause any carcinogenic effects (26).

Metabolism and toxicokinetics

^{14}C-Maneb oral rat 55% excreted in urine and faeces within 3 days. Body organs contained 1.2%, 0.18% after 24 hr and 5 days, respectively, as metabolites ethylenediamine and ethylenebisthiuram monosulfide (27).
Acid hydrolysis in the stomach results in the production of ethylenediamine and carbon disulfide, the latter being expired in air. The ethylenediamine is absorbed, some is oxidised to glycine and oxalic acid, and ultimately carbon dioxide. The remainder is excreted in urine together with inorganic sulfate. Maneb is also transformed into ethylenebisthiuram monosulfide, it then forms ethylene thiourea and then carbon disulfide which is expired in air (27).

Irritancy

1% skin patch test (72 hr) caused no irritation (28).

Sensitisation

In a 1% skin patch test (72 hr), 3 out of 125 agricultural workers experienced an allergic reaction (28).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 with metabolic activation positive (29).
Salmonella typhimurium TA100, TA98 with and without metabolic activation negative (29).
Escherichia coli WP2 *uvr A* reverse mutation with and without metabolic activation negative (30).
Saccharomyces cerevisiae D3 mitotic recombination with metabolic activation positive (30).
Saccharomyces cerevisiae D_7 without metabolic activation negative (29).
In vitro human lung fibroblasts, unscheduled DNA synthesis positive (30).
In vivo chick embryo, eggs dipped in 0-27 g l^{-1} for 30 sec, significantly increased sister chromatid exchanges at ≥13.5 g l^{-1} (31).
In vivo mouse bone marrow cells slight increase in chromosomal aberrations (32).

Other effects

Any other adverse effects

Intraperitoneal ♂ mouse, single doses of 30, 60, 100, 200 or 1000 mg kg^{-1} caused an inhibitory effect on locomotor activity and aggressiveness (33).
A trace contaminant and degradation product of maneb, ethylene thiourea has caused thyroid effects, tumours and birth defects in laboratory animals (34).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (35).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (36).
WHO Toxicity Class Table 5 (37).

EPA Toxicity Class IV (34).
ADI 0.03 mg kg^{-1} body weight (34).
UK advisory value for drinking water 10 μg l^{-1} (38).

Other comments

Residues have been isolated from crops (4).
Genetic toxicity reviewed (39).
Residues on vegetables degrade to ethylene thiourea (*qv*) during cooking (20).
Use, occurrence, analysis, carcinogenicity and mammalian toxicity reviewed (20).

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M22 manganese

Mn

Mn **Mol. Wt.** 54.94 **CAS Registry No.** 7439-96-5

EINECS No. 231-105-1 **RTECS No.** OO 9275000

Uses In making steel and non-ferrous alloys.

Occurrence As oxide, sulfide, carbonate and silicate in the earth's crust, in soil, sediments, sea-floor nodules, plants and animals, but not as the free metal; constitutes 0.085% of earth's crust (1).

Physical properties

M. Pt. 1244°C **B. Pt.** 2095°C **Specific gravity** 7.47 (α-form) at 20°C, 7.26 (β) at 20°C, 6.37 (γ) at 1100°C, 6.28 (δ) at 1143°C with respect to water at 4°C **Volatility** v.p. 1.0 mmHg at 1292°C

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable fraction of aerosol)
JP-OEL 0.3 mg m^{-3}
SE-LEVL 1 mg m^{-3} (total dust); 0.5 mg m^{-3} (respirable dust)
UK-LTEL 1 mg m^{-3} (fume); 5 mg m^{-3} (as Mn) **UK-STEL** 3 mg m^{-3} (fume)
US-TWA 0.2 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (28 day) rainbow trout 2.91 mg l^{-1} (salt) (2).

Invertebrate toxicity

EC_{50} *Selenastrum capricornutum* 3.1 mg l^{-1} (salt) (3).
LC_{50} (48 hr) *Daphnia magna* 5.7 mg l^{-1} (sulfide salt) (4).
LC_{50} (48-96 hr) *Asellus aquaticus* 333-771 mg l^{-1} for Mn(II) salt (5).

Bioaccumulation

In chironomid larvae age and body weight affected the extent of retention. Among 4th instar larvae, younger individuals had higher concentrations than older instars (6).
Levels may be concentrated up to a factor of 10, 100 and 100,000 by land mammals, fish and marine plants, respectively (1).

Environmental fate

Degradation studies

Soil microorganisms in well aerated soils at >pH 5.5 can oxidise the divalent form rapidly. Oxidation is very slow in highly acid soils (7).

Adsorption and retention

Radiolabel study using two whole soils and the natural aggregates of one of the soils. Waterlogging, air drying and incubation at 100 cm suction treatments were applied. Irrespective of treatment, accumulation occurred in spots in the aggregates and throughout the whole soils. The manganese was converted rapidly into easily reducible forms by a microbe-dependent process in the soils and the spots were concluded to be areas where divalent manganese was oxidised microbially to insoluble oxides (8).
Mobilisation of manganese is favoured by low pH (9).

In river water enhanced mobility exhibited during denitrification phases, probably due to decreased redox potential and associated manganese oxyhydroxide reduction (10).

Mammalian & avian toxicity

Acute data

LD_{50} injection chicken egg 765 μg egg^{-1} (as chloride) (11).

Sub-acute and sub-chronic data

Intratracheal rat (1 month) 12.5 mg kg^{-1} daily of welding dust containing 7.5-11% manganese caused changes to the cardiac-respiratory system, including effects to metabolism and macrophage morphology and atelectasis and emphysema. No fibrogenic activity was observed (12).

Carcinogenicity and chronic effects

Compounds found not to be carcinogenic (13).

Teratogenicity and reproductive effects

Gross malformations to chick foetuses following injection to egg on day-2 of incubation (as chloride) (11).

Metabolism and toxicokinetics

The gastro-intestinal and respiratory tracts are the major routes for absorption in humans, reaching in the former <5% for healthy adults (14-16).
Absorption rate is influenced by dietary levels of iron and manganese, iron deficiency, age and type of manganese compound (15,17).
Calcium may enhance absorption in the gastro-intestinal tract (18).
Total body load in a 70 kg man ~10-20 mg and is widely distributed (19,20).
Mitochondria-rich tissues (pancreas, liver, intestines and kidney) contain high concentrations (21,22).
Bound to β_1-globulin, probably transferrin; it is transported in the plasma (23,24).
It is able to pass through the blood-brain barrier and placenta (25).
$t_{1/2}$ ~37 days (15).
Inorganic forms are mainly excreted faecally via bile with only 0.1-1.3% of daily intake eliminated in urine (26-28).

Irritancy

500 mg (24 hr) instilled into rabbit eye or administered to skin caused mild irritation, and well defined erythema with slight oedema, respectively (29).

Genotoxicity

Salmonella typhimurium TA98, TA102, TA1535, TA1537 with metabolic activation negative; TA1537 without metabolic activation positive (30).
Mouse polychromatic red blood cells in bone marrow and blood lymphocytes did not significantly induce micronuclei (31).

Other effects

Other adverse effects (human)

Early signs of neurotoxic dysfunction in individual humans occupationally or environmentally exposed to manganese vary, but collectively they show a pattern of slowing motor functions, increased tremor, reduced response speed, enhanced olfactory sense, possible memory and intellectual deficits, and mood changes (32).
In an occupational exposure study significantly higher incidence of dyspnoea during exercise, cough in cold season and episodes of acute bronchitis were observed. Lung ventilatory parameters were slightly altered. Reaction time, hand tremor and audioverbal short-term memory were significantly altered. There was a slight increase in the amount of circulating neutrophils and in the values of certain serum parameters. A blood threshold concentration at ~1 μg 100 ml whole $blood^{-1}$ is suggested by the response to the eye-hand coordination test. A time-weighted average exposure to airborne dust of ~1 mg m^{-3} for <20 yr may cause preclinical signs of poisoning (33).

Lesions of the central nervous system have been shown to be most severe in the pallidum and striatum following autopsy of chronic poisoning cases. Chronic poisoning is a danger in the mining and processing of manganese ores, welding and in the manganese alloy and dry-cell battery industries. Psychological and neurological symptoms characterise the condition (14,34,35).
Effects on communities in the vicinity of manganese production plants have been reported (36-38).

Any other adverse effects
Caused depletion of dopamine, and probably serotonin, in the basal ganglia of rabbits, rats and monkeys (39-41).
Liver necrosis and reduced blood pressure effects reported (42,43).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Manganese: guide level 20 $\mu g\ l^{-1}$ and maximum admissible concentration 50 $\mu g\ l^{-1}$ (44).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (45).

Other comments

Seedlings of four tree species from northern Japan were grown hydroponically in solutions containing nutrients and 1, 10, 50 or 100 mg l^{-1} for 50 days. Managanese accumulation in the leaves of all species caused a decline in photosynthetic rate and carboxylation efficiency but had little effect on the maximum efficiency of photochemistry. Early successional species (*Betula ermanii* and *Alnus hirsuta*) had a greater tolerance towards excess Mn in leaves than the mid- and late-successional species (*Ulmus davidiana var. japonica* and *Acer mono*) (46).
Environmental pollutant from iron and steel works, mines, agrochemical production and use and production of dry-cell batteries and manganese oxide reviewed (1).
Availability increased by fertilisation of soil. Wheat production positively correlated to availability (47).
Toxicity reviewed (48).
Pathology, bioavailability, metabolism and biochemistry reviewed (49-53).
An essential trace element necessary for the formation of connective tissue and bone, lipid and carbohydrate metabolism, reproduction and growth. Daily requirement is 2-3 mg (19,20).
Conversion of sulfur dioxide into sulfuric acid is promoted by atmospheric manganese compounds (54).
The divalent form is 2.5-3 times more toxic than the trivalent form (1).
Influence of route of administration (oral gavage, intraperitoneal injection, intratracheal installation) and chemical form ($MnCl_2.4H_2O$, MnO_2) on the absorption and cerebral distribution of manganese in rats investigated (55).
Toxicity data refer to bioavailable forms.

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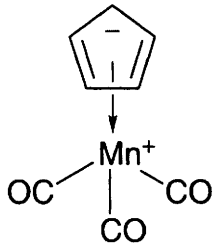
M23 manganese cyclopentadienyl tricarbonyl



$C_8H_5MnO_3$ **Mol. Wt.** 204.06 **CAS Registry No.** 12079-65-1

Synonyms tricarbonyl (η^5-2,4-cyclopentadien-1-yl)manganese; tricarbonyl-π-cyclopentadienyl-manganese; Cymantrene; cyclopentadienylmanganese tricarbonyl; MCT

EINECS No. 235-142-4 **RTECS No.** OO 9720000

Uses Additive in unleaded petrol.

Physical properties

M. Pt. -1°C **B. Pt.** 232-233°C

Occupational exposure

FR-VME 0.1 mg m^{-3} (as Mn)
UK-LTEL 0.1 mg m^{-3} (as Mn) **UK-STEL** 0.3 mg m^{-3} (as Mn)
US-TWA 0.1 mg m^{-3} (as Mn)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 80, 150 mg kg^{-1}, respectively (1).
LC_{50} (2 hr) inhalation rat 120 mg m^{-3} (2).
LD_{50} intraperitoneal rat 14 mg kg^{-1} (3).
LD_{50} intravenous mouse 710 μg kg^{-1} (4).

Sub-acute and sub-chronic data

Inhalation (10 month) rabbits, guinea pigs, rats 0.7-1 mg m^{-3} caused central nervous system muscarinic effects, decreased resistance to infection and a decrease in diuresis with increase in urinary albumin content (1).

Metabolism and toxicokinetics

Following subcutaneous administration to rats, manganese accumulated in the lung in a nonlipid-soluble form, suggesting accumulation of metabolites rather than parent compound. A strong correlation between pulmonary manganese concentration and toxicity was observed. It was suggested that monooxygenase mediated metabolites were involved in lung toxicity and manganese accumulation (5).

Other effects

Any other adverse effects

Subcutaneous ♂ rat 0.5, 1.0 or 2.5 mg Mn kg^{-1} at 24 hr bronchoalveolar lavage albumin, protein content and lactate dehydrogenase activities increased. Lung manganese content was significantly raised (5).

Legislation

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

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M24 manganese dioxide

MnO_2

MnO_2 **Mol. Wt.** 86.94 **CAS Registry No.** 1313-13-9

Synonyms manganese oxide; battery manganese; manganese(IV) oxide; manganese binoxide

EINECS No. 215-202-6 **RTECS No.** OP 0350000

Uses In dry-cell batteries. Oxidising agent. Porcelain paint. Pigments. In therapeutics.

Occurrence As the mineral pyrolusite and in seawater.

Physical properties

M. Pt. 535°C (decomp.) **Specific gravity** 5.03

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable fraction of aerosol)
JP-OEL 0.3 mg m^{-3} (as Mn)
SE-LEVL 1 mg m^{-3} (as Mn) (total dust); 0.5 mg m^{-3} (as Mn) (respirable dust)
UK-LTEL 5 mg m^{-3} (as Mn)
US-TWA 0.2 mg m^{-3} (as Mn)
Supply classification harmful
Risk phrases Harmful by inhalation and if swallowed (R20/22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the eyes (S2, S25)

Ecotoxicity

Fish toxicity
Common carp (140 day) 0.0137 mg g^{-1} caused a measurable change in length and/or weight (1).

Mammalian & avian toxicity

Acute data
LD_{100} subcutaneous mouse 550 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 442 mg kg^{-1} (3).
LD_{Lo} intravenous rabbit 45 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Inhalation (95 × 1 hr) monkey 0.6-3.0 mg m^{-3} over 4 months caused central nervous system effects (5).
Intratracheal (4 month) rat 0.3 mg m^{-3} for 5-6 hr daily caused inflammatory changes (4).

Injection (14.5 month) monkey 2000 and 3500 mg with interval of 3 months caused the proliferation of bizarre cells and extensive loss of neurones in the pallidum and subthalamic nucleus (6).
Subcutaneous (3.5 month) squirrel monkey 400 mg divided into two doses administered with a 5 wk interval caused muscular rigidity and tremor (7).

Metabolism and toxicokinetics

Oral ♂ mouse (100 day) 2 g Mn kg^{-1}. Levels of manganese in liver, kidney and hair were the highest followed by bone, pancreas and prostate gland. The leukocyte level was significantly reduced (8).
Largely cleared from the lungs by ciliary action and a proportion of this is absorbed from the gut (9).

Genotoxicity

Salmonella typhimurium TA1535/psk1002 did not induce SOS reaction (10).

Other effects

Any other adverse effects

Inhalation of fine dust containing relatively low concentration causes pneumonitis. When induced in rat by intratracheal administration, shedding of bronchial and alveolar epithelium is seen with mononuclear cell infiltration of the alveolar walls and alveoli (11).
Other effects include peribronchial and perivascular sclerosis, inflammatory changes, appearance of collagenic threads, accentuation of blood vessels and reduced resistance to infection (12-15).
Hepatic effects also reported (13).
Inhalation at 10-20 mg m^{-3} for 4 hr daily during 3 to 6 months caused changes to lung tissue and reduced number of red blood cells (9).
Investigation of the lung inflammatory respone of mice to intratracheal installation of MnO_2 dusts with different specific surface areas (0.16, 0.5, 17 and 62 m^2 g^{-1}) showed that the amplitude of the response was dependent on the total surface area in contact with the biological system (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Manganese: guide level 20 µg l^{-1} and maximum admissible concentration 50 µg l^{-1} (17).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Pollutant from mining, steel casting, metallurgical processing and metal welding and cutting (19,20).
Toxicity data refer to bioavailable forms. Dissolves in HCl.
Influence of route of administration (oral gavage, intraperitoneal injection, intratracheal installation) and chemical form ($MnCl_2.4H_2O$, MnO_2) on the absorption and cerebral distribution of manganese in rats investigated (21).

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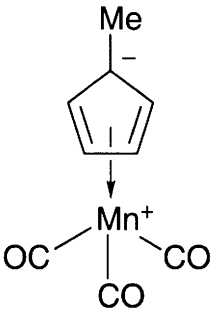
M25 manganese 2-methylcyclopentadienyl tricarbonyl



$C_9H_7MnO_3$ **Mol. Wt.** 218.09 **CAS Registry No.** 12108-13-3

Synonyms manganese, tricarbonyl[(1,2,3,4,5-π)-1-methyl-2,4-cyclopentadien-1-yl]-; manganese, tricarbonyl(methyl-π-cyclopentadienyl)-; methylcymantrene; MMT; 2-methylcyclopentadienyl manganesetricarbonyl

EINECS No. 235-165-5 **RTECS No.** OP 1450000

Uses Antiknock agent, used as an octane improver in unleaded gasoline.

Physical properties

M. Pt. –1°C **B. Pt.** 233°C **Flash point** 96°C **Specific gravity** 1.38 **Volatility** v.p. 4.7×10^{-2} mmHg at 20°C
Solubility Water: 70 ppm at 25°C

Occupational exposure

FR-VME 0.2 mg m^{-3} (as Mn)
UK-LTEL 0.2 mg m^{-3} (as Mn) **UK-STEL** 0.6 mg m^{-3} (as Mn)
US-TWA 0.2 mg m^{-3} (as Mn)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 230 mg kg^{-1} (1).
LD_{50} oral rat 50 mg kg^{-1} (2).
LD_{50} oral mice 152 mg kg^{-1} (solvent propylene glycol) (3).
LD_{50} oral mice 999 mg kg^{-1} (solvent corn oil) (3).

LC_{50} (4 hr) inhalation rat 76 mg m^{-3} (1).
LC_{50} (4 hr) inhalation mouse 58 mg m^{-3} (4).
LD_{50} dermal rabbit 140 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 152 mg kg^{-1} (5).
LD_{50} intraperitoneal rat 12.1 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 23 mg kg^{-1} (2).

Metabolism and toxicokinetics

Subcutaneous Sprague-Dawley rats 4 mg kg^{-1}, blood, lung, liver and kidney manganese levels increased between 1.5 and 96 hr, with peak organ levels occurring at 3-6 hr. Manganese concentration in lung, liver and kidney averaged 13-, 4- and 4-fold higher, respectively, than in the blood, indicating the accumulation and retention of it in these tissues. Maximal pulmonary toxicity occurred 24-48 hr after injection. No hepatic or renal injury occurred (6).

Other effects

Any other adverse effects

Subcutaneous (24 hr) ♂ rats 0.5, 1.0 or 2.5 mg manganese kg^{-1}. The pneumotoxic response was characterised by large increases in lavage albumin and protein content, with smaller increases in lactate dehydrogenase activity. Lung manganese levels were significantly elevated after treatment (7).

Inhibits the binding of [^{3}H]-*tert*-butyl-bicyclo-*o*-benzoate in mouse brain membranes with a median inhibitory concentration value of 240 μg kg^{-1} (8).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

Environmental effects, environmental toxicology, human health effects and workplace experience reviewed (10-12).

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M26 manganese nitrate

$Mn(NO_3)_2$

MnN_2O_6 **Mol. Wt.** 178.95 **CAS Registry No.** 10377-66-9

Synonyms manganese dinitrate

EINECS No. 233-828-8 **RTECS No.** QU 9780000

Uses Preparation of porcelain colorants. Intermediate in the manufacture of reagent grade MnO_2.

Physical properties

M. Pt. 37.1°C (tetrahydrate); 25.0°C (hexahydrate) **Specific gravity** 2.13 (tetrahydrate); 1.8 (hexahydrate)
Solubility Water: freely soluble. Organic solvents: acetonitrile, dioxane, tetrahydrofuran

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable fraction of aerosol)
JP-OEL 0.3 mg m^{-3} (as Mn)
SE-LEVL 1 mg m^{-3} (as Mn) (total dust); 0.5 mg m^{-3} (as Mn) (respirable dust)
UK-LTEL 5 mg m^{-3} (as Mn)
US-TWA 0.2 mg m^{-3} (as Mn)

UN No. 2724 **HAZCHEM Code** 1Y **Conveyance classification** oxidising substance

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 56 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Manganese: guide level 20 μg l^{-1} and maximum admissible concentration 50 μg l^{-1}; nitrate: guide level 25 mg l^{-1} and maximum admissible concentration 50 mg l^{-1} (2).
Included in Schedule 4 (Release into 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

M27 manganese tetroxide

Mn_3O_4

Mn_3O_4 **Mol. Wt.** 228.81 **CAS Registry No.** 1317-35-7

Synonyms manganese oxide (Mn_3O_4); manganese oxide; trimanganese tetraoxide; M34

EINECS No. 215-266-5 **RTECS No.** OP 0895000

Occurrence As the mineral hausmannite.

Physical properties

M. Pt. 1564°C **Specific gravity** 4.80

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 1 mg m^{-3}
JP-OEL 0.3 mg m^{-3} (as Mn)
SE-LEVL 1 mg m^{-3} (as Mn) (total dust); 0.5 mg m^{-3} (as Mn) (respirable dust)
UK-LTEL 1 mg m^{-3}
US-TWA 0.2 mg m^{-3} (as Mn)

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Inhalation rat (2 month) (concentration unspecified) no noticeable histological changes in lung (1).

Metabolism and toxicokinetics

Clearance $t_{1/2}$ from rat lung in 2-month inhalation study was several hours (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Soluble in HCl.

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

M28 D-mannitol

$CH_2OHCH(OH)CH(OH)CH(OH)CH(OH)CH_2OH$

$C_6H_{14}O_6$ **Mol. Wt.** 182.17 **CAS Registry No.** 69-65-8

Synonyms cordycepic acid; manna sugar; mannistol; mannitol; 1,2,3,4,5,6-hexanehexol; Diosmol; Isotol; Osmitrol; Resectisol; Mannit

EINECS No. 200-711-8 **RTECS No.** OP 2060000

Uses In making artificial resins and plasticisers. Pharmaceutical excipient and diluent. Anticaking and free-flow agent, flavouring agent and stabiliser in food industry. Diuretic. Renal function diagnostic aid. Used in reducing intracranial and intra-ocular pressure.

Occurrence Plants.

Physical properties

M. Pt. 166-168°C **B. Pt.** 290-295°C at 3.5 mmHg **Specific gravity** 1.52 at 20°C **Partition coefficient** log P_{ow} −3.10 (1)

Solubility Water: 182 g l^{-1}. Organic solvents: aniline, ethanol, glycerol, pyridine

Environmental fate

Degradation studies

BOD (5 day test), 59% ThOD; COD 87% ThOD (0.05 N $K_2Cr_2O_7$); and ThOD, 1.15 (2).

Utilised by microbes of industrial activated sludge (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 13.5, 22 g kg^{-1}, respectively (4,5).

LD_{50} intraperitoneal mouse 14 g kg^{-1} (6).

Carcinogenicity and chronic effects

Oral F344 rat and B6C3F_1 mouse (103 wk) 0, 2.5 or 5.0% in diet had no effect on survival or mean body weight. Feed consumption was approximately the same as controls. ♀ rats had increased incidence of gastric fundal gland dilation and a mild nephrosis in the renal tubular epithelium of mice was observed. Retinopathy and cataracts occurred at increased frequency in high-dose ♂ and low- and high-dose ♀ rats (7,8).

Non-carcinogenic to rat and mouse (9).

Oral rat, mouse up to highest tested dose of 50,000 ppm non-carcinogenic (10).

National Toxicology Program tested rats and mice orally in feed. No evidence of carcinogenicity (8).

Teratogenicity and reproductive effects

In vitro chick embryo neural retina cells not developmentally toxic; lowest-observed-effect concentration >7.3 g l^{-1} (11).

In vivo rat developmentally toxic intravenous dose 12.5 g l^{-1} kg^{-1} (12).

Metabolism and toxicokinetics

In man gastro-intestinal tract absorption is minimal. Following intravenous injection and before any significant metabolism by the liver can take place rapid excretion from the kidneys occurs. Elimination $t_{1/2}$ 100 min. The eye is not penetrated and nor is the blood-brain barrier crossed (13).

Sensitisation

Hypersensitivity reactions have been reported (species unspecified) (13).

Genotoxicity

Salmonella typhimurium (strain unspecified) with or without metabolic activation negative (14).
In vitro mouse lymphoma L5178Y with and without metabolic activation negative (15).
In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exhanges and chromosomal aberrations negative (16).
Drosophila melanogaster wing spot test negative (17).

Other effects

Other adverse effects (human)

Fluid and electrolyte imbalance including circulatory overload and acidosis at high doses. Expansion of extracellular volume can precipitate pulmonary oedema. Can cause tissue dehydration. Dehydration of the brain may lead to central nervous system symptoms. Causes diarrhoea when given orally. Headache, thirst, vomiting, dizziness, chills, nausea and fever are some of the side-effects when administered intravenously (13).
In renal failure patients, central nervous system involvement, large osmolality gap, fluid overload and severe hyponatraemia were seen following intravenous administration over 1 to 3 days (18).
Following intravenous injection of 20% mannitol, one patient suffered focal osmotic nephrosis (19).
Oliguric renal failure reported (20,21).

Any other adverse effects

Non-toxic to mouse lymphoma L5178Y cells for concentrations up to 5000 $\mu g\ ml^{-1}$ (15).

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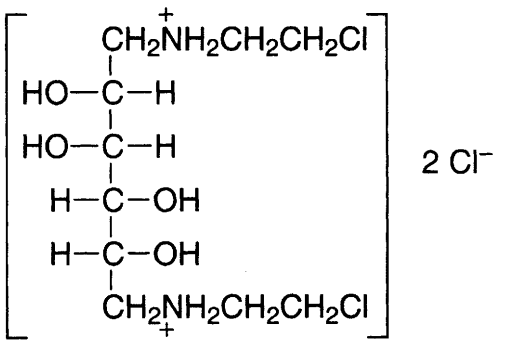
M29 mannomustine hydrochloride



$C_{10}H_{24}Cl_4N_2O_4$ **Mol. Wt.** 378.12 **CAS Registry No.** 551-74-6

Synonyms mannomustine (dihydrochloride); 1,6-bis(2-chloroethylamino)-1,6-dideoxy-D-mannitol dihydrochloride; 1,6-dideoxy-1,6-di(2-chloroethylamino)-D-mannitol dihydrochloride; 1,6-di(2-chloroethylamino)-1,6-dideoxy-D-mannitol dihydrochloride; mannitol mustard; BCM; Degranol

Uses Antineoplastic.

Physical properties

M. Pt. 239-241°C (dec.)

Solubility Water: soluble. Organic solvents: ethanol (slightly)

Mammalian & avian toxicity

Acute data

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

LD_{50} subcutaneous mouse 120 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).

Intraperitoneal injection 100 ♂ and 100 ♀ C3 mice 2.5 mg kg^{-1} weekly for 52 weeks. Lymphatic leukaemia was observed in 25% ♂ and 23% ♀ mice, and other leukaemias occurred in 7% ♂ and 4% ♀ mice. In 200 controls, the incidence of lymphatic leukaemia was 3.3%, that of other leukaemias was 0.5%, and of other tumours 9% (4).

Teratogenicity and reproductive effects

Mannomustine given to rats on the 13th day of gestation was not teratogenic, but the offspring were about half the normal size at birth (5).

Metabolism and toxicokinetics

Intravenous injection 6-week-old Wistar rats 100 mg kg^{-1} radiolabelled compound. Thirty minutes after injection, 2.1% of radioactivity was detected in the liver and 3.1% in the kidneys. After 12 hours, these values had fallen to 0.28% and 0.21%, respectively. Of a 8-15 mg kg^{-1} dose, 63% was excreted in the urine, and no activity was detected in the blood serum after 6 hours (6).

In humans, ~50% of a single dose of 1 mg kg^{-1} was removed from the blood within 20 min (7).

Genotoxicity

Escherichia coli/mouse host-mediated assay positive at 1 mg kg^{-1} (8).

In vitro cultured human lymphocytes chromosomal aberrations and sister chromatid exchange positive (9).

In vitro human T lymphocytes chromosomal aberrations positive in differentiated and non-differentiated cells (10).

Other comments

Alkylating agent (10).
A study of 16 neoplasm inhibitors found no strong correlation between carcinogenic and immunosuppressive activity (1).

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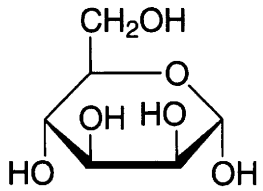
M30 D-mannose



$C_6H_{12}O_6$ **Mol. Wt.** 180.16 **CAS Registry No.** 3458-28-4

Synonyms carubinose; mannose; D-(+)-mannose; seminose

EINECS No. 222-392-4

Physical properties

M. Pt. 133°C (α form); 133-140°C (mixture of anomers) **Specific gravity** 1.54 (β) at 20°C
Solubility Water: 2500 g l^{-1} (β). Organic solvents: absolute ethanol, methanol, pyridine

Environmental fate

Anaerobic effects
Utilised by *Blastocladiella ramosa* and *Blastocladiella pringsheimii* producing lactic, succinic, acetic and propionic acids (1).

Degradation studies
Degraded in soil (2).

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Infused (12 hr) pregnant rats during early neurulation, day 9.5-10 of development. The number of resorbed conceptions was increased. At term no foetal gross anomalies, but mean body weight and mean weight and protein content of livers, kidneys, hearts and brains were reduced. Skeletal development was significantly delayed (3).

In vitro rat embryos were cultured from day-9.5 of gestation. 3 or 6 mg ml^{-1} (48 hr) caused inhibition of yolk sac expansion, smaller embryo size, delayed morphological development and abnormalities. Similar effects were seen in shorter-duration exposures, including delayed neural-fold closure or an irregular neural groove (4).

Other comments

Mannose recognition has a role in lymphocyte entry to spleen and lymph node (5).

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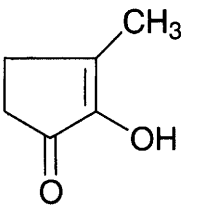
M31 maple lactone



$C_6H_8O_2$ **Mol. Wt.** 112.13 **CAS Registry No.** 80-71-7

Synonyms 2-hydroxy-3-methyl-2-cyclopenten-1-one; Corylon; Corylone; Cycloten; Cyclotene

EINECS No. 201-303-2 **RTECS No.** GY 7298000

Physical properties

M. Pt. 106-107°C

Solubility Organic solvents: ethanol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig 1400 mg kg^{-1} (1).

LD_{Lo} intraperitoneal rat, mouse 500 mg kg^{-1} (1).

Genotoxicity

In vitro human lymphoma cells, sister chromatid exchanges positive (2).

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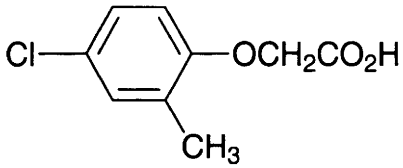
M32 MCPA



$C_9H_9ClO_3$ **Mol. Wt.** 200.62 **CAS Registry No.** 94-74-6

Synonyms (4-chloro-*o*-tolyloxy)acetic acid; 2-methyl-4-chlorophenoxyacetic acid; 4-chloro-2-methylphenoxyacetic acid; Methoxone; Herbivit; Agricorn; Bartol; Bordermaster

EINECS No. 202-360-6 **RTECS No.** AG 1575000

Uses Herbicide.

Physical properties

M. Pt. 118-119°C **Specific gravity** 1.56 at 25°C with respect to water at 15.5°C **Volatility** v.p. 1.5×10^{-6} mmHg at 21°C

Solubility Water: 825 mg l^{-1} at 25°C. Organic solvents: diethyl ether, ethanol, toluene, xylene

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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves – Wear eye/face protection (S2, S26, S37, S39)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) bluegill sunfish 100 mg l^{-1} (1).

LC_{50} (24 hr) brown trout 147 mg l^{-1} static bioassay (2).

LC_{50} (96 hr) rainbow trout 232 mg l^{-1} (3).

Invertebrate toxicity

The pulmonate snail *Lymnaea stagnalis* L was exposed to 10 or 100 mg l^{-1} MCPA for 2 months. No effect was observed on snail mortality, but reproductive output was affected (4).

LC_{50} *Xenopus* embryos 3607 mg l^{-1}. Growth retardation occurs at 2000 mg l^{-1}; MCPA does not present a high teratogenic risk (5).

Reported to be non-toxic to bees (3).

Environmental fate

Degradation studies

In soil degraded to 4-chloro-2-methylphenol followed by ring hydroxylation and ring opening. Duration of

residual activity in the soil was reported to be 3-4 months following an application of 3 kg ha^{-1}. $t_{1/2}$ <7 days after initial 'lag phase' (3).

A consortium of three bacteria isolated from topsoil, viz. *Alcaligenes denitrificans*, *Pseudomonas glycinea* and *Pseudomonas marginalis*, is able to degrade MCPA (6).

A consortium of soil bacteria collected from a rice field degraded 500 mg MCPA l^{-1} within 12 days at an initial pH 6.5, falling to pH 4.0 due to the dechlorination step in the degradative pathway which makes this an acid-yielding reaction. MCPA was not degraded above pH 8.5 and only partial degradation occurred at initial pH 5.5 or 7.5 (7).

Abiotic removal

Photolytic $t_{1/2}$ 20-24 days in sunlight (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 550, 800 mg kg^{-1}, respectively (3,9).

LD_{50} oral bobwhite quail 377 mg kg^{-1} (3).

LD_{50} dermal rabbit 4.8 g kg^{-1} (♂), 3.4 g kg^{-1} (♀) (10).

Sub-acute and sub-chronic data

Chick embryos were treated on day-0 of incubation with 0.4 and 2.0 mg. Toxic effect on the liver of 19-day-old embryos was noted by a depression of ethoxycoumarin *O*-deethylase, and an increase in NADPH-cytochrome P_{450} reductase activities for the higher dose. The activity of glutathione *S*-transferases were increased at the lower dose and significantly reduced at the higher dose (11).

Oral rat (2 wk) ≤200 mg kg^{-1} day^{-1}, 5 day wk^{-1} showed hypolipidaemia and peroxisome proliferation in the liver. Lowest-observed-adverse-effect level 100 mg kg^{-1} (12).

Oral dog (1 yr) 0, 0.15, 0.75 and 3.75 mg kg^{-1} day^{-1}, renal toxicity was observed at the two highest doses and was characterised by elevated serum levels of creatine, urea and potassium, coloration of the kidneys and increased storage of pigment in the renal tubules (10).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, no adequate data for carcinogenicity to animals, IARC classification group 2B (13).

Oral rat, mouse (24 month) no-observed-effect level 20 ppm (about 1.3 mg kg^{-1} daily) and 100 ppm (about 18 mg kg^{-1} daily), respectively (3).

Following (1 yr) exposure of 100 crested newts to concentration of ≤400 mg l^{-1} in water, putative preneoplastic nodules of the liver and tumour-like lesions of the lower jaw were occasionally observed in animals which survived more than 22 months, but there was no significant increase in occurrence over the control group (14).

In a cohort study of exposed and potentially exposed workers, there was a slight, but not significant, excess of deaths from soft tissue sarcoma (15).

In a cohort study in the former German Democratic Republic, involving 1658 ♂ subjects potentially exposed to 2,4-D and 4-chloro-2-methylphenoxyacetic acid for at least 5 yr, 124/169 neoplasms were verified as cancerous. Between 1970 and 1978, 50 cases of bronchial carcinoma occurred (27.5 expected). One case of soft-tissue sarcoma and 5 of lymphatic neoplasms were observed (16).

In a cohort study involving 4563 workers in two Danish chemical plants which produced 2,4-D, dichloroprop, 2,4,5-T and 4-chloro-2-methylphenoxyacetic acid and its sodium salt, the observed number of individual cancers did not differ statistically or significantly from expected numbers (17).

A number of case studies demonstrated an increased risk of soft-tissue sarcomas and malignant lymphoma among exposed agricultural workers. Similar studies did not demonstrate significantly increased risks to exposed workers of colon, liver and nasal cancer (18,19).

The occurrence of acute myelomonocytic leukaemia was reported in a farmworker in a follow-up study 5 yr after exposure (10).

Teratogenicity and reproductive effects

Oral rabbits (16-18 days gestation) 75 mg kg^{-1} day^{-1} and oral rats (6-15 days gestation) 125 mg kg^{-1} day^{-1} did not induce any foetotoxic or teratogenic effects (10).

Induced 54% inhibition of testicular DNA synthesis in mice at 200 mg kg^{-1} (route and duration unspecified) (20).

Metabolism and toxicokinetics

In five volunteers given 15 μg kg^{-1} orally, the highest plasma concentrations were seen after 1 hr. Urinary excretion was almost complete by 24 hr at which time ~40% of the dose had been recovered (21).

Dermal absorption was reported to be an important factor in occupational exposure: urinary concentrations reached 12 μg ml^{-1} in exposed workers while the TWA concentrations in air samples were <0.1 mg m^{-3} (21).

Following oral administration to rats, rapidly absorbed and excreted almost exclusively in the urine with only a small proportion in the faeces. Only moderate metabolism occurs and there is only a small amount of conjugate formation (22).

Irritancy

Dermal rabbit (duration unspecified) 0.5 g induced a slight erythema. The skin became sclerotic after 5-6 days and healed by day-12 (23).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (24).

Escherichia coli WP2 with and without metabolic activation negative (24).

Escherichia coli (SOS chromotest) with and without metabolic activation negative (25).

Salmonella typhimurium TA97a with and without metabolic activation positive (26).

Saccharomyces cerevisiae without metabolic activation positive (27).

Weakly positive results were obtained for sister chromatid exchanges in Chinese hamster cells *in vivo* and *in vitro* (28).

Weakly active in inducing sex-linked recessive lethal mutation, but did not induce aneuploidy in *Drosophila melanogaster* (29,30).

Caused changes in density and melting profile of nuclear DNA in seedlings and callus of *Zea mays* (31).

Aspergillus nidulans with metabolic activation induced mitotic crossing-over (26).

Did not induce a significant increase in sister chromatid exchanges in lymphocytes of workers exposed to 2,4-D and 4-chloro-2-methylphenoxyacetic acid (32).

Other effects

Other adverse effects (human)

Detected in urine of exposed workers (18).

An exposed farmer was reported to exhibit reversible aplastic anaemia, muscular weakness, haemorrhagic gastritis and signs of slight liver damage that were followed by pancytopenia of all the myeloid cell lines (33).

Any other adverse effects

In the presence of 20-80 mg *in vitro*, lower concentrations stimulated state 4 respiration, decreased the respiratory control ratio and the ADP/oxygen ratio in rat liver mitochondria. At higher concentrations, all bioenergetic markers, respiration in state 4,3 and uncoupled state and the ADP/oxygen ratios were inhibited in a dose-dependent manner (34).

MCPA was found to potentiate the activity of lipid metabolising enzymes in the peroxisomal fraction from rat liver (35).

Legislation

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

WHO revised guidelines for drinking water quality: guide level 2 μg l^{-1} (37).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (38).

WHO Toxicity Class III (39).

EPA Toxicity Class III (formulation) (3).

Other comments

In higher plants metabolism involves hydroxylation followed by glycosylation and incorporation into wall material (22).
Results of a long-term greenhouse trial of pesticide mixtures containing 25, 257 and 2579 µg MCPA on forest species (the deciduous *Carpinus betulus* and *Fagus sylvatica*, and the coniferous *Abies alba* and *Picea excelsa* species) suggest that changes in physiological parameters (transpiration, photosynthesis, stomatal conductance and chlorophyll) are indicative of complex effects of pesticides on plant metabolism (40).
MCPA metabolism in excised seedlings of barley and tomato proceeded via initial hydrolysis to the free phenoxyacetic acid, followed by conjugation with carbohydrates. A minor metabolite of MCPA in barley seedlings was formed by hydroxylation at the methyl carbon and subsequent glycosylation (41,42).
Residues have been detected in water, sediment and crops (43).
Oxidation product of the related herbicide 4-(4-chloro-2-methylphenoxy)butanoic acid.
Environmental fate and effects of MCPA in Canada reviewed (44).
Human carcinogenic potential reviewed (45).
Reviews on physico-chemical properties, human health effects, exposure levels, workplace experience, environmental effects, experimental toxicology and epidemiology listed (46).
Metabolic pathways reviewed (47).

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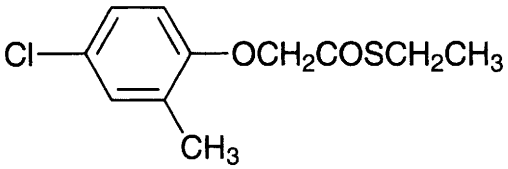
M33 MCPA-thioethyl



$C_{11}H_{13}ClO_2S$ **Mol. Wt.** 244.74 **CAS Registry No.** 25319-90-8

Synonyms (4-chloro-2-methylphenoxy)ethanethioic acid, *S*-ethyl ester; [(4-chloro-*o*-tolyl)oxy]thioacetic acid, *S*-ethyl ester; Herbit; HOK 7501; Phenothiol

EINECS No. 246-831-4 **RTECS No.** AG 2650000

Uses Hormone-type herbicide.

Physical properties

M. Pt. 41-42°C **B. Pt.** 165°C at 7 mmHg **Volatility** v.p. 1.58×10^{-4} mmHg at 20°C
Solubility Water: 2.3 mg l^{-1} at 25°C. Organic solvents: acetone, *n*-hexane, xylene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 2.5 mg l^{-1} (1).

Invertebrate toxicity
LD_{50} (contact) >40 µg bee^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral Japanese quail >1000 mg kg^{-1} (1).
LD_{50} oral ♂, ♀ rat, ♂ ♀ mouse 749-877 mg kg^{-1} (1).
LD_{50} dermal ♂ mouse >1500 mg kg^{-1} (1).
LD_{50} intraperitoneal ♂, ♀ rat 530-570 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Oral (2 yr) rat no-effect level in diet 100 mg kg^{-1} (1).
Oral (2 yr) mouse no-effect level in diet 20 mg kg^{-1} (1).

Teratogenicity and reproductive effects
Non-teratogenic and no reproductive effects to rats (1).

Irritancy
Non-irritating to rabbit skin and eyes (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class III (5).

References

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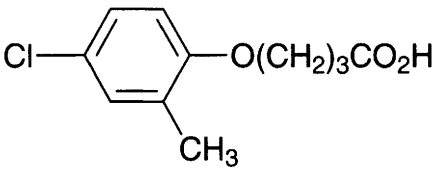
M34 MCPB



$C_{11}H_{13}ClO_3$ **Mol. Wt.** 228.68 **CAS Registry No.** 94-81-5

Synonyms 4-(4-chloro-2-methylphenoxy)butanoic acid; 4-(4-chloro-*o*-tolyloxy)butyric acid; 4-(4-chloro-2-methylphenoxy)butyric acid; Bexone; Tropotox; Butoxone; Butizyl; Divopan; Trifolex

EINECS No. 202-365-3 **RTECS No.** ES 8575000

Uses Selective systemic herbicide.

Physical properties

M. Pt. 100°C **Partition coefficient** log P_{ow} 3.53 (1)
Solubility Water: 44 mg l^{-1} at 25°C. Organic solvents: acetone, dichloromethane, ethanol, hexane, 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) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) rainbow trout 75 mg l^{-1} (2).

LC_{50} (48 hr) fathead minnow 11 mg l^{-1} (2).

Invertebrate toxicity

Reported to inhibit growth, respiration and phosphorus uptake at a minimal concentration of 573 mg l^{-1} in *Chlamydomonas globosa, Chlorella pyrenoidosa* and *Stichococcus bacillaris* (3).

Not toxic to bees (2).

Environmental fate

Degradation studies

Anaerobic activation at 28°C, 50% digested in 16-20 days (4).

In soil, metabolism involves degradation of the side-chain to 4-chloro-2-methylphenol, ring hydroxylation and ring opening. Duration of residual activity in soil 6 wk (2).

Mammalian & avian toxicity

Acute data

LC_{50} oral ring-necked pheasant, mallard duck >5000 mg kg^{-1} in diet (5).

LD_{50} oral rat, mouse 680, 800 mg kg^{-1}, respectively (6,7).

LD_{50} dermal rat 1000 mg kg^{-1} (8).

Inhalation rats (1 hr) 100 mg l^{-1} produced no adverse effects in rats (9).

Sub-acute and sub-chronic data

Oral mice (2 months) 400 mg kg^{-1}, no fatalities were observed, although a depression in body weight gain was recorded (9).

Intraperitoneal rats (duration unspecified) 23 mg caused decreased thyroid hormone levels by interference with the T4 binding site of transthyretin (10).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, IARC classification group 2B (11).

Metabolism and toxicokinetics

Metabolised in guinea pigs to 2-methyl-4-chlorophenoxyacetic acid, which is then excreted in the urine (12).

Irritancy

Mild eye and mucous membrane irritant (species unspecified) (13).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (14).

Escherichia coli WP2 hcr with and without metabolic activation negative (14).

Escherichia coli PQ37 with and without metabolic activation SOS chromotest negative (15).

Gene conversion *Saccharomyces cerevisiae* negative (16).

Induced a slight but statistically significant increase in mutation rates in the pelargonium flower (17).

Other effects

Other adverse effects (human)

Epidemiology studies show an increased risk of cancer, notably soft-tissue sarcomas and non-Hodgkin's lymphomas, in people occupationally exposed to chlorophenoxy herbicides. A historical cohort study of mortality is reported in an international register of 18,910 production workers or sprayers from 10 countries. Exposure was reconstructed through questionnaires, factory or spraying records, and job histories. Cause-specific national death rates were used as reference. No excess was observed in all-cause mortality, for all neoplasms, for the most

common epithelial cancers, or for lymphomas. Risks appeared to be increased for cancers of the testes, thyroid, other endocrine glands, nose, and nasal cavity, based on small numbers of deaths. The excess of soft-tissue sarcomas among sprayers is compatible with a causal role of chlorophenoxy herbicides (18).

Any other adverse effects

In vitro human and rabbit blood platelet aggregation, induced by ADP, adrenaline or collagen, was inhibited dose dependently on concentrations between 0.1-2.0 mg ml^{-1} plasma (19).

Uncoupler of oxidative phosphorylation in mammalian tissues (13).

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 III (22).

EPA Toxicity Class III (formulation) (2).

Other comments

Recommended herbicide dose 1 mg kg^{-1} soil; larger doses give transient increase in ammonia, nitrite ion production by soil microflora (23).

Physico-chemical properties, human health effects, experimental toxicology, exposure levels and epidemiology reviewed (24).

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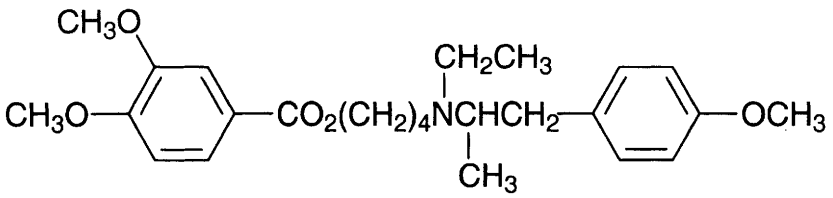
M35 mebeverine



$C_{25}H_{35}NO_5$ **Mol. Wt.** 429.56 **CAS Registry No.** 3625-06-7

Synonyms 3,4-dimethoxybenzoic acid, 4-[ethyl[2-(4-methoxyphenyl)-1-methylethyl]amino]butyl ester; veratric acid, 4-[ethyl(*p*-methoxy-α-methylphenethyl)amino]butyl ester

EINECS No. 222-830-4 **RTECS No.** YX 5250000

Uses Gastro-intestinal antispasmodic.

Occurrence Has been detected at levels of 0.29 μg in river water (1).

Physical properties

M. Pt. 129-131°C

Solubility Organic solvents: ethanol

Other effects

Other adverse effects (human)

Cystic fibrosis patient developed a perforated stercoral ulcer (2,3).

Other comments

Administered as the hydrochloride or embonate.

References

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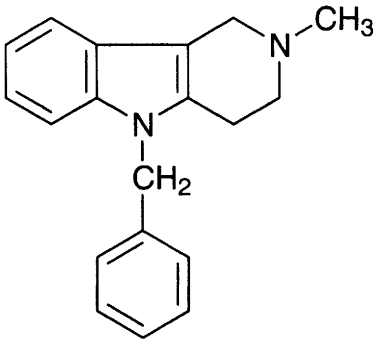
M36 mebhydrolin



$C_{19}H_{20}N_2$ **Mol. Wt.** 276.38 **CAS Registry No.** 524-81-2

Synonyms 2,3,4,5-tetrahydro-2-methyl-5-(phenylmethyl)-1*H*-pyrido[4,3-*b*]indole; 5-benzyl-2,3,4,5-tetrahydro-2-methyl-1*H*-pyrido[4,3-b]indole; 3-methyl-9-benzyl-1,2,3,4-tetrahydro-γ-carboline; *N*-methyl-9-benzyl tetrahydro-γ-carboline; Incidal

EINECS No. 208-364-4

Uses Antimuscarinic and central sedative (antihistamine) used in the relief of hypersensitivity reactions and in pruritic skin disorders.

Physical properties

M. Pt. 95°C **B. Pt.** 207-215°C at 1 mmHg

Solubility Organic solvents: acetone, chloroform, ethanol, methanol

Mammalian & avian toxicity

Metabolism and toxicokinetics

Absorbed slowly from the gastro-intestinal tract. Following extensive metabolism only small amounts of unchanged drug are detected in urine. Plasma $t_{1/2}$ ~4 hr (1).

Other effects

Other adverse effects (human)

Granulocytopenia and agranulocytosis reported (1).

Other comments

Administered as the base or as the napadisylate salt.

Has been detected in river water at levels of 0.15 μg mebhydrolin l^{-1} (2).

References

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M37 mecarbam

$$(CH_3CH_2O)_2PS(S)CH_2C(O)N(CH_3)CO_2CH_2CH_3$$

$C_{10}H_{20}NO_5PS_2$ **Mol. Wt.** 329.38 **CAS Registry No.** 2595-54-2

Synonyms *S*-[*N*-ethoxycarbonyl-*N*-methylcarbamoylmethyl] *O,O*-diethyl phosphorodithioate; ethyl *N*-[diethoxythiophosphorylthio]acetyl-*N*-methylcarbamate; 6-ethoxy-2-methyl-3-oxo-7-oxa-5-thia-2-aza-6-phosphanonanoic acid, ethyl ester, 6-sulfide; (mercaptoacetyl)methylcarbamic acid, ethyl ester, *S*-ester with *O,O*-diethyl phosphorodithioate; Marfotoks; MS 1053; Murfotox; Murphotox; Pestan

EINECS No. 219-993-9 **RTECS No.** FB 3850000

Uses Insecticide. Acaricide.

Physical properties

B. Pt. 144°C at 0.02 mmHg **Specific gravity** 1.222 at 20°C

Solubility Water: <1 g l^{-1}. Organic solvents: aliphatic hydrocarbons, miscible with alcohols, ketones, esters and aromatic and chlorinated hydrocarbons

Occupational exposure

Supply classification toxic, dangerous for the environment

Risk phrases Toxic in contact with skin and if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R50/53)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (24, 48, 96 hr) harlequin fish 8, 7 and 4 g l^{-1}, respectively (1).

Environmental fate

Degradation studies

Persists in soil for 4 to 6 wk (2).

Abiotic removal

Below pH 3 subject to hydrolysis (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 36-53, 106 mg kg^{-1}, respectively (3,4).

LC_{50} (6 hr) inhalation rat 0.7 mg l air^{-1} (2).

LD_{50} dermal rat 380->1220 mg kg^{-1} (2,5).

LD_{Lo} subcutaneous guinea pig 50 mg kg^{-1} (6).

Sub-acute and sub-chronic data

Oral (6 month) rat 1.6 mg kg^{-1} day^{-1} no effects, but 4.56 mg kg^{-1} day^{-1} caused slight depression in growth rate (2).

Metabolism and toxicokinetics

Hydrolysis, oxidative desulfuration and degradation of the carbamoyl moiety was the principal metabolic pathway in the rat. A minor pathway was O-deethylation (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).
WHO Toxicity Class Ib (9).
EPA Toxicity Class I (10).
ADI 0.002 mg kg^{-1} body weight (10).

References

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M38 mechlorethamine

$$(ClCH_2CH_2)_2NCH_3$$

$C_5H_{11}Cl_2N$ **Mol. Wt.** 156.05 **CAS Registry No.** 51-75-2

Synonyms 2,2-dichloromethyldiethylamine; chlormethine; 2,2'-dichloro-*N*-methyldiethylamine; bis(2-chloroethyl)methylamine; bis(β-chloroethyl)methylamine; di(2-chloroethyl)methylamine; *N*,*N*-di(chloroethyl)methylamine; methylbis(2-chloroethyl)amine; nitrogen mustard; Mustargen; Mustine

EINECS No. 200-120-5 **RTECS No.** AI 1750000

Uses Warfare agent. Hydrochloride used as an antineoplastic agent.

Physical properties

M. Pt. –60°C **B. Pt.** 87°C at 18 mmHg **Specific gravity** 1.118 at 25°C with respect to water at 4°C **Volatility** v.p. 0.17 mmHg at 25°C ; v.den. 5.9
Solubility Water: very slightly soluble. Organic solvents: carbon disulfide, carbon tetrachloride, dimethylformamide

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 10 mg kg^{-1} (1).
LC_{50} (2 min) inhalation rat 600 mg m^{-3} (1).
LC_{50} (30 min) inhalation mouse 1500 mg m^{-3} (1).
LD_{50} dermal rabbit 12 mg kg^{-1} (1).
LD_{50} intravenous rat 1.1 mg kg^{-1} (1).

Metabolism and toxicokinetics
Following intravenous injection in humans, it is rapidly converted into a reactive ethyleneiminonium ion. It is usually cleared from the blood within a few min. A very small proportion is excreted unchanged in the urine (2).

Irritancy
20 μg instilled into rabbit eye for 30 min caused irritation (3).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation positive (4).
In vitro 9L cells, sister chromatid exchange positive (5).
In vitro dominant lethal mutation in mouse spermatogonia positive (6).
In vitro mouse bone-marrow micronucleus assay positive (7).

Other effects

Any other adverse effects
Interstrand cross-linking of DNA is believed to account for the cytotoxicity of this alkylating agent and to account for its activity in the treatment of cancer (8).

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M39 mechlorethamine *N*-oxide

$$(CH_2ClCH_2)_2N(CH_3)O$$

$C_5H_{11}Cl_2NO$ **Mol. Wt.** 172.05 **CAS Registry No.** 126-85-2

Synonyms 2,2′-dichlorodiethyl-*N*-methylamine *N*-oxide; 2-chloro-*N*-(2-chloroethyl)-*N*-methylethanamine, *N*-oxide; 2,2′-dichloro-*N*-methyldiethylamine *N*-oxide; HN_2 oxide mustard; MBAO; mechlorethamine oxide; nitrogen mustard oxide; methylbis(β-chloroethyl)amine *N*-oxide; nitrogen mustard amine oxide; nitrogen mustard *N*-oxide; NMO; oxy-NH_2

RTECS No. IA 2200000

Uses Chemical intermediate in synthesis of the hydrochloride salt, which is marketed in Europe and Japan as an antineoplastic agent. In the USA 2,2′-dichloro-*N*-methyldiethylamine *N*-oxide has never been produced or marketed as the commercial product; however, it has been tested as an antineoplastic agent and as an insect chemosterilant.

Physical properties

Solubility Organic solvents: benzene

Mammalian & avian toxicity

Acute data
LD_{50} intravenous rat 60 mg kg^{-1} (1).

Carcinogenicity and chronic effects

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

Intravenous rat (52 wk) 4.2 mg kg^{-1} (body weight), total dose 218 mg kg^{-1} body weight, 27% of animals developed malignant tumours, 4% of animals developed benign tumours compared with 6% and 5% in controls, respectively. Other tumours included 3 sarcomas in the abdominal cavity, 7 reticular cell tumours, 1 osteosarcoma and 1 angiosarcoma in the muscle. Malignant tumours in controls included 3 mammary carcinomas and 1 phaeochromocytoma (1).

Dermal C3H/He ♂, ♀ mice (17-20 wk) 0.05 ml of 1% solution in acetone daily 6 day wk^{-1}. 9/37 treated mice developed tumours within 33-74 wk; no tumours developed in controls. The study could not be evaluated by IARC due to the small numbers of animals tested (3).

Subcutaneous mice (4 wk) 650 mg kg^{-1} body weight. 27/47 animals developed thymic lymphomas and 20/47 animals developed lung adenomas in mice surviving >80 days. Lung carcinomas and Harderian gland adenomas in 8/38 and 6/38 of mice surviving >180 days. Other tumours included liver tumours, ovarian tumours, haemangioma of the duodenum and papilloma of the forestomach. 15/69 control animals developed lung adenomas. Average survival time was 260 days (4).

Metabolism and toxicokinetics

When ^{14}C labelling of methyl group was carried out, radioactivity was detected in <4 hr, after 5 mg kg^{-1} was injected in dogs (5).

Microsomal fractions of rat liver and cultured cell lines of hepatic tissue can metabolise the compound to nitrogen mustard. The metabolism is mediated by NADPH or NADH; an anaerobic pathway is preferred. Purified cytochrome P_{450} reductase can initiate metabolism. The nitrogen mustard metabolite can be detected by its ability to induce unscheduled DNA synthesis in the liver (6).

Genotoxicity

In vivo mouse peritoneum, Ehrlich ascites tumour cells induced chromosomal aberrations (7).

In vivo mice induced dominant lethal mutations (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorines: guide level 1 μg l^{-1} (9).

Other comments

Immunosuppressive effect in humans under treatment for nephrotic syndrome and in patients receiving skin grafting have been reported in Japan (10).

In Japan used in human medicine to treat lymphomas and oat-cell carcinomas of the lung; administered orally 0.5 mg kg^{-1} (body weight) day^{-1} for 5-12 days or intravenously 0.5-2 mg kg^{-1} (body weight) day^{-1} (11).

Not produced commercially in the USA or Europe.

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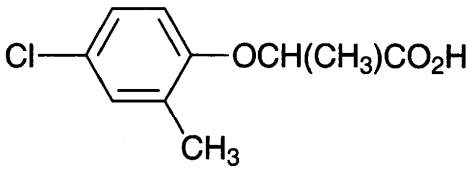
M40 mecoprop



$C_{10}H_{11}ClO_3$ **Mol. Wt.** 214.65 **CAS Registry No.** 93-65-2

Synonyms (±)-2-(4-chloro-2-methylphenoxy)propanoic acid; (*RS*)-2-(4-chloro-*o*-tolyloxy)propionic acid; (±)-2-[(4-chloro-*o*-tolyl)oxy]propionic acid; MCPP; CMPP; isocornox; Astrix; Acemeco; Calligal; Chemitex

EINECS No. 202-264-4 **RTECS No.** UE 9750000

Uses Herbicide.

Physical properties

M. Pt. 94-95°C **Partition coefficient** log P_{ow} 0.1004 (1) **Volatility** v.p. 2.33×10^{-6} mmHg at 25°C
Solubility Water: 620 mg l^{-1} at 20°C. Organic solvents: acetone, chloroform, diethyl ether, ethanol, ethyl acetate

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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves and eye/face protection (S2, S26, S37/39)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) trout 150-220 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish >100 mg l^{-1} (1).

Invertebrate toxicity
Reported to be non-toxic to bees (1).

Environmental fate

Degradation studies
In soil, degraded by microorganisms to 4-chloro-2-methylphenol, followed by ring hydroxylation at the 6-position and ring opening. Duration of residual activity in soil reported to be ~2 months (1).
Biotransformation rate in surface waters 0.0005 – 0.24 day^{-1} ($t_{1/2}$ 3-1400 days). In small hydrological systems such as field ditch and channels mecoprop appears to be transformed rapidly, but it persists for longer in larger water bodies such as main discharge channels and lakes (2).

Abiotic removal
Photodecomposes slowly on dry soil surfaces. On moist soil surfaces photodecomposition occurs in two days with transformation kinetics fitting the Hoerl function (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 930-1166 mg kg^{-1} (1).
LD_{50} oral mouse 650 mg kg^{-1} (1).

LD_{50} oral Japanese quail 740 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >12.5 mg l^{-1} air (1).
LD_{50} dermal rabbit 900 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral rat (90 day) 4.5-13.5 mg kg^{-1} day^{-1} in diet, no adverse effects reported. Oral dog (90 day) 4 mg kg^{-1} day^{-1} in diet, no adverse effects reported (1).
Oral rat (21 day) no-effect level via diet 65 mg kg^{-1} day^{-1}. Rats receiving 100 mg kg^{-1} diet for 210 days suffered only a slight enlargement of the kidneys (1).

Carcinogenicity and chronic effects
Limited evidence for carcinogenicity to humans, IARC classification group 2B (4).
Oral rat (2 yr) 1.1 mg kg^{-1} day^{-1} in diet, no adverse effects reported (1).
In a cohort study of chemical workers exposed to chlorophenoxy herbicides including mecoprop, no overall increase in cancer incidence was observed, but there were significantly increased risks for soft-tissue sarcoma and lung cancer in some subcohorts, which were not necessarily those with the highest exposures (duration and concentrations unspecified) (4,5).

Teratogenicity and reproductive effects
Oral mice (6-15 days gestation) ≥300 mg kg^{-1} was embryotoxic and ≥400 mg kg^{-1} caused skeletal malformations (6).

Metabolism and toxicokinetics
Following oral administration to mammals predominantly eliminated unchanged in the urine (1).
In one human case of serious intoxication the plasma concentration was found to be 298 mg l^{-1} 3-4 hr after ingestion. The plasma $t_{1/2}$ was ~17 hr (7).

Irritancy
Skin irritant. Highly irritating to the eyes (1).

Genotoxicity

Salmonella typhimurium TA1535, TA1536, TA1537, TA1538 with and without metabolic activation negative (8).
Escherichia coli PQ37 with and without metabolic activation negative (9).

Other effects

Other adverse effects (human)
In two cases of serious intoxication, both patients had central nervous system involvement, became unconscious and had inadequate respiration. Muscle cramps and rhabdomyolysis with renal failure were noted. Shortly after admission a serious decrease in arterial blood pressure developed. In one patient this was demonstrated to be caused by a reduction in peripheral vascular resistance (duration and exposure concentration unspecified) (8).
Detected in the urine of exposed farmers (10).
In two cases of intentional ingestion of Verdone (2,4-D and mecoprop) level of consciousness was depressed. No evidence of muscle damage noted. Minor liver and renal damage in one patient (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (12).
WHO revised guidelines for drinking water quality: guide level 10 μg l^{-1} (13).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (14).
WHO Toxicity Class III (15).
EPA Toxicity Class III (formulation) (1).

Other comments

Residues have been detected in soil, crops and water. Mecoprop exists as a mixture of two optically active isomers of which only the (*R*)-(+)-form (mecoprop-P) is herbicidally active.
Metabolic pathways reviewed (16).

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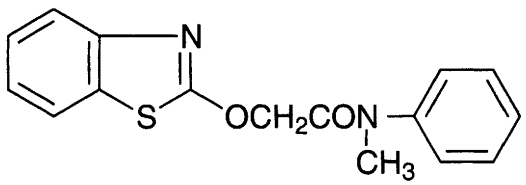
M41 mefenacet



$C_{16}H_{14}N_2O_2S$ **Mol. Wt.** 298.37 **CAS Registry No.** 73250-68-7

Synonyms 2-(2-benzothiazolyloxy)-*N*-methyl-*N*-phenylacetamide; FOE 1976; NTN 801; 2-benzothiazol-2-yloxy-*N*-methylacetanilide

EINECS No. 277-328-8 **RTECS No.** AB 4542550

Uses Herbicide.

Physical properties

M. Pt. 134.8°C **Partition coefficient** log P_{ow} 3.23 (1) **Volatility** v.p. 4.8×10^{-9} mmHg at 20°C
Solubility Water: 4 mg l^{-1} at 20°C. Organic solvents: dichloromethane, hexane, isopropanol, toluene

Occupational exposure

Supply classification dangerous for the environment
Risk phrases Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R51)
Safety phrases Avoid release to the environment. Refer to special instructions/safety data sheet (S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) trout, carp 6.8-8.0 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, dog >5000 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat 0.02 mg l^{-1} air (dust) (1).

LD_{50} dermal rat, mouse >5000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral (2 yr) rat 100 mg kg^{-1} no-effect level (1).

Legislation

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

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

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

WHO Toxicity Class Table 5 (5).

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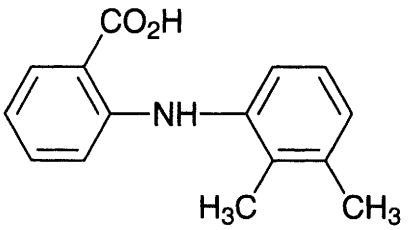
M42 mefenamic acid



$C_{15}H_{15}NO_2$ **Mol. Wt.** 241.29 **CAS Registry No.** 61-68-7

Synonyms 2-[(2,3-dimethylphenyl)amino]benzoic acid; *N*-2,3-xylylanthranilic acid; mephenamic acid; C.I. 473; Coslan; Mefacit; Ponstan; Ponstil

EINECS No. 200-513-1 **RTECS No.** CB 4550000

Uses Anti-inflammatory, analgesic and antipyretic.

Physical properties

M. Pt. 230-231°C (effervescence)
Solubility Water: 0.041 g l^{-1} at 25°C and pH 7.1. Organic solvents: chloroform, ethanol, methanol

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 525, 740 mg kg^{-1}, respectively (1,2).
LD_{50} intravenous mouse, cat, rat 96-112 mg kg^{-1} (3,4).
LD_{50} intraperitoneal mouse 120 mg kg^{-1} (5).

Metabolism and toxicokinetics
Absorbed from the human gastro-intestinal tract with peak plasma concentrations occurring 2 to 4 hr after ingestion. $t_{1/2}$ 2-4 hr. Bound to plasma proteins. Over 50% may be recovered as unchanged drug or conjugated metabolites in the urine (6).
Has been detected in human breast milk (7).

Sensitisation
Skin rashes, urticaria and occasionally allergic glomerulonephritis. May precipitate asthma (6).

Other effects

Other adverse effects (human)
Gastro-intestinal disturbances, particularly diarrhoea, are the most common side-effects (6).
Nephrotoxicity has been reported as a problem in elderly patients (8).
Bullous pemphigoid and fixed eruptions of the skin (9-11).
Central nervous system toxicity, especially convulsions, and coma have occurred in overdose cases (12-14).
Haemolytic anaemia, pancytopenia, agranulocytosis and bone-marrow aplasia recorded (6).

Other comments

Detected at levels of 1.17 μg mefanamic l^{-1} in river water (15).

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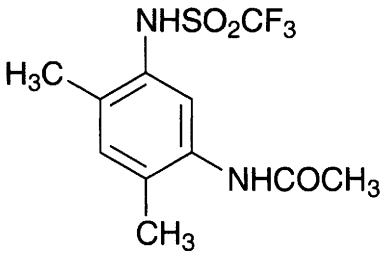
M43 mefluidide



$C_{11}H_{13}F_3N_2O_3S$ **Mol. Wt.** 310.30 **CAS Registry No.** 53780-34-0

Synonyms *N*-[2,4-dimethyl-5-[[(trifluoromethyl)sulfonyl]amino]phenyl]acetamide; Embark; MBR 12325; VEL 3973; 5′-[1,1,1-trifluoromethanesulfonamido]acet-2′,4′-xylidide

EINECS No. 258-767-4 **RTECS No.** AE 2460000

Uses Plant growth regulator, herbicide.

Physical properties

M. Pt. 183-185°C **Volatility** v.p. $<7.5 \times 10^{-5}$ mmHg at 25°C

Solubility Water: 0.18 g l^{-1} at 23°C. Organic solvents: acetone, methanol, 1-octanol, dichloromethane, benzene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish >100 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (6 hr) *Daphnia magna* 40 mg l^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ < 1 wk in soil. 5-Amino-2,4-dimethyltrifluoromethane sulfone anilide is a metabolite (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck, bobwhite quail >4620 mg kg^{-1} (2).

LD_{50} oral mouse, rat 1920, <4000 mg kg^{-1}, respectively (3,4).

LD_{50} dermal rabbit >4000 mg kg^{-1} (2).

Sub-acute and sub-chronic data

LC_{50} (8 day) oral mallard duck, bobwhite quail >10,000 mg kg^{-1} in diet (2).

Oral (90 day) rat no-effect level in diet 6000 mg kg^{-1} (2).

Oral (90 day) dog no-effect level in diet 1000 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Oral rat (2 yr) 100 mg kg^{-1} diet, no-effect level (2).

Metabolism and toxicokinetics

Excreted unchanged when orally administered to mammals (2).

Irritancy

Mild irritant to rabbit eye. Dermal rabbit non-irritating (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
WHO Toxicity Class III (7).

Other comments

Relation of pH to toxicity studied in the toad (8).

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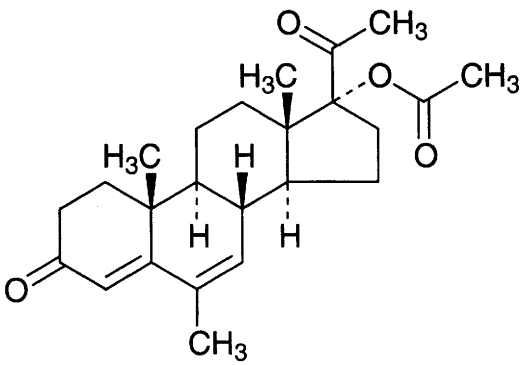
M44 megestrol acetate



$C_{24}H_{32}O_4$ **Mol. Wt.** 384.52 **CAS Registry No.** 595-33-5

Synonyms 17-hydroxy-6-methylpregna-4,6-diene-3,20-dione acetate; 17α-acetoxy-6-methylpregna-4,6-diene-3,20-dione; 6-dehydro-6-methyl-17α-acetoxyprogesterone; 6-methyl-$\Delta^{4,6}$-pregnadien-17α-ol-3,20-dione acetate; Megace; Megestat; Niagestin; Ovaban

EINECS No. 209-864-5 **RTECS No.** TU 4075000

Uses Orally active progestogen, formerly used in combinations as oral contraceptive. Used in palliative treatment of breast and endometrial carcinomas. Used in veterinary medicine as an oestrus regulator.

Physical properties

M. Pt. 214-216°C
Solubility Water: 2 mg l^{-1} at 37°C. Organic solvents: acetone, chloroform, ethanol, diethyl ether

Mammalian & avian toxicity

Acute data

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

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity in animals. For progestins overall there is inadequate evidence for carcinogenicity in humans, IARC classification group 2B (2).

Megestrol acetate has been tested alone or in combination with ethinyloestradiol in mice, rats, dogs and monkeys by oral administration, and in rats by subcutaneous injection. When tested alone in dogs it produced nodular hyperplasia, and benign and malignant mammary tumours; in mice, tested with ethinyloestradiol, it also produced malignant mammary tumours. In rats, with ethinyloestradiol, results were negative or inadequate. In monkeys, no tumours were reported (2,3).

Oral ♀ dogs 0.01, 0.1 or 2.5 mg kg^{-1} day^{-1} for 4 yr. Decreased evidence of oestrus was observed. Mean haemoglobin, packed cell volume and total erythrocyte values were decreased, and mean total leukocyte counts and erythrocyte sedimentation rates were increased for the middle- and high-dose groups. Disturbances of blood clotting mechanisms were not evident. At 4 yr, signs of diabetes (bilateral cataracts, elevated serum glucose concentrations and glycosuria) were observed in 2/16 high-dose treated dogs (4).

Teratogenicity and reproductive effects

No significant effect of exposure on the frequency of abnormal karyotypes or on sex ratio was observed in 124 abortuses of women who had used oral contraceptives (11 had taken 4 mg megestrol acetate with 0.05 mg mestranol), compared with 122 abortuses of women who had never taken oral contraceptives (5).

Metabolism and toxicokinetics

Megestrol acetate is metabolised much more slowly than progesterone. *In vitro* studies of its metabolism by rat and rabbit liver enzymes found that the 17α-acetoxy group, the 6(7)-double bond and the 6-methyl group hinder enzymatic metabolism (7).

In humans, absorption of orally administered megestrol acetate from the gastro-intestinal tract is variable, with peak plasma concentration occurring 1-3 hr after dosage. It is mostly excreted unchanged in the urine; only 5-8% of the dose is excreted as metabolites (6).

Genotoxicity

In vitro human lymphocytes chromosomal aberrations negative (8).

In vivo mouse induction of unscheduled DNA synthesis and inhibition of DNA synthesis positive at 200 mg kg^{-1} (9).

Other effects

Other adverse effects (human)

Four women taking megestrol acetate experienced severe pain in the hands, similar to that of carpal tunnel syndrome (10).

Megestrol acetate has been associated with hyperglycaemia and diabetes mellitus in AIDS patients, weight gain in patients treated for breast cancer, adrenocortical deficiency and hypernoea (6).

Other comments

Biological activity of progestins reviewed (11).

General review of oral contraception (12).

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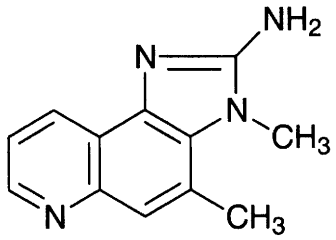
M45 MeIQ



$C_{12}H_{12}N_4$ **Mol. Wt.** 212.25 **CAS Registry No.** 77094-11-2

Synonyms 3,4-dimethyl-3*H*-imidazo[4,5-*f*]quinolin-2-amine; 2-amino-3,4-dimethylimidazo[4,5-*f*]quinoline

RTECS No. NJ 5907000

Occurrence Isolated from broiled fish and meat and beef extract.

Physical properties

M. Pt. 296-298°C

Solubility Organic solvents: dimethyl sulfoxide, ethanol, methanol

Environmental fate

Abiotic removal

Sensitive to activation by sunlight and fluorescent light (1).

Exposure of an acetone solution of the compound to sunlight for 1 hr resulted in conversion of the 2-amino group into a 2-nitro group (2).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).

Oral rat (58 wk) 14 doses of 10 mg kg^{-1} were administered in drinking water, a small number of Zymbal gland tumours were detected. Short exposures to low doses produced persistent procarcinogenic lesions. Secondary factors, promoters or high cell turnover may, over time, develop these lesions into cancer (3).

Gavage ♀ CFI mice, Sprague-Dawley rats (unspecified dose) administered twice with a 4-day interval induced colon cancer (4).

Fed CDF_1 mice (91 wk) 0.04 or 0.01% induced hepatocellular carcinomas and hepatocellular adenomas in ♀. Incidence of squamous cell carcinomas and papillomas were higher in both sexes (5).

In vivo rat liver medium-term bioassay (6 wk) showed increased foci (6).

Metabolism and toxicokinetics

Rapidly absorbed, metabolised and excreted in urine bile and faeces within 24 hr of oral administration to rats (2).
Metabolised along a number of pathways, including *N*-hydroxylation, aromatic hydroxylation, sulfonation and glucuronidation both *in vivo* and *in vitro* (2).
Activated to mutagenic form via *N*-hydroxylation by human hepatic cytochrome P_{450} (2).
MeIQ was not mutagenic to *Salmonella typhimurium* TA98/1,8-DNP6 (defective in esterifying activity) but was mutagenic to TA98 with metabolic activation, suggesting the ultimate mutagenic form is a reactive ester of the *N*-hydroxy derivative (2).

Genotoxicity

Salmonella typhimurium TA98, pYG 121 with metabolic activation positive (7,8).
Salmonella typhimurium NM 2009 with metabolic activation positive (9).
In vitro Chinese hamster V79 cells with metabolic activation induced sister chromatid exchange (10). *Drosophila melanogaster* DNA-repair test positive (11).
Intraperitoneal rat (2 hr) 80 mg kg^{-1} no DNA damage observed in stomach, small and large intestine, liver, kidney or testis. Intraperitoneal ♂ F344 rat 80 mg kg^{-1} or fed 0.03% MeIQ (13 day) induced DNA damage in large intestine, liver and kidney (12).
In vitro human mammary epithelial cells were treated with 500 μM MeIQ. The mean number of DNA adducts per 108 nucleotides was 6.63 (13).

Other comments

In vivo and *in vitro* mice bacterial mutation assays demonstrated that bran in the diet reduced the genotoxicity potential by restricting uptake of MeIQ from the gut lumen. Feeding mice a high-fat diet led to its hepatic conversion into an active genotoxin (14).
Toxicology and genetic effects reviewed (2).

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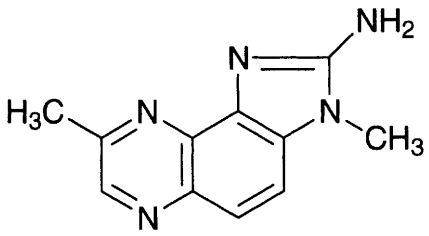
M46 MeIQx



$C_{12}H_{11}N_5$ **Mol. Wt.** 225.25 **CAS Registry No.** 77500-04-0

Synonyms 3,8-dimethyl-3*H*-imidazo[4,5-*f*]quinoxalin-2-amine; 2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline

RTECS No. NJ 5925500

Occurrence Has been detected in cooked fish, chicken, mutton and beef.

Physical properties

M. Pt. 295-300°C (with slight decomp.)

Solubility Organic solvents: dimethyl sulfoxide, methanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (1).

Oral ♂ F344 rats (56 wk) 100, 200 and 400 ppm. Tumours developed dose-dependently in liver, Zymbal glands and skin, but were lacking in the control group. Rats given 100 ppm developed benign tumours, rats given 200 and 400 ppm developed carcinomas (2).

Projected aggregate tumorigenic potency in ♂ humans (by surface area) 8.7 mg kg^{-1} day^{-1}, and 5.0 mg kg^{-1} day^{-1} for ♀ humans (3).

Newborn ♂ B6C3F mice were injected intraperitoneally with 0, 0.625 and 1.25 µmol of MeIQx dissolved in 5, 10 and 20 µl of dimethyl sulfoxide and administered at 1, 8 and 15 days after birth, respectively. A significant increase in hepatocellular adenomas was observed at 12 months: controls 5/44, low dose 8/24 and high dose 17/20 (1).

In vivo rat liver medium-term bioassay (6 wk) showed increased foci (4).

Metabolism and toxicokinetics

Oral, intravenous, intraperitoneal mouse (duration unspecified) 7-16% excreted unchanged, with 15-35% in the urine and 30-55% in the faeces (5).

In rabbit and human liver, activation of MEIQx was catalysed by cytochrome P_{450}IA2 (5).

Metabolised to 2-hydroxyamino-3,8-dimethylimidazo[4,5-*f*]quinoxaline by microsomal cytochrome P_{450} and is further activated to an acetylated form (6).

Incubation with mixed human faecal microflora under anaerobic conditions yielded 2-amino-3,6-dihydro-3,8-dimethylimidazo[4,5-*f*]quinoxalin-7-one as the major metabolite, but with low overall conversion (7).

In rat hepatocytes, ten metabolites were identified, including 2-(hydroxyamino)-3,8-dimethylimidazo[4,5-*f*]quinoxaline and its *N*-hydroxy-*N*-glucuronide (8).

Sulfate and glucuronide derivatives were detected in the urine of cynomolgus monkeys fed 2-amino-3,8-dimethylimidazo[4,5-*f*]quinoxaline (9).

In six ♂ humans fed 320 g of cooked ground beef, MeIQx was detected in urine after 12 hr (none was detected before the meal). 2-5% of ingested amount was excreted unchanged in urine (1).

After oral administration to mice (amount unspecified) 20-25% was excreted within 6 hr (1).

Activated by human liver microsomes to a DNA-reactive species (1).
Isolated rat liver cells transformed MeIQx into ten metabolites including *N*-hydroxy, 4- or 5-hydroxy, 8-hydroxymethyl and *N*-3-demethylated derivatives, sulfate and glucuronide derivatives of these compounds and sulfamate and glucuronide derivatives of MeIQx (1).
After intragastric administration to rats, 40 and 49% were recovered in urine and faeces, respectively, 20-25% in bile within 24 hr (1).
MeIQx was not mutagenic to *Salmonella typhimurium* TA98/1,8-DNP_6 (defective in esterifying activity) but mutagenic to TA98, suggesting that the ultimate mutagenic form is a reactive ester of the *N*-hydroxy derivative (1).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation positive (10).
Salmonella typhimurium NM 2009 with metabolic activation positive (11).
In vitro human lymphocyte cells with metabolic activation induced a low frequency of sister chromatid exchange (12).
Chronic and acute treatment of mice with MeIQx did not induce *DL6-1* mutations (13).
In vitro hamster hepatocytes unscheduled DNA synthesis weak dose-related response observed (14).
Drosophila melanogaster DNA-repair test positive (15).
Alkaline single cell gel electrophoresis assay detected statistically significant DNA damage in mouse liver, kidney, and brain following a single intraperitoneal injection of 13 mg kg^{-1} (16).

Other comments

The geometric mean value of MeIQx concentrations at 11 locations in the Yodo River systems (Japan) was 4.8 ng g^{-1} blue rayon equivalent (17).
Excreted in the urine of men after consumption of fried ground beef patties with 1.8-4.9% of the amount consumed excreted unchanged within 12 hr (1).
The binding of mutagens known to occur in fried or broiled food, including MeIQx, was investigated *in vitro*. Results showed water-insoluble fibre components were responsible for most of the binding capacity. There was a significant correlation between Klason lignin content and the binding of mutagens. Dietary fibre from sorghum had the highest binding capacity (18).
Toxicology and genetic effects reviewed (1).

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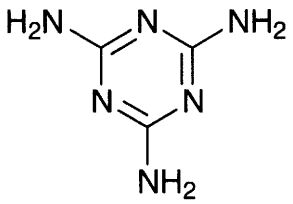
M47 melamine



$C_3H_6N_6$ **Mol. Wt.** 126.12 **CAS Registry No.** 108-78-1

Synonyms 1,3,5-triazine-2,4,6-triamine; cyanuramide; cyanurotriamide; isomelamide; Theoharn; 2,4,6-triaminotriazine

EINECS No. 203-615-4 **RTECS No.** OS 0700000

Uses Forms synthetic resins with formaldehyde which are used in the manufacture of laminates, surface coating resins, plastics, paper products, textile resins.

Physical properties

M. Pt. <250°C **B. Pt.** sublimes **Specific gravity** 1.573 at 16°C with respect to water at 4°C **Volatility** v.p. 50 mmHg at 315°C ; v.den. 4.34

Solubility Organic solvents: very slightly soluble in hot ethanol

Ecotoxicity

Bioaccumulation

Non accumulative or low accumulative (1).

Environmental fate

Nitrification inhibition

Nitrosomonas sp. 100 mg l^{-1} caused no inhibition of ammonium oxidation (2).

50 mg l^{-1} (threshold concentration) caused no inhibition of nitrifying bacteria (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 3160-3300 mg kg^{-1} (4,5).

LD_{100} intraperitoneal mouse 800 mg kg^{-1} (5).

LD_{100} intraperitoneal rat 3200 mg kg^{-1} (5).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (6).

National Toxicology Program tested (103 wk) rats and mice orally 2250 or 4500 ppm via food. No evidence of carcinogenicity in mice (♂ and ♀) or ♀ rats was reported. However, ♀ rats developed chronic inflammation of the kidneys and ♂ mice developed acute and chronic inflammation and epithelial hyperplasia of the urinary bladder and an increased incidence of bladder stones. ♂ rats developed transitional-cell carcinomas with incidences significantly higher in the high-dose group. There was an association between bladder stones and bladder tumours (7,8).

Teratogenicity and reproductive effects

Intraperitoneal administration of 70 mg kg^{-1} to rats on days 5 and 6, 8 and 9, or 12 and 13 of gestation caused no toxic effects or gross malformations of foetuses (9).

Metabolism and toxicokinetics

50% of an oral dose of 250 mg kg^{-1} recovered in urine of rats after 6 hr (10).

[^{14}C]melamine ♂ rat 90% excreted in urine within 24 hr; analysis showed that the melamine was not metabolised. Negligible radioactivity was detected in exhaled air or faeces whilst it was found concentrated in the kidney and bladder. By 24 hr virtually no radioactivity was detected in tissues (11).

Irritancy

0.5% patch test negative for irritancy and allergic reactions (12).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, with and without metabolic activation negative (13).

Escherichia coli microscreen assay (metabolic activation unspecified) positive (14).

In vitro mouse lymphoma L5178Y tk^+/tk^{-1} with and without metabolic activation negative (15).

In vitro Chinese hamster ovary cells with and without metabolic activation, sister chromatid exchanges equivocal and chromosomal aberrations negative (16).

Drosophila melanogaster fed on a diet containing melamine did not develop sex-linked recessive lethal mutations (17).

In vitro mouse bone marrow did not induce micronuclei (18).

Other effects

Other adverse effects (human)

Exposure to melamine-formaldehyde resins has caused dermatitis (19).

Any other adverse effects

X-Ray and infrared analysis of bladder stones obtained from melamine treated ♂ rats indicated the principal component was melamine (20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (21).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (22).

Other comments

Toxicity and hazards reviewed (23,24).

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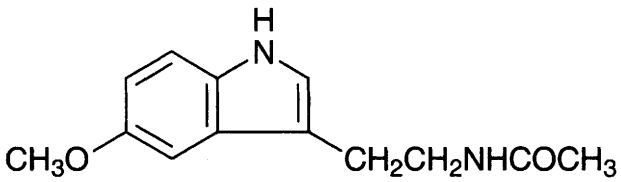
M48 melatonin



$C_{13}H_{16}N_2O_2$ **Mol. Wt.** 232.28 **CAS Registry No.** 73-31-4

Synonyms *N*-[2-(5-methoxy-1*H*-indol-3-yl)ethyl]acetamide; *N*-acetyl-5-methoxytryptamine

EINECS No. 200-797-7 **RTECS No.** AC 5955000

Uses Potential to alleviate jet lag and delayed sleep phase syndrome.
Occurrence Hormone produced in the pineal gland.

Physical properties

M. Pt. 116-118°C

Ecotoxicity

Toxicity to other species

In late pre- to pro-metamorphic *Rana catesbeiana* injected with ^{3}H-melatonin the highest uptake of label occurred in intestine, ventral skin and pituitary, the lowest in thyroid and brain, and intermediate in hindlimb, tail and gills. The simultaneous injection of 0.007 or 0.2 μg thyroxine caused an increase in the uptake of labelled melatonin into peripheral tissues that undergo major metamorphic changes but not into neural or endocrine organs (1).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 180 mg kg^{-1} (2).

Metabolism and toxicokinetics

The major metabolite is 6-hydroxymelatonin (3).

Radiolabelled (^{3}H) melatonin injected into spotted skunk jugular vein 1-3 hr before darkness. Relatively high amounts were found, after 22 min, in the pineal gland, liver, pituitary gland, ovary and kidney. Relatively small amounts were found in the brain, uterus, temporalis muscle and pancreas. The lung had the least (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 with and without metabolic activation negative (3).
In vitro mouse spleen lymphocytes DNA replication was unaffected by concentrations between 0.02 and 2×10^{-5} g (5).

Other effects

Any other adverse effects
Daily administration of 25 μg to gerbil led to increased eye lens weight. Wistar/NIN rats increased lens weight was dependent on time of administration (noon and 5pm) (6).
Intramuscular administration over 30 days to adult ♂ Indian finches inhibited thyroid activity, seasonal gonadal growth and activity and luteinising hormone-dependent plumage pigmentation. Inhibition of body weight growth was dependent on time of administration and dose (7).
Intravenously or intracerebroventricularly to rats did not produce any cardiovascular or ventilatory effects (8).

Other comments

Precursor is *N*-acetylserotonin (5).
Enhances both natural and acquired immunity in animals. Immune modulation and ageing reviewed (9).
Physiology, pharmacology, actions in optic and central nervous systems, oncology interactions reviewed (10-13).
Animal studies indicate that concentrations of γ-aminobutyric acid and serotonin are increased in the hypothalamus and midbrain and pyridoxal kinase activity is enhanced. Involved in oestrus, inhibition of gonadal development and protective changes in skin coloration. Secreted in a diurnal rhythm and may influence sleep patterns (14).

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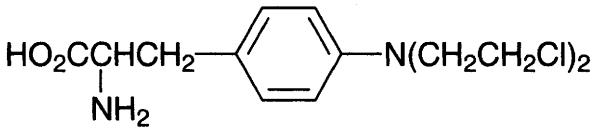
M49 melphalan



$C_{13}H_{18}Cl_2N_2O_2$ **Mol. Wt.** 305.20 **CAS Registry No.** 148-82-3

Synonyms 4-[bis(2-chloroethyl)amino]-L-phenylalanine; 3025 C.B.; levofalan; L-PAM; phenylalanine mustard; L-sarcolysine; Alkeran

EINECS No. 205-726-3 **RTECS No.** AY 3675000

Uses Antineoplastic chemotherapeutic agent.

Physical properties

M. Pt. 182-183°C (decomp.)

Solubility Organic solvents: ethanol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 11,200 μg kg^{-1} (1).

LD_{Lo} intravenous man 8140 mg kg^{-1} (2).

LD_{50} intravenous mouse 23 mg kg^{-1} (3).

Intravenous dog 0.75, 1.5 or 3.0 mg kg^{-1}. After 8-9 days post-administration lethargy, vomiting, general muscle weakness, dehydration and diarrhoea was observed at high dose. Necropsy revealed widespread lymphocytic depletion in all lymphoid tissues and in the bone marrow and spleen marked hypoplasia of haematopoietic tissue. A dose-related decrease in white blood cells occurred (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (5).

Patients developed acute non-lymphocytic leukaemia following treatment (6-10).

Dose-related increase in lung tumours in mice and peritoneal sarcomas in rats following intraperitoneal injection (11).

TD_{50} for tumours in ♀ mouse, ♂ mouse, ♀ rat, ♂ rat were, respectively, 0.10, 0.11, 0.078 and 0.047 mg kg^{-1} day^{-1} (12).

Metabolism and toxicokinetics

600 μg kg^{-1} body weight administered to cancer patients. When given orally systemic availability was very variable. Mean plasma terminal phase $t_{1/2}$ 90 min and mean 24 hr excretion in urine was 10.9% of dose. Mean peak plasma level was 280 ng ml^{-1} (13).

Following absorption it is quickly distributed throughout body water and is believed to be inactivated mainly by spontaneous hydrolysis. 50-60% is protein bound initially, rising to 80-90% after 12 hr (14).

Sensitisation

Skin rashes and hypersensitivity reactions may occur (species unspecified) (14).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation positive (15).

Salmonella typhimurium TA1537, TA1538 with and without metabolic activation negative (16).

In vitro human lymphocytes induced sister chromatid exchange in cells from heroin addicts and controls, with incidence higher in the former (17).

Drosophila melanogaster wing spot test positive (18).

Mouse germ cell mutagenicity studies gave positive result in dominant lethal test in ♂, heritable translocations and postmeiotic and premeiotic specific locus mutations (19).
In vivo bone marrow cells of ♂ B6C3F mouse micronucleus test and chromosomal aberrations induction positive (20).

Other effects

Other adverse effects (human)
Neutropenia, thrombocytopenia, bone-marrow depression, gastro-intestinal effects, haemolytic anaemia, vasculitis, pulmonary fibrosis, oedema, neurotoxicity, vesiculation of the skin and thrombophlebitis reported (14). Ovarian failure occurred in three young women given high doses (21).

Legislation

Land disposal regulated under the Federal Resource Conservation and Recovery Act (22).

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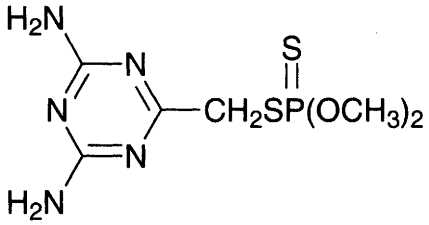
M50 menazon



$C_6H_{12}N_5O_2PS_2$ **Mol. Wt.** 281.30 **CAS Registry No.** 78-57-9

Synonyms phosphorodithioic acid, *S*-[(4,6-diamino-1,3,5-triazin-2-yl)methyl] *O,O*-dimethyl ester; phosphorodithioic acid, *S*-[(4,6-diamino-*s*-triazin-2-yl)methyl] *O,O*-dimethyl ester; *S*-[(4,6-diamino-1,3,5-triazin-2-yl)methyl] *O,O*-dimethyl phosphorodithioate; Abol X; Azidithion; Sayfos; Saphicol; Saphizon

EINECS No. 201-123-4 **RTECS No.** TD 5600000

Uses Superseded aphicide and fungicide.

Physical properties

M. Pt. 160-162°C (decomp.) **Volatility** v.p. 1×10^{-6} mmHg at 25°C

Solubility Water: 240 mg l^{-1} at 20°C. Organic solvents: ethanol glycol, 2-ethoxyethanol, 2-methoxyethanol, tetrahydrofurfurol

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R52/53)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S61)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) harlequin fish 220 mg l^{-1} (1).

Carp, ≥0.1 mg l^{-1} decreased blood corpuscles, cardiovascular activity and growth rate (2).

Rainbow trout and stickleback 30 mg l^{-1} caused death in 2-4 hr. Test conditions: total hardness 0-17 mg l^{-1}; methyl orange alkalinity 14 mg l^{-1}; and pH 7.6 (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken 487 mg kg^{-1} (4).

LD_{50} oral rat, mouse 427, 890 mg kg^{-1}, respectively (5,6).

LD_{50} oral mouse 427 mg kg^{-1} (6).

Dermal rabbit (24 hr) 500-800 mg kg^{-1} caused no local or systemic effects (1).

Sub-acute and sub-chronic data

Oral rat (90 day) no-effect level 30 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects

Oral rat (2 yr) 250, 1000, 4000 mg kg^{-1} diet showed no significant effect other than inhibition of cholinesterase activity (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (7).
Pesticides are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Residues have been found in meat and fish.

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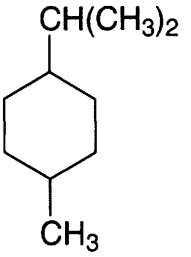
M51 *trans-p*-menthane



$C_{10}H_{20}$ **Mol. Wt.** 140.27 **CAS Registry No.** 1678-82-6

Synonyms 1-isopropyl-4-methylcyclohexane; 1-methyl-4-(1-methylethyl)-*trans*-cyclohexane

Mammalian & avian toxicity

Irritancy

At 2% and 5% in ethanol, recovery from oedema and erythema occurred within 48 hr in rats and rabbits (1).

References

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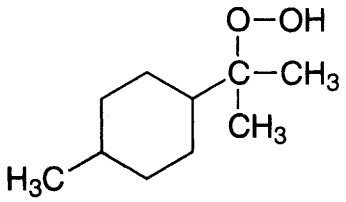
M52 *p*-menthane hydroperoxide



$C_{10}H_{20}O_2$ **Mol. Wt.** 172.27 **CAS Registry No.** 26762-92-5

Synonyms 1-methyl-1-(4-methylcyclohexyl)ethyl hydroperoxide; *p*-menth-8-yl hydroperoxide

EINECS No. 247-987-6 **RTECS No.** OS 9450000

Physical properties

Flash point 71°C **Specific gravity** 0.910-0.925 at 15.5°C with respect to water at 4°C

Occupational exposure

Supply classification oxidising, corrosive

Risk phrases May cause fire – Harmful by inhalation – Causes burns (R7, R20, R34)

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 acids – 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)

Genotoxicity

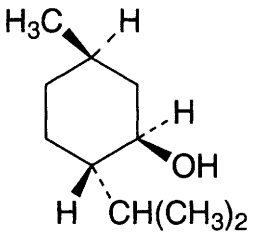
Salmonella typhimurium TA97 with and without metabolic activation weakly positive (1).

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (1).

References

1. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-157

M53 menthol



$C_{10}H_{20}O$ **Mol. Wt.** 156.27 **CAS Registry No.** 1490-04-6

Synonyms 5-methyl-2-(1-methylethyl)cyclohexanol; 2-isopropyl-5-methylcyclohexanol; 5-methyl-2-isopropylcyclohexanol; menthyl alcohol; *p*-menthan-3-ol

EINECS No. 216-074-4 **RTECS No.** OT 0350000

Uses In liqueurs, perfumery, confectionery, cigarettes, cough drops. A topical antipruritic. Veterinary local anaesthetic and antiseptic and internally as carminative and gastric sedative.

Occurrence In peppermint oil and from *Mentha* spp.

Physical properties

M. Pt. 41-43°C **B. Pt.** 212°C **Flash point** 110.6°C **Specific gravity** 0.890 **Volatility** v.p. 1 mmHg at 56°C ; v.den. 5.38

Solubility Water: slightly soluble in water. Organic solvents: chloroform, diethyl ether, ethanol, glacial acetic acid, liquid petroleum, light petrol

Ecotoxicity

Bioaccumulation

Confirmed to be non-accumulative or low accumulative (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3180 mg kg^{-1} (2).

LD_{Lo} oral cat 1500 mg kg^{-1} (3).

LD_{Lo} intraperitoneal rat, mouse 1500, 1800 mg kg^{-1}, respectively (4,5).

LD_{50} intramuscular rat 10 g kg^{-1} (6).

LD_{Lo} intravenous cat ~37 mg kg^{-1} (5).

Metabolism and toxicokinetics

Excreted in urine and bile as a glucuronide (7).

Irritancy

750 μg instilled into rabbit eye caused severe irritation (8).

Sensitisation

May cause hypersensitivity reactions including contact dermatitis (7).

Other effects

Other adverse effects (human)

Ataxia, confusion, nystagmus, euphoria and diplopia were experienced when recommended dose of a preparation was exceeded (9).

Apnoea and collapse reported in infants following local application to nostrils. Taken orally, nausea, vomiting, vertigo, abdominal pain, ataxia, drowsiness and coma have been reported (7).

Other comments

Toxicity reviewed (10).

References

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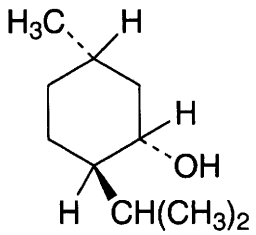
2. *Food Cosmet. Toxicol.* 1964, **2**, 327.
3. *Abdernalden's Handbuch der Biologischen Arbeitsmethoden* 1935, **4**, 1289.
4. *Ann. Pharm. Fr.* 1952, **10**, 481.
5. *Arch. Int. Pharmacodyn. Ther.* 1939, **63**, 43.
6. *Naunyn-Schmiedeberg's Arch. Pharmakol.* 1954, **222**, 244.
7. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
8. *Am. J. Ophthalmol.* 1946, **29**, 1363.
9. O'Mullane, N. M. et al *Lancet* 1982, **i**, 1121.
10. *BIBRA Toxicity Profile* 1991, British Industrial Biological Research Association, Carshalton, UK

M54 DL-menthol



$C_{10}H_{20}O$ **Mol. Wt.** 156.27 **CAS Registry No.** 15356-70-4

Synonyms 5-methyl-2-(1-methylethyl)cyclohexanol, (1α,2β,5α)-(±)-; (±)-*cis*-1,3-*trans*-1,4-menthol; (±)-menthol; hexahydrothymol; menthacamphor; menthol; menthomenthol; peppermint camphor

EINECS No. 239-388-3 **RTECS No.** OT 0525000

Uses Cigarettes, pharmaceutical rubs and liniments, nasal sprays, antipruritic lotions, expectorants, cough drops and foot powders.

Occurrence In the oils of *Mentha arvensis*.

Physical properties

M. Pt. 43-44°C **B. Pt.** 103-104°C at 9 mmHg **Flash point** 91°C **Specific gravity** 0.904 at 15°C with respect to water at 15°C

Solubility Organic solvents: ethanol, diethyl ether, acetone, benzene

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2900, 3100 mg kg^{-1}, respectively (1,2).

LD_{Lo} subcutaneous rat 1 g kg^{-1} (3).

LD_{Lo} intraperitoneal cat, rabbit 1500, 2000 mg kg^{-1}, respectively (1,3).
LD_{50} intraperitoneal guinea pig 865 mg kg^{-1} (4).

Carcinogenicity and chronic effects
National Toxicology Program administered orally in feed 3750 or 7500 ppm to Fischer 344 rats and either 2000 or 4000 ppm to B6C3F1 mice for 103 wk. Mean body weights were slightly lower but no other effects were observed. ♀ rats showed the only dose-related trend in mortality. Non-carcinogenic (5,6).

Irritancy
Dermal rabbit (24 hr) 500 mg caused well-defined erythema and slight oedema (7).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (8).
In vitro mouse lymphoma L5178Y with and without metabolic activation negative (9).

Other effects

Any other adverse effects
Lethal to *in vitro* mouse lymphoma L5178Y cells at 200 μg ml^{-1} with and without metabolic activation. Metabolic activation tended to reduce the toxicity of non-lethal concentrations (9).

References

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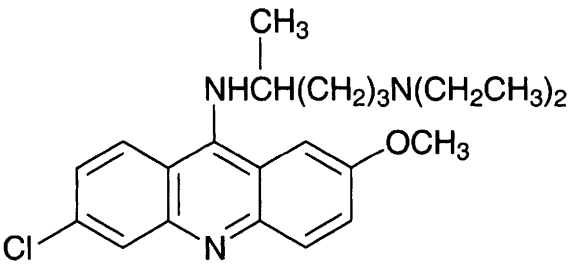
M55 mepacrine



$C_{23}H_{30}ClN_3O$ **Mol. Wt.** 399.96 **CAS Registry No.** 83-89-6

Synonyms quinacrine; Acrichin; Acrinamione; atabrine; antimalarina; 6-chloro-9-[[4-(diethylamino)-1-methylbutyl]amino]-2-methoxyacridine; N^1,N^1-diethyl-N^4-(6-chloro-2-methoxy-9-acridinyl)-1,4-pentanediamine

EINECS No. 201-508-7 **RTECS No.** AR 7875000

Uses Anthelmintic. Antimalarial drug.

Physical properties

M. Pt. 248°C (decomp.)
Solubility Water: 3% (dihydrochloride). Organic solvents: ethanol, methanol

Ecotoxicity

Fish toxicity
Not toxic to brown trout, bluegill sunfish, goldfish or yellow perch 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 and 12.8°C (1).

Environmental fate

Nitrification inhibition
50% inhibition of nitrite oxidation at 50 mg l^{-1} (quinacrine dihydrochloride) (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken, mouse 710, 1300 mg kg^{-1}, respectively (3,4).
LD_{50} subcutaneous mouse 240 mg kg^{-1} (5).
LD_{50} intravenous mouse, rabbit 8, 50 mg kg^{-1} respectively (6).

Sub-acute and sub-chronic data
Oral dog 375-500 mg $animal^{-1}$ day^{-1} for 15 days. These doses were lethal to most animals. Disturbances in the histology of the eyes were reported (7).

Metabolism and toxicokinetics
Rapidly and completely absorbed following intraperitoneal injection to rabbits and humans. Mean absorption $t_{1/2}$ ~7 min (8).
Readily absorbed from the human gastrointestinal tract. Crosses the placenta. Significant amounts can still be detected in the urine for at least 2 months after therapy is discontinued (9).
In rabbits metabolites include 6-chloro-9-(4-ethylamino-1-methylbutylamino)-2-methoxyacridine (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, with and without metabolic activation positive TA100, TA1535 with and without metabolic activation negative (dihydrochloride) (11).
Drosophila melanogaster zeste somatic eye colour mutation assay and sex-linked recessive lethal assay positive (12).
In vitro mouse BALB/c3T3 1-13 cells, DNA damage positive (13).

Other effects

Other adverse effects (human)
The most common adverse effects from therapeutic use are dizziness, headache and gastro-intestinal disturbances. Transient acute toxic psychosis and central nervous stimulation have also been reported (14).

Other comments

Quinacrine dihydrochloride CAS RN 000069-05-6

References

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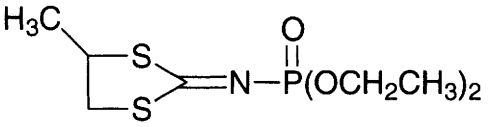
M56 mephosfolan



$C_8H_{16}NO_3PS_2$ **Mol. Wt.** 269.33 **CAS Registry No.** 950-10-7

Synonyms diethyl 4-methyl-1,3-dithiolan-2-ylidenephosphoramidate; (4-methyl-1,3-dithiolan-2-ylidene)phosphoramidic acid, diethyl ester; phosphonadithioimidocarbonic acid, cyclic propylene *P,P*-diethyl ester; Cytrolane; AC 47470; imidocarbonic acid, phosphonodithio-, cyclic propylene

EINECS No. 213-447-3 **RTECS No.** JP 1050000

Uses Superseded insecticide and acaricide.

Physical properties

B. Pt. 120°C at 0.001 mmHg **Specific gravity** 1.539 at 26°C **Partition coefficient** log P_{ow} 1.0414 (1)
Solubility Water: 57 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, dichloroethane, ethanol, toluene, xylene

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Very toxic in contact with skin and if swallowed – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R27/28, R51/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S36/37/39, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 2 mg l^{-1} (1).
LC_{50} (96 hr) carp 55 mg l^{-1} (1).

Invertebrate toxicity
LD_{50} topical application bee 3.5 µg bee^{-1} (1).

Environmental fate

Degradation studies
$t_{1/2}$ in soil 7-13 day. Rate of degradation decreased with decreased soil pH (2).

Accelerated degradation by soil following as little as one exposure can reduce efficiency as an insecticide; >95% degraded in previously treated hop yard soils after 8 wk at 15°C compared with 23-35% in untreated soil (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral Japanese quail 13 mg kg^{-1} (1).
LD_{50} oral chicken 2.8 g kg^{-1} (4).
LD_{50} oral rat, mouse 9, 11 mg kg^{-1}, respectively (1,4).
LD_{50} dermal rabbit 10-29 mg kg^{-1} (1,5).

Sub-acute and sub-chronic data

Oral rat (90 day) 15 mg kg^{-1} diet caused a reduction in erythrocyte and brain cholinesterase activities, but no significant effect on weight gain (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).
WHO Toxicity Class Ia (8).
EPA Toxicity Class I (1).

Other comments

Environmental pollutant.

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
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M57 meprobamate

$$NH_2C(O)OCH_2C(CH_3)(CH_2CH_2CH_3)CH_2OC(O)NH_2$$

$C_9H_{18}N_2O_4$ **Mol. Wt.** 218.25 **CAS Registry No.** 57-53-4

Synonyms Miltown; 2-methyl-2-propyl-1,3-propanediol dicarbamate; carbamic acid, 2-methyl-2-propyltrimethylene ester; Bamate; Bamo; Meprospam

EINECS No. 200-337-5 **RTECS No.** TZ 0175000

Uses Anxiolytic with hypnotic, sedative and some muscle relaxant properties. Used to treat anxiety disorders and for short-term management of insomnia, although largely superseded by benzodiazepines.

Physical properties

M. Pt. 104-106°C
Solubility Water: 0.34% (w/w) at 20°C. Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral starling 127 mg kg^{-1} (1).
LD_{50} oral rat, mouse 750, 1000 mg kg^{-1}, respectively (2,3).
LD_{50} intravenous mouse, rat 230, 350 mg kg^{-1}, respectively (4,5).

Teratogenicity and reproductive effects
Two studies reported significantly higher rates of severe congenital defects following administration to women during early pregnancy (6,7), while another did not (8).
Teratogenic and embryotoxic in mice after subcutaneous administration of 0.75 mg g^{-1} on day 10 or 12 of pregnancy. Principal abnormalities were club foot or affected fingers and toes (9).
Not teratogenic in rats or rabbits (dose, duration and route unspecified) (10).
1000 μg ml^{-1} affected crown-rump length, differentiation, yolk sac size and vascularisation, and 300 μg l^{-1} affected morphology in whole rat embryos cultured during early stages of organogenesis (11).
Rodent embryo limb bud cell culture *in vitro* teratogen screen positive (inhibited cartilage formation) (12).

Metabolism and toxicokinetics
Elimination from blood in rabbits unaffected by daily doses of 0.4 g kg^{-1} ethanol and accelerated by 1.6 g kg^{-1} (13).
Readily absorbed from human gut; plasma concentrations peak after 1-3 hr. Widely distributed; extensively metabolised in the liver and excreted in urine mainly as a hydroxylated metabolite and its glucuronide conjugate. <10% excreted unchanged. $t_{1/2}$ 6-16 hr, but may be prolonged after chronic administration. Crosses the placenta and appears in human milk at 4 × maternal plasma concentration (14).

Sensitisation
Hypersensitivity may occur in patients, causing rashes, urticaria, purpura, angioedema, bronchospasm and anuria. Erythema multiforme and exfoliative or bullous dermatitis have also been reported (14).

Other effects

Other adverse effects (human)
Barbiturate-like profile of action. When administered at 600-3600 mg to men with previous histories of drug misuses, they reported mood and sleep sedation effects but not tranquilisation. Likelihood of abuse equals or exceeds that of Lorazepam, but is less likely to produce adverse behavioural effects (15).
Lowest lethal dose in humans (route unspecified) 441 mg kg^{-1} (16).
Side-effects include drowsiness, nausea, vomiting, diarrhoea, paraesthesia, weakness, headache, paradoxical excitement, dizziness, ataxia and visual disturbances. Hypotension, tachycardia and cardiac arrhythmias may occur. Blood disorders including agranulocytosis, eosinophilia, leucopenia, thrombocytopenia and aplastic anaemia have been reported. Caution is required for use in patients with impaired liver or kidney function, mental or respiratory function depression. It may cause convulsions in epileptics. It is unsafe for patients with acute porphyria and its effects are enhanced by alcohol and other central nervous system depressants (14).

Legislation

Controlled substance (depressant) listed in US Code of Federal Regulations, TA621, Part 1308.14, 1987.

Other comments

2.6 μg l^{-1} predicted in River Lee (17).

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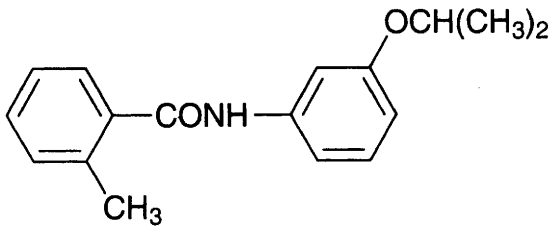
M58 mepronil



$C_{17}H_{19}NO_2$ **Mol. Wt.** 209.29 **CAS Registry No.** 55814-41-0

Synonyms 2-methyl-*N*-[3-(1-methylethoxy)phenyl]benzamide; 3′-isopropoxy-*o*-toluanilide; 3′-isopropoxy-2-methylbenzanilide; Basitac

RTECS No. CV 5581700

Uses Systemic fungicide, mainly used to treat *Puccinia* and *Typhula* infection in wheat.

Physical properties

M. Pt. 92-93°C **Flash point** 225°C **Partition coefficient** log P_{ow} 3.66 **Volatility** v.p. 4.2×10^{-7} mmHg at 20°C
Solubility Water: 12.7 mg l^{-1} at 20°C. Organic solvents: acetone, acetonitrile, benzene, hexane, methanol

Occupational exposure

JP-OEL 5 mg m^{-3}

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) carp, rainbow trout 8-10 mg l^{-1} (1).

Invertebrate toxicity
LD_{50} oral honey bee >0.1 mg bee^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral hen >8 g kg^{-1} (1).
LD_{50} oral rat, mouse >10 g kg^{-1} (1).
LC_{50} (6 hr) rat >1.32 mg l^{-1} (1).
LD_{50} dermal rabbit, rat >10 g kg^{-1} (1).

Carcinogenicity and chronic effects
No-effect level in 2-yr feeding trial in ♂ rats 5.9 mg kg^{-1}; ♀ rats 72.9 mg kg^{-1} (1).

Irritancy
Non-irritating to eyes and skin of rabbits (1).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (2).
WHO Toxicity Class Table 5 (3).
EPA Toxicity Class IV (1).
ADI 0.05 mg kg^{-1} (4).

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M59 mercaptoacetic acid

$$HSCH_2CO_2H$$

$C_2H_4O_2S$ **Mol. Wt.** 92.12 **CAS Registry No.** 68-11-1

Synonyms 2-sulfanylethanoic acid; 2-mercaptoethanoic acid; thioglycolic acid; Thiovanic Acid

EINECS No. 200-677-4 **RTECS No.** AI 5950000

Uses Reagent for iron, tin, molybdenum and silver. In manufacture of thioglycolates.

Physical properties

M. Pt. –16.5°C **B. Pt.** 104-106°C at 11 mmHg **Flash point** 125°C **Specific gravity** 1.325 at 20°C with respect to water at 4°C **Volatility** v.p. 10 mmHg at 18°C
Solubility Water: miscible. Organic solvents: miscible with benzene, chloroform, diethyl ether, ethanol

Occupational exposure

FR-VME 1 ppm (5 mg m^{-3})
SE-LEVL 1 ppm (4 mg m^{-3}) **SE-STEL** 2 ppm (8 mg m^{-3})
UK-LTEL 1 ppm (3.8 mg m^{-3})

US-TWA 1 ppm (3.8 mg m^{-3})

UN No. 1940 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Causes burns (R23/24/25, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the eyes – Take off immediately all contaminated clothing – 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, S25, S27, S28, S45)

Ecotoxicity

Fish toxicity
5 ppm (24 hr) did not cause symptoms of sickness in rainbow trout, bluegill sunfish, yellow perch or goldfish. Test conditions: pH 7.0; dissolved oxygen content 7.5 ppm; total hardness (soap method) 300 ppm; methyl orange alkalinity 300 ppm; free carbon dioxide 5 ppm; and temperature 12.8°C (1).

Environmental fate

Degradation studies
Activated sludge (special respirometer) BOD 20°C 1-5 days observed, feed 662 mg l^{-1} acclimation: 1 day: no removal or oxidation (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 242 mg kg^{-1} (3).
LD_{Lo} dermal rabbit 300 mg kg^{-1} (4).
LD_{50} intraperitoneal rat, mouse 70, 138 mg kg^{-1}, respectively (3,5).

Irritancy
Corrosive irritant to skin (6).

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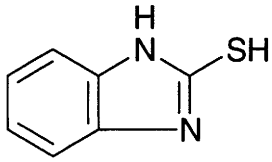
M60 2-mercaptobenzimidazole



$C_7H_6N_2S$ **Mol. Wt.** 150.20 **CAS Registry No.** 583-39-1

Synonyms 2-sulfanylbenzimidazole; 2-benzimidazolethiol; *o*-phenylenethiourea; autigene MB; USAF EK-6540

EINECS No. 209-502-6 **RTECS No.** DE 1050000

Physical properties

M. Pt. 301-305°C

Ecotoxicity

Invertebrate toxicity

EC_{50} (5-30 min) *Photobacterium phosphoreum* 86.4 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 476, 1250 mg kg^{-1}, respectively (2,3).

LD_{50} intravenous mouse 180 mg kg^{-1} (4).

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (5).

Irritancy

500 mg applied to skin or eyes of rabbits for 24 hr caused mild irritation (2).

100 mg instilled into rabbits' eyes caused moderate to severe irritation with corneal involvement persisting >24 hr but with recovery within 21 days (6).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).

Other comments

Physical properties reviewed (8).

Reviews on human health effects, experimental toxicity and workplace experience listed (9).

Impurities in 2-mercaptobenzimidazole produced in Shanghai, China reported as responsible for mutagenicity in the Ames test (10).

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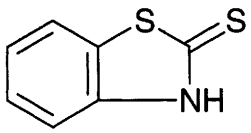
M61 2-mercaptobenzothiazole



$C_7H_5NS_2$ **Mol. Wt.** 167.26 **CAS Registry No.** 149-30-4

Synonyms 2-sulfanylbenzothiazole; captax; MBT; 2-benzothiazolethiol; rotax; NCI-C56519; USAF GY-3

EINECS No. 205-736-8 **RTECS No.** DL 6475000

Uses Rubber vulcanisation accelerator. Salts used as fungicide.

Physical properties

M. Pt. 180-182°C **Specific gravity** 1.42

Solubility Water: practically insoluble. Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

Supply classification harmful

Supply classification dangerous for the environment

Risk phrases May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R43, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – Wear suitable gloves – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S24, S37, S60, S61)

Ecotoxicity

Fish toxicity

Fatal concentration (48 hr) goldfish 2 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (5-30 min) *Photobacterium phosphoreum* 0.681 ppm Microtox test (2).

Killed microorganisms present in municipal treatment plant sludge in 2-3 days (3).

Bioaccumulation

No or low accumulation (4).

Environmental fate

Degradation studies

Non-biodegradable (4).

Did not degrade during Pitter's kinetic test of biodegradation (3).

TOC, COD and BOD_5 57.8, 230 and 5.5 mg l^{-1} O_2 respectively; γ irradiation did not improve biodegradation (3).

Biological purification of wastewaters can be achieved as long as the concentration of MBT in the influent does not exceed 100 mg l^{-1} (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1490-1560 mg kg^{-1} (6,7).

LD_{50} intraperitoneal mouse, rat 100, 300 mg kg^{-1}, respectively (8,9).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via gavage 5 days wk^{-1} for 103 wk. No evidence of carcinogenicity in ♂ mice dosed with 375 or 750 mg kg^{-1}, equivocal evidence in ♀ mice, some evidence of carcinogenicity in ♂ and ♀ rats (10).

Increased tumour rates in NTP study were adrenal gland phaeochromocytoma in ♂ and ♀ rats, pituitary gland adenoma in ♀ rats, leukaemia and adenoma of the pancreas and preputial gland in ♂ rats, and liver adenoma and carcinoma in ♀ mice (11).

Reduced weight gain and renal histopathological changes reported in mice fed 1920 ppm in the diet for 20 months (6).

Metabolism and toxicokinetics

Rats and guinea pigs absorbed 16.1-17.5% and 33.4%, respectively, of a topical radiolabelled dose. 72 hr after intravenous administration 90.9-100% appeared in urine of rats; results were similar after oral administration. No unchanged mercaptobenzothiazole was detected in urine, but two metabolites were identified; one was a thioglucuronide derivative and the other possibly a sulfonic acid derivative (12).

Irritancy

5 and 10% solutions caused skin irritation in guinea pigs (13).

Sensitisation

Cross-sensitisation to morpholinylmercaptobenzothiazole reported in guinea pigs (13).

Hypersensitivity reported in a miner, and cross-sensitisation to the rubber additive 2,2′-dibenzothiazyl disulfide (14).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative. Equivocal results also reported (15).

Mouse lymphoma L5178Y cell assay without metabolic activation negative, with metabolic activation positive; induced sister chromatid exchanges and chromosomal aberrations in Chinese hamster ovary cells with metabolic activation, but only sister chromatid exchanges without metabolic activation (16,17).

Other comments

The toxicity towards microorganisms has been particularly attributed to its metal chelating properties and/or its interference with membrane-bound (co)enzymes (5).

Report compiled by the German Advisory Committee on Existing Chemicals under the German Chemical Act (18).

Reviews on human health effects, experimental toxicity, environmental effects, ecotoxicology and exposure levels listed (19).

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M62 2-mercaptoethanol

$$HOCH_2CH_2SH$$

C_2H_6OS **Mol. Wt.** 78.14 **CAS Registry No.** 60-24-2

Synonyms 2-sulfanylethanol; 2-hydroxyethyl mercaptan; monothioethylene glycol; 2-thioethanol; thioglycol; 2-ME; USAF EK-4196

EINECS No. 200-464-6 **RTECS No.** KL 5600000

Uses In organic synthesis, biochemical research tool, catalyst.

Physical properties

B. Pt. 157°C (decomp) **Flash point** 73°C **Specific gravity** 1.1168 at 20°C with respect to water at 20°C
Volatility v.p. 1 mmHg at 20°C ; v.den. 2.69
Solubility Water: miscible. Organic solvents: benzene, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
May alleviate toxicity of heavy metals in N_2-fixing cyanobacteria in aquatic ecosystems (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 190, 244 mg kg^{-1}, respectively (2).
LC_{50} (15 min) inhalation mouse 13,200 mg m^{-3} (2).
LD_{50} dermal guinea pig 300 mg kg^{-1} (3).
LD_{50} intravenous mouse 480 mg kg^{-1} (4).

Irritancy
Severe eye irritant in rabbits after application of 2280 mg (duration unspecified) (5).
0.1 ml instilled into rabbit's eye caused corneal damage lasting >21 days (6).

Genotoxicity

Interferes with microtubule in mouse embryo cells *in vitro* (7).

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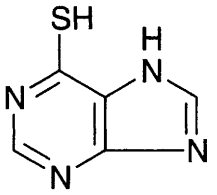
M63 6-mercaptopurine



$C_5H_4N_4S$ **Mol. Wt.** 152.18 **CAS Registry No.** 50-44-2

Synonyms 6-sulfamylpurine; 6-purinethiol; purine-6-thiol; 1,7-dihydro-6*H*-purine-6-thione; 6-thiopurine; Leukerin; Ismipur; Purinethol

EINECS No. 200-037-4 **RTECS No.** UO 9800000

Uses Antineoplastic used for treatment, chiefly in maintenance programmes, of acute myeloblastic leukaemia and chronic myelocytic leukaemia. It acts as an antimetabolite.

Physical properties

M. Pt. 313-314°C (decomp.)
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 260 mg kg^{-1} (1).
LD_{50} intraperitoneal ♂ mouse 240 mg kg^{-1} (2).

Carcinogenicity and chronic effects
No evidence for carcinogenicity in limited studies in experimental animals, insufficient data to make an evaluation in humans, IARC classification group 3 (3).

Teratogenicity and reproductive effects
Transient profound oligospermia reported in a man treated with 150 mg day^{-1} 6-mercaptopurine plus 80 mg day^{-1} prednisone (4).
Of two babies born to a woman treated with 6-mercaptopurine and radiation during both pregnancies, one had severe multiple anomalies including microphthalmia, corneal opacities, cleft palate and thyroid and ovarian hypoplasia; received busulfan during the pregnancy which resulted in the anomalous baby (5).
Rats fed 1000 μg zinc g^{-1} diet showed fewer adverse effects on reproduction and embryogenesis than those fed less zinc; the rats received 27.5 mg kg^{-1} on day-11 of pregnancy (6).
In utero exposed mice were sterile or had small litters and more dead foetuses (7). 50% foetal death occurred in rats after oral administration of 5 mg kg^{-1} on days 7 and 8 of pregnancy (8).
Malformations reported in rats and mice given 50 mg kg^{-1} on days 5-9 or 6-12 (rats) and 6-8 (mice) of pregnancy; central nervous system anomalies occurred at 0.5-1 mg kg^{-1} (9,10).
Gut, liver, limb, palate, mandible and tongue malformations reported in Syrian hamsters after intraperitoneal administration of 5-9 mg kg^{-1} on day-9 of pregnancy; the teratogenic effect was less marked if dosed on day-8 or 10-11 (11).

Metabolism and toxicokinetics
In humans, variably and incompletely absorbed from the gut; 40-50% of oral doses have been reportedly absorbed (3,12).
Absolute bioavailability is somewhat lower and varies widely between individuals, which may be due to thiopurine methyltransferase activity (resulting in methylation and inactivation of mercaptopurine instead of formation of active nucleotides) (12).

Distributed widely after absorption (12); after intravenous administration to mice concentrations were highest in the liver, gut and other organs but low in the brain (3).
Crosses the blood-brain barrier to some extent; it was found in subtherapeutic levels (10% of plasma level) in cerebrospinal fluids (3,12).
Plasma $t_{1/2}$ is 10-90 min after intravenous injection (12) and 90 min after oral administration (3); it is not found in plasma after 8 hr (12).
Activated intracellularly by conversion into nucleotide derivatives (6-thionucleotides) (3,12).
Intracellular metabolites are 6-methylmercaptopurine, ribonucleoside mono-, di- and triphosphates (3).
Rapidly and extensively metabolised in the liver by methylation, oxidation and formation of inorganic sulfates. Considerable amounts are oxidised to thiouric acid by xanthine oxidase (12).
Excreted in urine unchanged (46% of an oral dose and 71% of an intravenous dose over 24 hr) and as 6-thiouric acid; 6-methylthio-2,8-dihydroxypurine; 6-methylthio-8-hydroxypurine glucuronide; inorganic sulfate; and 6-methylsulfinyl-8-hydroxypurine. The first two predominate after intravenous administration and the latter two after oral (3).
In mice given a single intraperitoneal dose of 10 mg kg^{-1} 21.4% was excreted unchanged in urine, 18.9% as 6-thiouric acid and 29.5% as inorganic sulfate. Blood $t_{1/2}$ 14 min in mice and 9 min in rats (3).

Genotoxicity

Salmonella typhimurium TA1535, G46 without metabolic activation positive (13).
Induced sister chromatid exchanges in human peripheral lymphocytes and bone marrow cells *in vitro* (14,15).
In vivo mouse bone marrow micronucleus test positive (16,17).
Induced chromosomal aberrations in bone marrow cells of rats and Chinese hamster after intraperitoneal administration and in mice after oral or parenteral administration (18).

Other effects

Other adverse effects (human)
Major toxic effect is white cell depression. Higher doses used in the past (2.5-5 mg kg^{-1} day^{-1}) caused reversible jaundice. Less common side-effects include nausea, mucosal ulceration, skin rash and fever (3).
Crystalluria with haematuria, and skin hyperpigmentation have been observed rarely (12).
Its effects are enhanced by allopurinol. It may diminish warfarin activity. Its hepatoxicity may be enhanced by doxorubicin, and concurrent administration of methotrexate increases plasma concentrations of mercaptopurine (12).

Any other adverse effects
6-Mercaptopurine had pronounced effects on zinc, copper, calcium and magnesium metabolism in maternal and foetal rat tissue which may play a role in teratogenesis (6).
Predominant toxicity in rats and mice is bone marrow and gut epithelial damage and liver necrosis (3).

Other comments

Urine and faeces produced by patients up to 48 hr and 5 days, respectively, should be handled wearing protective clothing (12).
Destruction of mercaptopurine wastes to non-mutagenic residues by oxidation with potassium permanganate in sulfuric acid has been described (19).

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M64 mercury

Hg

Hg **Mol. Wt.** 200.59 **CAS Registry No.** 7439-97-6

Synonyms quicksilver; hydrargyrum; NCI-C60399; RCRA Waste No. U151

EINECS No. 231-106-7 **RTECS No.** OV 4550000

Uses Cathode in sodium chloride electrolysis. In the electrical industry, in control instruments in the home and industry and in laboratory and medical instruments. In gold extraction. In dental amalgam.

Occurrence Abundance in earth's crust 0.5 ppm.

Obtained by roasting cinnabar (mercuric sulfide).

Natural mercury arises from the Earth's crust through volcanic gases and evaporation from oceans and amounts to between 25,000 and 125,000 tonnes per yr. The three major mercury species are: elemental mercury Hg^0, inorganic mercury Hg^{2+}, and methyl mercury CH_3Hg^+. 99% of atmospheric mercury exists as Hg^0. However, particulate mercury accounts for all of the mercury wet and dry deposition (1,2).

Physical properties

M. Pt. -38.87°C **B. Pt.** 356.72°C **Specific gravity** 13.534 at 25°C **Volatility** v.p. 0.0012 mmHg at 20°C

Solubility Water: 0.28 μmol l^{-1} (25°C)

Occupational exposure

DE-MAK 0.012 ppm (0.1 mg m^{-3})

FR-VME 0.05 mg m^{-3} (vapour)

JP-OEL 0.05 mg m^{-3}

SE-LEVL 0.03 mg m^{-3} (vapour)

UK-LTEL 0.025 mg m^{-3}

US-TWA 0.025 mg m^{-3}

UN No. 2809 **HAZCHEM Code** 2Z **Conveyance classification** corrosive substance

Supply classification toxic

Risk phrases Toxic by inhalation – Danger of cumulative effects (R23, R33)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7, S45)

Ecotoxicity

Fish toxicity

LC_{50} (28 day) rainbow trout 0.005 mg l^{-1} (3).

LC_{50} (96 hr) fathead minnow, snakehead fish 0.17, 0.9 mg Hg l^{-1} (as $HgCl_2$), respectively (4,5).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 0.0052 mg l^{-1} (6).

LC_{50} (96 hr) *Lymnaea acuminata, Nais communis, Ilyodrilus frantzi, Aplexa hypnorum* 0.023-0.36 mg l^{-1} (7-9).

The cyanobacterium *Pharmidium fragile* was exposed to increasing concentrations of mercury from 0.01 to 1.5 mg l^{-1}. A decrease in dry biomass yield, protein content, chlorophyll a, and carotenoids was observed with increased mercury concentration. Malate dehydrogenase, glutamate dehydrogenase, and nitrate reductase activities were suppressed by increased mercury concentration, whereas glutamic-oxalacetic transaminase and glutamic-pyruvic transaminase were not affected (10). .

Bioaccumulation

Levels of mercury were determined in invertebrates and edible fish collected in Sao Miguel Island in the Azores between 1993 and 1994. Mean concentrations of total mercury in the edible crab were 0.864 and 1.265 μg g^{-1} dry weight in the gills and midgut gland, respectively. Mean total mercury concentration in white seabream muscle tissue ranged from 0.043 to 0.371 μg g^{-1} wet weight (11).

Environmental fate

Degradation studies

BOD, COD and MnO_4^{-1} values showed 40-60% reduction of organic matter when mercury content in feed solution was ≥400 μg dm^{-3} in bench-scale experiments of mercury toxicity in biological aerobic filters treating synthetic wastewater (12).

Abiotic removal

Colloidal manganese oxides may sorb inorganic mercury and thereby affect cycling in lake waters (13).

Adsorption and retention

High organic matter content increases the transport of mercury from watersheds, therefore increasing the available supply to fish (14,15).

Mammalian & avian toxicity

Acute data

LC_{50} (30 hr) inhalation rabbit 29 mg m^{-3} (16).

Carcinogenicity and chronic effects

Metallic mercury and inorganic mercury compounds are not classifiable as to their carcinogenicity to humans, IARC group 3 (17).

The WHO reported no evidence that inorganic mercury is carcinogenic, and the EPA classify it as group O (not classifiable as to human carcinogenicity) (18) .

Teratogenicity and reproductive effects

Increased resorptions reported in rats exposed by inhalation to 500 or 1000 μg m^{-3} on days 10-15 of pregnancy. Exposure throughout gestation caused cranial defects at 500 and reduced maternal and foetal weights at 1000 μg m^{-3} (19).

Metabolism and toxicokinetics

Experiments on guinea pigs exposed to mercury vapour suggest that foetal hepatic metallothionein plays a significant defense role against mercury crossing the placenta and is involved in regulating mercury distribution in the foetus (20).

In humans 80% of the vapour is retained by the body, but the liquid is poorly absorbed via the gut (<1%). Most is then deposited in the kidney. Metabolism can be via oxidation of metallic to divalent mercury, reduction of divalent to metallic mercury, methylation of inorganic mercury and conversion of methylmercury into divalent

inorganic mercury. Oxidation of metallic mercury vapour is too slow to prevent passage through the blood-brain barrier, placenta and other tissues. Elimination in humans is mainly via urine and faeces, although some is exhaled. $t_{1/2}$ is a few days or weeks for most of the absorbed mercury, but in years for a fraction, possibly due to formation of a selenium complex (18).

After short-term human exposure, the first phase of elimination from blood had $t_{1/2}$ 2-4 days, accounting for 90% of the mercury. The second phase $t_{1/2}$ was 15-30 days (18).

Elemental mercury vapour easily penetrates the placental barrier and, after oxidation, accumulates in rodents' foetal tissue. In guinea pigs exposed to 200-300 μg m^{-3}, 2 hr day^{-1} (duration unspecified) or a single 150 min exposure to 8-11 mg m^{-3}, mercury concentrations in foetal lungs, brain, heart, kidneys and blood were much lower (5-100 ×) than in maternal tissues; mercury concentration in foetal liver was 2 × higher than in maternal liver (18).

One day after cessation of exposure, rats exposed to Hg vapour for 7 days had brain tissue levels of 7-8 μg Hg g^{-1} tissue and brain metallothionein levels about twice control levels. Brain Hg levels fell gradually, $t_{1/2}$ 26 days, but metallothionein levels induced by Hg remained unchanged for >2 wk. Most Hg was found in the cytosol fraction bound to metallothionein (21).

Irritancy

Metallic mercury may cause contact dermatitis; mercurial pharmaceuticals cause Pink disease in children and mercury vapour may cause Kawasaki disease (18).

Other effects

Other adverse effects (human)

The standard of epidemiological evidence is such that the effect of mercury vapour on the menstrual cycle and foetal development in the absence of signs of intoxication is open to question (18).

Acute inhalation of the vapour may cause chest pains, dyspnoea, cough, haemoptysis, pneumonitis and may be fatal. The central nervous system is the critical organ of vapour exposure. Sub-acute exposure may cause psychotic reactions; occupational exposure may cause erethism and, after continuing exposure, fine tremor (initially of the hands). Occupational exposure is also associated with proteinuria, and kidney effects have been reported at exposure levels below those causing central nervous system effects (18).

A subject who had been diagnosed with pulmonary and systemic mercury microembolism more than 11 years previously following intravenous mercury injection was found still to have mercury microemboli in both lungs and elsewhere, and showed signs of interstitial lung impairment, peripheral axonopathy and asthenozoospermia (22).

Thirty-three Hg-exposed workers from a Hg-producing plant, mean age 27 yr and mean exposure period 19 months, who at the time of testing and for the 3 previous months had urinary Hg levels below the currently accepted limit of 50 μg g^{-1} creatinine, had a significant reduction in the number of their B lymphocytes compared with unexposed control workers. No correlation was found between B lymphocyte changes and urinary Hg concentrations, length of exposure, and worker age (23).

Skin uptake of metallic mercury vapour in human volunteers is only 1% of inhalation uptake (18).

Acute, prolonged exposure to elemental mercury and its vapour caused acute, inorganic mercury toxicity and long-term, probably irreversible, neurological sequelae in 53 construction workers. Their earliest symptoms were rapidly resolving metal fume fever. Central nervous system symptoms and abnormal performance on neuropsychological tests persisted for the prolonged period of follow-up (570 days). Serial mercury in the blood and urine confirmed the long $t_{1/2}$ and large volume of distribution of mercury. Estimated $t_{1/2}$, assuming linear first-order kinetics, 42 days. Blood mercury levels did not correlate with severity of symptoms, but there were significant correlations between neuropsychological tests and indices of mercury exposure (24).

Colour vision was evaluated in 21 mercury-exposed workers. Mean urinary mercury content was 115 ± 6.15 μg g^{-1} creatinine. Dose-related subclinical colour vision impairment was observed in exposed workers. One year later under improved working conditions the workers were reexamined. Mean urinary mercury was found to be 10.0 μg g^{-1} and colour perception had improved significantly (25).

Any other adverse effects

Mercury is a potent neurotoxin in vertebrates because they lack external barriers or internal detoxifying systems (26,27).

HeLa cells *in vitro* have shown inhibition of DNA, RNA and protein synthesis (hydroxide) (28).

Legislation

Community Right-To-Know List. Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 $\mu g\ l^{-1}$ (29).
Included in Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (30).
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 5g 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 (31).

Other comments

Limited measurements of methyl mercury (2-14% of total mercury) indicated that disturbed wetland environments produce more methyl mercury than undisturbed (13).
Anthropogenic sources contribute to atmospheric deposition. Sources include waste incinerators, landfills, hazardous waste sites, sewage treatment plants, coal-combustion power plants and chlor-alkali production plants.
The biological effects of mercury depend on dose-response relationships for methyl mercury and the organism. Assessment of risks to the health of humans and other organisms who consume organisms that accumulate mercury from aquatic ecosystems require consideration of the atmosphere as a potentially important source (13).
Few data are available on the biological effects of mercury that actually occur in the aquatic environment. Pre mid-1980s laboratory studies of mercury toxicity to aquatic species were undertaken using unrealistically high water concentrations. The bias resulted from field measurements on contaminated sites. Post mid-1980s improvements in analytical techniques have allowed more accurate determinations and this accounts for the decrease in environmental concentrations reported (32-34).
Concern about the use of mercury amalgams in dental work and the potential toxic effects to humans has prompted some countries including the USA, Canada, Sweden and Germany to review their existing legislation on permitted use.
Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (35).
Toxicity (36-38), neurotoxicity (39,40), teratology (41), mutagenicity (42-44) and health hazards from use in dental amalgam (45,46) reviewed.
Carcinogenic risks to humans evaluated (17).
Aquatic pollution (47), biotransformation (48), bioavailability (49,50) and bioaccumulation reviewed (51-53).
The toxicity and environmental fate of organomercury compounds has been comprehensively reviewed (54).
Occupational exposure to mercury is discussed (55,56).
Effects of mercury on wildlife reviewed (57).

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M65 mercury(II) acetate

$$(CH_3C(O)O)_2Hg$$

$C_4H_6HgO_4$ **Mol. Wt.** 318.68 **CAS Registry No.** 1600-27-7

Synonyms acetic acid, mercury(2+) salt; diacetoxymercury; mercuric diacetate; mercuryl acetate

EINECS No. 216-491-1 **RTECS No.** AI 8575000

Uses Chemical intermediate and catalyst, with fungicidal properties (1).

Physical properties

M. Pt. 178-180°C **Specific gravity** 3.28

Solubility Water: 400 g l^{-1} at 20°C. Organic solvents: ethanol

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Hg) (inhalable dust fraction)

JP-OEL 0.05 mg m^{-3} (as Hg)

SE-LEVL 0.03 mg m^{-3} (as Hg)

UN No. 1629 **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

Intestinal transport rate for nutrients decreased in *Channa punctatus* exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days.

Disrupted metabolism in *Notopterus notopterus* exposed to 44 μg l^{-1} for 30 days (2).

Teratogenic to rainbow trout after exposure of eggs to 0.12-0.21 μg l^{-1} (Hg^{2+}) 4 days post-hatch, and after parenteral exposure to 0.70-0.79 μg l^{-1} (Hg^{2+}) for 400 days (2).

LC_{Lo} (1 hr) trout 5 ppm (3).

LC_{Lo} (2 hr) bluegill sunfish 5 ppm (3).

LC_{Lo} (3 hr) goldfish 5 ppm (3).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 9.3 μg l^{-1}; EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (Hg^{2+}) (2).

IC_{50} *Pseudomonas fluorescens* 7.65 μg of Hg at pH 6. Toxicity reduces with increasing pH and may be linked with the ability of the microorganism to methylate inorganic mercury (4,5).

Toxicity is also reduced by presence of cysteine in medium due to binding of mercury to thiol groups (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 24, 41 mg kg^{-1}, respectively (6).

LD_{50} dermal rat 570 mg kg^{-1} (7).

LD_{50} intraperitoneal mouse 6.5 mg kg^{-1} (7).

LD_{50} subcutaneous mouse 20 mg kg^{-1} (8).

Teratogenicity and reproductive effects

Embryotoxicity was studied in golden hamsters given 4-100 mg kg^{-1} orally, 4-50 mg kg^{-1} subcutaneously, 2-8 mg kg^{-1} intraperitoneally or 4 mg kg^{-1} intravenously on day-8 of pregnancy. Major manifestations of embryo damage were increased resorption rate and small, retarded and oedematous embryos. Embryotoxicity based on resorption rate decreased in the order intraperitoneal >subcutaneous >oral (9).

Metabolism and toxicokinetics

Rats receiving the compound in diet are reported to have absorbed 50% of dose (10).

Uptake into isolated rat hepatocytes is concentration-dependent and causes inhibition of alcohol dehydrogenase and glutathione reductase activities (11).

Other effects

Any other adverse effects

In synaptosomal fractions of rat brain cerebral cortex, 5HT release can be induced at 34 mg l^{-1} and 5HT binding at 3.4 mg l^{-1} (12).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 μg l^{-1} (13).

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (14).

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 (15).

Other comments

The compound is generally classified as an inorganic mercury compound. The toxicology, absorption, distribution and metabolism of inorganic mercury compounds has been reviewed (16).

The toxicity and environmental fate of organomercury compounds has been comprehensively reviewed (17).

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M66 mercury ammonium chloride

$$Hg(Cl)NH_2$$

$HgNH_2Cl$ **Mol. Wt.** 252.07 **CAS Registry No.** 10124-48-8

Synonyms mercury amide chloride; aminomercuric chloride

EINECS No. 233-335-8 **RTECS No.** OV 7020000

Uses Topical anti-infective.

Physical properties

Specific gravity 5.38
Solubility Water: acetic acid, ammonium carbonate, sodium thiosulfate

Occupational exposure

DE-MAK 0.012 ppm (0.1 mg m^{-3})(as Hg)
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. 1630 **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)

Other effects

Other adverse effects (human)
Allergic dermatitis reported (1).
Prolonged use may cause local pigmentation of skin or eyelids and ptyalism. Oral ingestion causes epigastric pain, nausea and diarrhoea (1).

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} (2).
Included in Schedule 4 (Release into Air: 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).

Other comments

Should not be used therapeutically in conjunction with sulfur or iodine (1).
Reviews on physico-chemical properties, human health effects, ecotoxicology, experimental toxicology, environmental effects, exposure levels and workplace experience listed (5).
Aquatic toxicology reviewed (6).
Soluble in acetic acid, ammonium carbonate and sodium thiosulfate.

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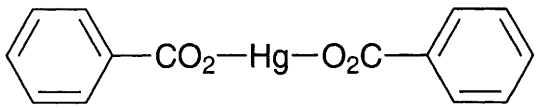
M67 mercury benzoate



$C_{14}H_{10}O_4Hg$ **Mol. Wt.** 442.82 **CAS Registry No.** 583-15-3

Synonyms mercuric benzoate

EINECS No. 209-499-1 **RTECS No.** OV 7060000

Uses Formerly used as an antisyphilitic.

Physical properties

M. Pt. 165°C

Solubility Water: soluble in 90 parts cold water. Organic solvents: ethanol

Occupational exposure

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)
US-TWA 0.1 mg m^{-3} (as Hg)

UN No. 1631 **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)

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} (1).
Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).
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 (3).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (4).
Aquatic toxicology reviewed (5).
Protect from light.

References

1. *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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M68 mercury(I) bromide

Hg_2Br_2

Hg_2Br_2 **Mol. Wt.** 560.99 **CAS Registry No.** 10031-18-2

Synonyms mercurous bromide

RTECS No. OV 7410000

Physical properties

B. Pt. 390°C (subl.) **Specific gravity** 7.307 **Volatility** v.den. 19.3

Occupational exposure

DE-MAK 0.01 ppm (0.08 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)
US-TWA 0.025 mg m^{-3} (as Hg)

UN No. 1634 **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)

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} (1).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).
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 (3).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (4).
Toxicity of inorganic mercury and environmental effects reviewed (5,6).
Aquatic toxicology reviewed (7).

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3. *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.
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.
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M69 mercury(II) bromide

$HgBr_2$

$HgBr_2$ **Mol. Wt.** 360.40 **CAS Registry No.** 7789-47-1

Synonyms mercuric bromide

EINECS No. 232-169-3 **RTECS No.** OV 7415000

Physical properties

M. Pt. 237°C **B. Pt.** 322°C (subl.) **Specific gravity** 6.109 at 25°C **Volatility** v.p. 1 mmHg at 136.5°C
Solubility Water: soluble in 200 parts water. Organic solvents: ethanol, methanol

Occupational exposure

DE-MAK 0.01 ppm (0.08 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. 1634 **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 knifefish exposed to 44 μg l^{-1} (Hg^{2+}) for 30 days (1).
Teratogenic to rainbow trout after egg exposure 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_{50} oral mouse, rat 35-40 mg kg^{-1} (2).

LD_{50} dermal rat 100 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 5 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

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (6).

Toxicity of inorganic mercury and environmental effects reviewed (7,8).

Toxicity of mercuric compounds discussed (9).

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M70 mercury(I) chloride

HgCl

HgCl **Mol. Wt.** 236.04 **CAS Registry No.** 7546-30-7

Synonyms mercurous chloride; subchloride of mercury; mercury monochloride; Cyclosan; Precipite blanc; C.I. 77764

EINECS No. 231-430-9 **RTECS No.** OV 8750000

Uses Used as a purgative, and in teething powders for children, now banned. Also previously used in ointments for the treatment of syphilis, and as an insecticide.

Physical properties

M. Pt. 400-500°C (sublimes) **Specific gravity** 7.15
Solubility Water: 2 mg l^{-1} at 25°C. Organic solvents: ethanol

Occupational exposure

DE-MAK 0.01 ppm (0.08 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)
US-TWA 0.025 mg m^{-3} (as Hg)
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 *Channa punctatus* exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days.
Disrupted metabolism in *Notopterus notopterus* 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).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 166-210 mg kg^{-1} (2,3).
LD_{50} oral mouse 180 mg kg^{-1} (2).
LD_{Lo} oral dog 1-2 g dog^{-1} (3).
LD_{Lo} oral horse 12-16 g $horse^{-1}$ (3).
LD_{50} dermal rat 1.5 g kg^{-1} (2).
LD_{50} intraperitoneal mouse 10 mg kg^{-1} (2).

Teratogenicity and reproductive effects
Injection into chick eggs caused death of all embryos at 0.5 mg and an 80% reduction in hatchability at 0.25 mg (4,5).

Metabolism and toxicokinetics

After oral ingestion, most of the compound passes out of the stomach unchanged, and into the small intestine where some is converted into various irritant compounds. Most is eliminated in faeces within a week of ingestion (6).

Genotoxicity

Rec assay with *Bacillus subtilis* positive (7).

Induced sister chromatid exchanges in Chinese hamster cells *in vitro* (8).

Mouse glioma cells *in vitro* inhibited DNA synthesis and transport systems for DNA precursors (9).

Other effects

Other adverse effects (human)

When used in teething powders for infants, the compound has caused acrodynia. The swelling, rawness and pink coloration of limbs was due principally to renal and cardiovascular effects associated with salt and water loss (6,10).

Repeated use of the compound as a purgative has led to dementia, erethism, colitis, renal failure and death due to absorption of mercury from the gastro-intestinal tract (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 $\mu g\ l^{-1}$ (12).

Included in Schedule 4 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).

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 (14).

Other comments

Absorption, excretion and distribution of inorganic mercurial salts has been reviewed (3,15).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).

The molecular formula is sometimes written as Hg_2Cl_2 with the synonym dimercury dichloride.

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M71 mercury(II) chloride

$HgCl_2$

$HgCl_2$ **Mol. Wt.** 271.50 **CAS Registry No.** 7487-94-7

Synonyms mercuric chloride; mercury bichloride; mercury perchloride; calochlor; corrosive sublimate; mercury chloride

EINECS No. 231-299-8 **RTECS No.** OV 9100000

Uses Preserving wood and anatomical specimens. In electroplating and other metal processes. Topical antiseptic and disinfectant.

Physical properties

M. Pt. 277°C **B. Pt.** 302°C (volatalises) **Specific gravity** 5.44 at 25°C **Volatility** v.p. 1.4×10^{-4} mmHg at 34°C **Solubility** Water: 69 g l^{-1}. Organic solvents: benzene, diethyl ether, ethanol, glycerol, methanol

Occupational exposure

DE-MAK 0.01 ppm (0.08 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. 1624 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic if swallowed – Causes burns – Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed (R28, R34, R48/24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37/39, S45)

Ecotoxicity

Fish toxicity
Intestinal transport rate for nutrients decreased in *Channa punctatus* exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days.
Disrupted metabolism in *Notopterus notopterus* 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).

Trout, bluegill sunfish and goldfish exposed to 5 ppm exhibited signs of distress in 1, 3 and 4 hr, respectively. Test conditions: pH 7.0; dissolved oxygen content 7.5 ppm; total hardness (soap method) 300 ppm; methyl orange alkalinity 310 ppm; free carbon dioxide 5 ppm; and temperature 12.8°C (2).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 9.3 μg l^{-1} (1).

IC_{50} *Pseudomonas fluorescens* 4.85 μg Hg at pH 6. Toxicity reduces with increasing pH and may be linked with the ability of the microorganism to methylate inorganic mercury (3,4).

Toxicity is also reduced by presence of cysteine in medium due to binding of mercury to thiol groups (4).

Bioaccumulation

Rainbow trout were exposed for 96 hr to 50 μg l^{-1} (Hg^{2+}) at temperatures of 5, 10 and 20°C; bioconcentration factors were 5, 12 and 26, respectively (5).

Acartia clausia 24 hr exposure to 0.05-0.5 μg l^{-1}; bioconcentration factor 7500 (6).

The bioconcentration factor for *Acetabularia calyculus* cells exposed to 1 or 10 mg l^{-1} $HgCl_2$ for three days was the same for both concentrations, reaching a saturation level in the uptake of Hg. The cells synthesised a polypeptide (molecular weight 29,000 Daltons) in response to $HgCl_2$ exposure which was absent in non-treated cells. It is suggested that the great ability of *Acetabularia* to bioconcentrate Hg could be related to the synthesis of this Hg-induced polypeptide (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1.5 mg kg^{-1} (8).

LD_{Lo} oral dog 0.1-0.3 g dog^{-1} (9).

LD_{Lo} oral cattle 4-8 g $animal^{-1}$ (9).

LD_{50} dermal mouse 41 mg kg^{-1} (10).

LD_{50} subcutaneous mouse 4.5 mg kg^{-1} (11).

Intraperitoneal rat 1 mg kg^{-1} body weight. Acute renal failure and necrosis of the proximal tubules was observed (12).

Carcinogenicity and chronic effects

Metallic mercury and inorganic compounds are not classifiable as to their carcinogenicity to humans, IARC classification group 3 (13).

National Toxicology Program tested rats and mice via gavage. Some evidence for carcinogenicity in ♂ rats, equivocal evidence for carcinogenicity in ♀ rats and ♂ mice and no evidence for carcinogenicity in ♀ mice. A Post Peer Review of data is in progress (14).

Mercury(II) chloride in drinking water was not significantly tumorigenic to mice in lifetime studies (15).

Teratogenicity and reproductive effects

Increased incidence of post-implantation loss reported in rats given 16 or 24 mg kg^{-1} day^{-1} on days 6-15 of pregnancy. Foetal weight was reduced at 12 mg kg^{-1}. Delayed ossification and a range of major malformations occurred at 24 mg kg^{-1} (16).

Metabolism and toxicokinetics

Rapidly absorbed from the gastro-intestinal tract with effects being visible after 10-15 min (17).

Mercury is distributed throughout soft tissue including the brain and spinal cord in which tissues there is some localisation (18-20).

It can be detected in liver, erythrocytes and blood plasma as well as the kidney where particularly high levels are found in the renal cortex (18,21).

Complexes are formed with proteins at many sites (9,17).

Mercury is secreted in saliva, bile, gastro-intestinal juices and breast milk, and ultimately excreted in urine and faeces (9,17,22).

Covalent binding to thiol groups leads to interference with function of many enzymes and co-enzymes, and binding to the thiol groups of cysteine leads to accumulation in the keratin of hair, nails and skin (17,23).

Absorption across the rat small intestine is pH-dependent, and the moiety absorbed is thought to be Hg(OH)Cl or $Hg(OH)_2$ (24,25).

Irritancy

Severe eye and skin irritant (species unspecified) (26).

Sensitisation

Allergies to mercury(II) chloride have been reported as quite common in dentists and surgeons (27).

Genotoxicity

Bacillus subtilis rec assay positive (28).
In vitro mouse lymphoma forward mutation assay L5178 tk^+/tk^- positive (29).
In vitro induced sister chromatid exchanges in Chinese hamster ovary cells (30).
DNA cross-linking in Novikoff Ascites hepatoma cells *in vitro* was induced by concentrations of 135 mg l^{-1} (31).

Other effects

Other adverse effects (human)

Chronic poisoning with mercury can induce tremor and neuropsychiatric disturbances. These are probably due to a variety of actions on the nervous system, including that on 5HT mediated pathways (32).
Single oral doses of 21 and 29 mg kg^{-1} have been reported as fatal to humans, with damage to nervous system, gastro-intestinal tract and kidney (33,34).

Any other adverse effects

Inorganic mercury compounds are highly reactive neurotoxins altering nerve function by interference with Ca^{2+} transport, whereas kidney damage may be related to induction of abnormal protein production (35-38).
An auto-immune reaction may be involved in the nephritis induced by the compound (21,39).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 μg l^{-1} (40).
Included in Schedule 4 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (41).
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 (42).
WHO Toxicity Class Ia (43).

Other comments

The effects of inorganic and organomercury compounds on human reproduction and development have been reviewed (44,45).
Carcinogenic risk to humans evaluated (13).

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M72 mercury(II) cyanide

$Hg(CN)_2$

C_2HgN_2 **Mol. Wt.** 252.63 **CAS Registry No.** 592-04-1

Synonyms mercuric cyanide

EINECS No. 209-741-6 **RTECS No.** OW 1515000

Uses Topical antiseptic for human and animal use. Chemical intermediate.

Physical properties

M. Pt. 20°C (decomp.) **B. Pt.** decomposes at 320°C **Specific gravity** 3.996

Solubility Water: 1 g dissolves in 13 ml water. Organic solvents: ethanol, methanol, glycerol

Occupational exposure

DE-MAK 0.01 ppm (0.08 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. 1636 **HAZCHEM Code** 4X **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

Intestinal transport rate for nutrients decreased in *Channa punctatus* exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days.

Disrupted metabolism in *Notopterus notopterus* 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}; EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (Hg^{2+}) (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 26, 33 mg kg^{-1}, respectively (2).

LD_{Lo} intraperitoneal rat 7.5 mg kg^{-1} (3).

LD_{50} subcutaneous dog 2.7 mg kg^{-1} (4).

LD_{50} intravenous rabbit 2 mg kg^{-1} (5).

LD_{Lo} in ♀ humans has been reported as 10 mg kg^{-1} (6).

Metabolism and toxicokinetics

Absorption from rat small intestine is pH-dependent in the range 5.4-7.4. The higher pH favours absorption, which may involve hydroxylation of the compound (7).

Irritancy

May cause eye and skin irritation (species unspecified) (8,9).

Other effects

Other adverse effects (human)

The compound can be fatal by inhalation (8).

Acute poisoning may produce symptoms of cough, choking, diarrhoea, dizziness, rapid breath, headache and unconsciousness (9).

Symptoms of both mercury and cyanide poisoning are seen in humans, with those of cyanide being seen first (9).

Chronic poisoning may cause tremor and neuropsychiatric disturbances (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 $\mu g\ l^{-1}$ (11).

Included in Schedule 4 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

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 (13).

Other comments

Toxicology of inorganic mercury compounds reviewed (10,14).

Protect from light.

References

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11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
13. *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.
14. Korshun, M. N. *Gig. Sanit.* 1989, (1), 69-70 (Russ.) (*Chem. Abstr.* **110**, 149418q)

M73 mercury fulminate

$$Hg(O\text{-}C{\equiv}N)_2$$

$C_2HgN_2O_2$ **Mol. Wt.** 284.62 **CAS Registry No.** 628-86-4

Synonyms fulminic acid, mercury(II) salt

EINECS No. 211-057-8 **RTECS No.** OW 4055000

Uses Manufacture of explosives.

Physical properties

M. Pt. (explodes) **Specific gravity** 4.42 at 20°C
Solubility Water: miscible. Organic solvents: ethanol

Occupational exposure

DE-MAK 0.012 ppm (0.1 mg m^{-3}) (as Hg)
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. 2024 (liquid)

UN No. 2025 (solid) **Conveyance classification** toxic substance
Supply classification explosive, toxic
Risk phrases Extreme risk of explosion by shock, friction, fire or other sources of ignition – Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R3, R23/24/25, R33)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep in a cool place – This material and its container must be disposed of in a safe way – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S3, S35, S45)

Genotoxicity

Induced chromosomal aberrations (gaps, breaks and fragments), and a significant increase in the incidence of micronucleated lymphocytes among exposed workers (1).

Other effects

Other adverse effects (human)
Cases of mercury poisoning have been reported in exposed munitions workers (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 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

References

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2. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981-82, **2**, John Wiley and Sons, New York, USA.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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M74 mercury gluconate

$C_6H_{11}HgO_7$ **Mol. Wt.** 395.74 **CAS Registry No.** 63937-14-4

Synonyms mercurous gluconate

RTECS No. OW 4060000

Occupational exposure

JP-OEL 0.05 mg m^{-3} (as Hg)
SE-LEVL 0.03 mg m^{-3} (as Hg)

UN No. 1637 **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)

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} (1).
Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).
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 (3).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (4).
Aquatic toxicology listed (5).

References

1. *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.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. *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.

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. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264

M75 mercury(I) iodide

HgI

HgI **Mol. Wt.** 327.49 **CAS Registry No.** 7783-30-4

Synonyms mercurous iodide; mercury protoiodide; yellow mercury iodide

EINECS No. 231-988-3 **RTECS No.** OW 5075000

Uses Antibacterial.

Physical properties

M. Pt. 290°C **Specific gravity** 7.70
Solubility Water: insoluble

Occupational exposure

DE-MAK 0.01 ppm (0.08 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)
US-TWA 0.025 mg m^{-3} (as Hg)

UN No. 1638 **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)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 110 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 50 mg kg^{-1} (1).

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} (2).
Included in Schedule 4 (Release into Air. 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 87/156/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).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicity, exposure levels and workplace experience listed (5).
Toxicity of inorganic mercury and environmental effects reviewed (6,7).
Aquatic toxicology reviewed (8).

References

1. *Arch. Toxikol.* 1964, **20**, 226.
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.
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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.
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.
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8. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264

M76 mercury(II) iodide

HgI_2

HgI_2 **Mol. Wt.** 454.40 **CAS Registry No.** 7774-29-0

Synonyms mercuric iodide; mercury biniodide; red mercuric iodide

EINECS No. 231-873-8 **RTECS No.** OW 5250000

Uses Topical antiseptic.

Physical properties

M. Pt. 259°C **B. Pt.** 350°C (sublimes) **Specific gravity** 6.28
Solubility Water: 0.006 g 100 g^{-1} at 25°C. Organic solvents: acetone, ethanol, ethyl acetate

Occupational exposure

DE-MAK 0.01 ppm (0.08 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. 1638 **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 knifefish 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}; EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 17-18 mg kg^{-1} (2).
LD_{Lo} oral human 357 mg kg^{-1} (3).
LD_{50} dermal rat 75 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 4200 μg kg^{-1} (2).

Teratogenicity and reproductive effects
Teratogenic and reproductive effects reported in mice exposed to 4870 ng m^{-3} for 24 hr by inhalation on days 1-22 of pregnancy (4).

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} (5).
Included in Schedule 4 (Release into Air: 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

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (8).
Toxicity of inorganic mercury and environmental effects reviewed (9,10).
Toxicity of mercuric compounds discussed (11).

References

1. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264.
2. *Gig. Tr. Prof. Zabol.* 1981, **25**(7), 27.
3. *Z. Klin. Med. (1879)* 1927, **106**, 783.
4. *Gig. Sanit.* 1981, **46**(5), 73.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *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.
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. *Environmental Health Criteria 118: Inorganic Mercury* 1991, WHO/IPCS, Geneva, Switzerland.
10. *Environmental Health Criteria 86: Mercury-Environmental Aspects* 1989, WHO/IPCS, Geneva, Switzerland.
11. Korshun, M. N. *Gig. Sanit.* 1989, (1), 69-70 (Russ.) (*Chem. Abstr.* **110**, 149418q)

M77 mercury(I) nitrate

$$Hg_2(NO_3)_2$$

$Hg_2N_2O_6$ **Mol. Wt.** 525.19 **CAS Registry No.** 10415-75-5

Synonyms nitric acid, mercury(1+) salt; mercurous nitrate; mercury protonitrate

EINECS No. 233-886-4 **RTECS No.** OW 8000000

Uses For fire gilding and blackening brass.

Occupational exposure

DE-MAK 0.01 ppm (0.08 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)
US-TWA 0.025 mg m^{-3} (as Hg)

UN No. 1627 **HAZCHEM Code** 2Z **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 *Channa punctatus* exposed to 3 μg l^{-1} for 30 days. Disrupted metabolism in *Notopterus notopterus* exposed to 44 μg l^{-1} 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}; EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (Hg^{2+}) (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 170 mg kg^{-1} (2).

LD_{50} oral mouse 49 mg kg^{-1} (2).

LD_{50} dermal rat 2.33 g kg^{-1} (3).

LD_{50} intraperitoneal mouse 5 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 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: 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

Toxicology, absorption, distribution and metabolism of inorganic mercury compounds has been reviewed (8).

Normally exists as dihydrate, melting point 70°C.

References

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2. Grins, N. et al *Hyg. Sanit. (USSR)* 1981, **46**(8), 12.
3. *Gig. Tr. Prof. Zabol.* 1981, **25**(7), 27.
4. *Arch. Toxikol.* 1964, **20**, 226.
5. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
7. *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.
8. Oehme, F. W. (Ed.) *Toxicity of Heavy Metals in the Environment* Part 1, 1978, Marcel Dekker Inc., New York, USA

M78 mercury(II) nitrate

$$Hg(NO_3)_2$$

HgN_2O_6 **Mol. Wt.** 324.60 **CAS Registry No.** 10045-94-0

Synonyms nitric acid, mercury(2+) salt; mercuric nitrate; mercury pernitrate

EINECS No. 233-152-3 **RTECS No.** OW 8225000

Uses Chemical intermediate. Used in the manufacture of felt. Fungicide.

Physical properties

M. Pt. 79°C **B. Pt.** decomposes **Specific gravity** 4.3

Occupational exposure

DE-MAK 0.01 ppm (0.08 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. 1625 **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 *Channa punctatus* exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days.
Disrupted metabolism in *Notopterus notopterus* 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}; EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (Hg^{2+}) (1).
IC_{50} *Pseudomonas fluorescens* 8.03 μg l^{-1} Hg at pH 6. Toxicity reduces with increasing pH and may be linked with the ability of the microorganism to methylate inorganic mercury (2,3).
Toxicity is also reduced by presence of cysteine in medium, due to binding of mercury to thiol groups (3).

Environmental fate

Abiotic removal
The compound can be stabilised in industrial waste by the formation of insoluble complexes with pulverised fuel ash and Portland cement. Chemical and physical reactions are involved (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 25-26 mg kg^{-1} (5).

LD_{50} intraperitoneal mouse 7.2 mg kg^{-1} (6).
LD_{50} subcutaneous mouse 20 mg kg^{-1} (7).

Teratogenicity and reproductive effects
Chronic mercury poisoning in ♀ mice following administration of the compound caused disturbances of the oestrus cycle (8).

Irritancy
Can cause eye irritation, conjunctival and corneal ulceration (9).
Causes skin irritation and dermatitis (9).

Other effects

Other adverse effects (human)
Acute poisoning in humans produces symptoms including gastro-intestinal disturbance, anuria and anaemia (9).
Chronic poisoning with mercury can induce tremors and neuropsychiatric disturbances (9).
In humans symptoms are probably due to a variety of actions on the nervous system, including those on 5HT-mediated pathways (10).

Any other adverse effects
Ingestion in rats and mice caused diarrhoea (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 μg l^{-1} (11).
Included in Schedule 4 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).
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 (13).

Other comments

Toxicology, absorption, distribution and metabolism of inorganic mercury compounds reviewed (14).

References

1. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264.
2. Farrell, R. E. *Appl. Environ. Microbiol.* 1990, **56**(10), 3006-3016.
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4. Clark, A. J. et al *Chem. Environ. Proc. Int. Conf.* 1986, 680-689.
5. Grins, N. et al *Hyg. Sanit. (USSR)* 1981, **46**(8), 12-14.
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9. *Dangerous Prop. Ind. Mater. Rep.* 1988, **8**(4), 42-49.
10. Oudar, P. et al *Pharmacol. Toxicol. (Copenhagen)* 1989, **65**(4), 245-248.

11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
13. *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.
14. Oehme, F. W. (Ed.) *Toxicity of Heavy Metals in the Environment Part 1* 1978, Marcel Dekker Inc., New York, USA

M79 mercury nucleate

CAS Registry No. 12002-19-6

Synonyms mercurol

RTECS No. OV 3200000

Occupational exposure

DE-MAK 0.01 ppm (0.08 mg m^{-3})(as Hg)
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. 1639 · **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)

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} (1).
Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).
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 (3).

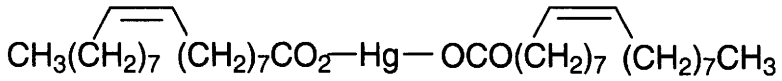
Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (4).
Aquatic toxicology reviewed (5).

References

1. *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.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. *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.
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. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264

M80 mercury oleate



$C_{36}H_{66}O_4Hg$ **Mol. Wt.** 763.51 **CAS Registry No.** 1191-80-6

Synonyms 9-octadecenoic acid, (Z)-, mercury salt; oleate of mercury

EINECS No. 214-741-4 **RTECS No.** OW 8600000

Uses Has been used as an ectoparasiticide and in antifouling paints.

Physical properties

M. Pt. 115°C
Solubility Organic solvents: diethyl ether, ethanol, oils

Occupational exposure

FR-VME 0.01 mg m^{-3} (as Hg)
JP-OEL 0.05 mg m^{-3} (as Hg)
SE-LEVL 0.03 mg m^{-3} (as Hg)

UN No. 1640 **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
5 ppm was lethal to rainbow trout, yellow perch and bluegill sunfish in 1 hr, 5 hr and 20 hr, respectively. Test

conditions: pH 7.0; dissolved oxygen content 7.5 ppm; total hardness (soap method) 300 ppm; methyl orange alkalinit y 310 ppm; free carbon dioxide 5 ppm; and temperature 12.8°C (1).

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} (2).
Included in Schedule 4 (Release into Air: 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).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (5).
Aquatic toxicology reviewed (6).

References

1. Wood, E. M. *The toxicity of 3400 chemicals to fish* 1987, EPA Report 500/6-87-002.
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. *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.
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.
6. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264

M81 mercury(I) oxide

Hg_2O

Hg_2O **Mol. Wt.** 417.18 **CAS Registry No.** 15829-53-5; 12653-71-3
Uses Treatment of apple canker and pruning cuts on fruit trees.

Physical properties

B. Pt. 500°C (decomp.)

Occupational exposure

DE-MAK 0.012 ppm (0.1 mg m^{-3})(as Hg)
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)
US-TWA 0.025 mg m^{-3} (as Hg)

UN No. 1641 **HAZCHEM Code** 2Z **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)

Legislation

Community Right-To-Know List.
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 $\mu g\ l^{-1}$ (1).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).
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 (3).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (4).
Toxicity of inorganic mercury and environmental effects reviewed (5,6).
Aquatic toxicology reviewed (7).

References

1. *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.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. *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.
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. *Environmental Health Criteria 118: Inorganic Mercury* 1991, WHO/IPCS, Geneva, Switzerland.
6. *Environmental Health Criteria 86: Mercury-Environmental Aspects* 1989, WHO/IPCS, Geneva, Switzerland.
7. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264

M82 mercury(II) oxide

HgO

HgO **Mol. Wt.** 216.59 **CAS Registry No.** 21908-53-2

Synonyms mercuric oxide red; mercuric oxide yellow; red oxide of mercury; C.I. 77760

EINECS No. 244-654-7 **RTECS No.** OW 8750000

Uses Chemical intermediate. Fungicide. Topical antiseptic. Pigment in marine bottom paints and porcelain paints (1).

Physical properties

M. Pt. 500°C (decomp.) **Specific gravity** 11.14

Solubility Water: 50 mg l^{-1}

Occupational exposure

DE-MAK 0.01 ppm (0.08 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. 1641 **HAZCHEM Code** 2Z **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

Toxic to fish (2).

Intestinal transport rate for nutrients decreased in *Channa punctatus* exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days.

Disrupted metabolism in *Notopterus notopterus* exposed to 44 μg l^{-1} (Hg^{2+}) for 30 days (3).

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 (3).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 9.3 μg l^{-1}; EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (Hg^{2+}) (3).

Environmental fate

Abiotic removal

Compound can be removed from wastewaters by flotation at pH 3-4.5 with potassium salts of saturated fatty acids (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 16-18 mg kg^{-1} (5).

LD_{50} dermal mouse 315 mg kg^{-1} (6).

LD_{50} intraperitoneal mouse 4.5 mg kg^{-1} (6).

Teratogenicity and reproductive effects
Oral administration of 2.16 mg to ♀ rats on day 12 or 19 of pregnancy retarded foetal growth and inhibited eye formation (7).

Metabolism and toxicokinetics
When introduced into rat duodenum, absorption and distribution through the body were rapid. Absorption showed different characteristics to that of many other inorganic mercury compounds such as mercury(II) chloride (8).

Irritancy
Strongly irritant (9).

Sensitisation
Strong allergen (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 $\mu g\ l^{-1}$ (10).
Included in Schedule 4 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
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 (12).
WHO Toxicity Class Ib (13).
EPA Toxicity Class I (2).

Other Comments

Toxicity reviewed (9).

References

1. Bezo, M. et al *Hung. Teljes* HU46, 240 28 Oct 1988.
2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
3. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264.
4. Scrylev, L. D. *Izv. Vyssh. Uchebn. Zaved., Tsvetn. Metall.* 1988, (6), 13-18 (Russ.) (*Chem. Abstr.* **110**, 218410v).
5. *IPCS Environmental Health Criteria 118: Inorganic Mercury* 1991, World Health Organisation, Geneva, Switzerland.
6. *Gig. Tr. Prof. Zabol.* 1981, **25**(7), 27.
7. Rizzo, A. M. et al *Proc. Western Pharm. Soc.* 1972, **15**, 52-54.
8. Endo, T. et al *Pharmacol. Toxicol. (Copenhagen)* 1990, **67**(5), 431-435.
9. *Dangerous Prop. Ind. Mater. Rep.* 1989, **9**(3), 49-57.
10. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
11. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
12. *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.
13. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

M83 mercury oxycyanide

$HgO \cdot Hg(CN)_2$

$C_2Hg_2N_2O$ **Mol. Wt.** 469.21 **CAS Registry No.** 1335-31-5

Synonyms mercury cyanide oxide; mercuric oxycyanide

EINECS No. 215-629-8 **RTECS No.** OW 1530000

Uses Topical antiseptic.

Physical properties

Specific gravity 4.44
Solubility Water: insoluble

Occupational exposure

DE-MAK 0.012 ppm (0.1 mg m^{-3})(as Hg)
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. 1642 (desensitised) **HAZCHEM Code** 2WE **Conveyance classification** toxic substance (desensitised)
Supply classification explosive, toxic
Risk phrases Extreme risk of explosion by shock, friction, fire or other sources of ignition – Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R3, 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 – This material and its container must be disposed of in a safe way – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S35, S45)

Mammalian & avian toxicity

Acute data
LD_{Lo} intravenous rabbit 2500 μg kg^{-1} (1).

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} (2).
Included in Schedule 4 (Release into Air: 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).

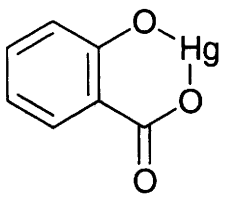
Other comments

Reviews on physico-chemical properties, human health effects and experimental toxicity listed (5).
Aquatic toxicology reviewed (6).
Violent poison. Explodes on impact or when exposed to flame.

References

1. *J. Pharmacol. Exp. Ther.* 1931, **41**, 21.
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. *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.
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.
6. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264

M84 mercury salicylate



$C_7H_4HgO_3$ **Mol. Wt.** 336.70 **CAS Registry No.** 5970-32-1

Synonyms mercuric salicylate; mercurisalicylic acid; salicylic acid, (hydromercuri)-, cyclic anhydride; 2-hydroxybenzoic acid, mercury complex

EINECS No. 227-760-8 **RTECS No.** OX 0300000

Uses Topical antiseptic.

Occupational exposure

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)

UN No. 1644 **HAZCHEM Code** 2Z **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

Acute data

LD_{Lo} subcutaneous mouse 10 mg kg^{-1} (1).

LD_{Lo} intramuscular rabbit 40 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 Schedules 4 and 6 (Release into Air/Land: 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 physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (6).

Aquatic toxicology reviewed (7).

Poison. Incompatible with alkali iodides.

References

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5. *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.
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M85 mercury(I) sulfate

Hg_2SO_4

Hg_2O_4S **Mol. Wt.** 497.24 **CAS Registry No.** 7783-36-0

Synonyms sulfuric acid, dimercury(1+) salt; mercurous sulfate

EINECS No. 231-993-0 **RTECS No.** OX 0480000

Uses Used in the manufacture of electrical batteries.

Physical properties

M. Pt. decomp. with heat **Specific gravity** 7.56
Solubility Water: 600 mg l^{-1} at 25°C

Occupational exposure

DE-MAK 0.01 ppm (0.08 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)
US-TWA 0.025 mg m^{-3} (as Hg)

UN No. 1645 **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 *Channa punctatus* exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days.
Disrupted metabolism in *Notopterus notopterus* 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}; EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (Hg^{2+}) (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 20.5 mg kg^{-1} (2).
LD_{50} oral mouse 152 mg kg^{-1} (2).
LD_{50} dermal rat 1.175 g kg^{-1} (3).
LD_{50} intraperitoneal mouse 11.5 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 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: 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

Toxicology, absorption, distribution and metabolism of inorganic mercury compounds reviewed (8).

References

1. Zillioux, E. J. et al *Environ. Toxicol. Chem.* 1993, **12**, 2245-2264.
2. Grins, N. et al *Hyg. Sanit. (USSR)* 1981, **46**(8), 12-14.
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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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8. Oehme, F. W. (Ed.) *Toxicity of Heavy Metals in the Environment* Part 1, 1978, Marcel Dekker Inc., New York, USA

M86 mercury(II) sulfate

$HgSO_4$

HgO_4S **Mol. Wt.** 296.65 **CAS Registry No.** 7783-35-9

Synonyms mercuric sulfate

EINECS No. 231-992-5 **RTECS No.** OX 0500000

Uses Battery electrolyte; with sodium chloride for extracting gold and silver from roasted pyrites.

Occurrence Accumulation of mercury in the environment results from atmospheric deposition. Both natural and anthropogenic sources contribute to atmospheric deposition; these include volcanoes, land erosion, incinerators, landfills, hazardous waste sites, sewage treatment plants, coal-combustion power plants and chlor-alkali production plants. The three major mercury species are: elemental mercury Hg^0; inorganic mercury Hg^{2+}; and methyl mercury CH_3Hg^+. Refer to mercury and methyl mercury entries for additional toxicity data on mercury salts.

Physical properties

Specific gravity 6.47

Solubility Water: decomposes

Occupational exposure

DE-MAK 0.01 ppm (0.08 mg m^{-3})
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. 2024 (liquid); 2025 (solid) **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R26/27/28, R33)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – After contact with skin, wash immediately with plenty of water – 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 *Notopterus notopterus* 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_{50} oral mouse, rat 25, 67 mg kg^{-1}, respectively (2,3).
LD_{50} dermal rat 625 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 6300 μg 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} (4).
Included in Schedule 4 (Release into Air: 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

Reviews on physico-chemical properties, human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels and workplace experience listed (7).

Physico-chemical properties, hazards and legislation in France reviewed (8).
Toxicity of inorganic mercury and environmental effects reviewed (9,10).

References

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2. *NTIS Report* PB214-270, Natl. Tech. Inf. Ser., Springfield, VA, USA.
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5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
6. *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.
7. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
8. *Cah. Notes Doc.* 1989, **137**, 711-716 (Fr.) (*Chem. Abstr.* **112**, 124221y).
9. *Environmental Health Criteria 118: Inorganic Mercury* 1991, WHO/IPCS, Geneva, Switzerland.
10. *Environmental Health Criteria 86: Mercury-Environmental Aspects* 1989, WHO/IPCS, Geneva, Switzerland

M87 mercury(II) thiocyanate

$$Hg(SCN)_2$$

$C_2HgN_2S_2$ **Mol. Wt.** 316.76 **CAS Registry No.** 592-85-8

Synonyms thiocyanic acid mercury(2+) salt; mercuric thiocyanate; mercuric sulfocyanate; mercuric sulfocyanide; mercury dithiocyanate

EINECS No. 209-773-0 **RTECS No.** XL 1550000

Uses Manufacture of fireworks and in photography.

Physical properties

M. Pt. 165°C (decomp.)
Solubility Water: 0.69 g l^{-1} at 25°C

Occupational exposure

DE-MAK 0.01 ppm (0.08 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. 1646 **HAZCHEM Code** 2Z **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

Intestinal transport rate for nutrients decreased in *Channa punctatus* exposed to 3 μg l^{-1} (Hg^{2+}) for 30 days.
Disrupted metabolism in *Notopterus notopterus* 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).
LC_{50} (24 hr) fathead minnow 0.39 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 9.3 μg l^{-1}; EC_{50} (48 hr) *Daphnia magna* 5.2 μg l^{-1} (Hg^{2+}) (1).
LC_{50} (24 hr) grass shrimp 0.09 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 46 mg kg^{-1} (3).
LD_{50} oral mouse 24.5 mg kg^{-1} (3).
LD_{50} dermal rat 685 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 3.5 mg kg^{-1} (3).

Metabolism and toxicokinetics

Absorption from rat small intestine is pH-dependent over the range 5.5-7.4, with higher pHs favouring absorption. Possibly hydroxylation of the compound may be involved (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 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: 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

Toxicology of inorganic mercury compounds reviewed (8,9).

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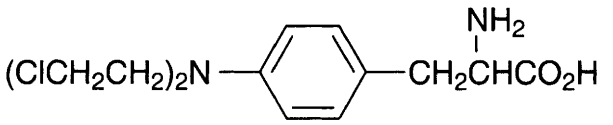
M88 merphalan



$C_{13}H_{18}Cl_2N_2O_2$ **Mol. Wt.** 305.20 **CAS Registry No.** 531-76-0

Synonyms DL-phenylalanine, 4-[bis(2-chloroethyl)amino]-; DL-3-[[*p*-bis(2-chloroethyl)amino]phenyl]alanine; DL-phenylalanine mustard; DL-sarcolysin; CB-3307

RTECS No. AY 3600000

Uses Antineoplastic agent, particularly for breast and ovarian cancer.

Physical properties

M. Pt. 172-174°C

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 23 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).

♂ mice receiving 1.25-2.5 mg kg^{-1} intraperitoneally three times per wk for 6 months developed a significantly increased number of tumours, particularly lymphosarcomas. ♂ rats receiving 0.75 mg kg^{-1} intraperitoneally showed an increased incidence of sarcomas, particularly of peritoneal and reticulum cells, while ♀ rats receiving the same dose showed an increased incidence of sarcomas, particularly of peritoneal and breast cells (3).

Virgin ♀ rats given a single intraperitoneal injection of 10 mg kg^{-1} developed an increased incidence of mammary fibroadenomas within 17 months (4).

Teratogenicity and reproductive effects

Merphalan has been shown to be teratogenic in rats, when given during the first 10 days of pregnancy, causing termination of pregnancy and various types of malformations (5).

Metabolism and toxicokinetics

Distribution throughout tissues in humans can be variable and lead to variable responses to treatment (6).

After administration by perfusion to cancer patients, 60% of dose can be removed within 45 min (7).

After intraperitoneal administration to rats of β-^{14}C-merphalan, there was selective binding of radioactivity to the soluble protein fraction of kidney after 2 days (1).

Merphalan reacts rapidly with heparinised blood *in vitro* (7).

Genotoxicity

Escherichia coli sd-4-73, streptomycin-independent reversion-induction positive (8).

Cytotoxicity is associated with the bis(chloroethyl)amino group (9).

Other effects

Other adverse effects (human)
Can cause neutropenia and thrombocytopenia (10).

Any other adverse effects
The compound exerts immunosuppressive effects in mice (11).

Other comments

Merphalan is a mixture of the two isomers medphalan and melphalan. The toxicology of the two isomers and merphalan itself have been reviewed (12).

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3. Weisburger, E. K. *Cancer* 1977, **40**, 1935-1949.
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5. Aleksandrov, V. A. *Dokl. Akad. Nauk SSSR* 1966, **171**, 146-149.
6. Albert, D. S. et al *Clin. Pharmacol. Ther.* 1979, **26**, 737.
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M89 merphos

$$P(SCH_2CH_2CH_2CH_3)_3$$

$C_{12}H_{27}PS_3$ **Mol. Wt.** 298.52 **CAS Registry No.** 150-50-5

Synonyms phosphorotrithious acid, tributyl ester; tributyl phosphorotrithioate; *S,S,S*-tributyl trithiophosphite; Folex; Deleaf defoliant; Butiphos

EINECS No. 205-761-4 **RTECS No.** TG 5600000

Uses Superseded herbicide. Chemical intermediate.

Physical properties

B. Pt. 150-152°C **Flash point** 60-63°C **Specific gravity** 0.987 at 20°C with respect to water at 4°C
Solubility Organic solvents: chloroform, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂, ♀ rat 1475 mg kg^{-1} (1).
LD_{50} dermal ♂ rat 690 mg kg^{-1}; ♀ rat 615 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 150 mg kg^{-1} (2).
LD_{Lo} subcutaneous atropinised chicken 600 mg kg^{-1} (1).

Sub-acute and sub-chronic data
In 90-day feeding trials, dogs and cats fed 750 mg kg^{-1} diet showed depression of cholinesterase activity, but no other pathological or histological effects (3).

Metabolism and toxicokinetics

Merphos can be absorbed from the gastro-intestinal tract or through skin. The compound is more toxic in rats via the dermal route (1).

Other effects

Any other adverse effects

Subcutaneous single injections of ≥600 mg kg^{-1} to atropinised chickens caused muscle weakness or paralysis for more than 90 days, onset time 3-21 days (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).

Other comments

Toxicity and environmental fate reviewed (6).

Metabolic pathways reviewed (7).

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1. Gaines, T. B. *Toxicol. Appl. Pharmacol.* 1969, **14**(3), 515-534.
2. *Proc. Soc. Exp. Biol. Med.* 1963, **114**, 509.
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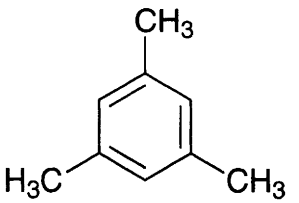
M90 mesitylene



C_9H_{12} **Mol. Wt.** 120.19 **CAS Registry No.** 108-67-8

Synonyms benzene, 1,3,5-trimethyl-; *s*-trimethylbenzene; trimethylbenzol; Fleet-X

EINECS No. 203-604-4 **RTECS No.** OX 6825000

Uses Chemical intermediate.

Physical properties

M. Pt. –44.8°C **B. Pt.** 164.7°C **Flash point** 44°C **Specific gravity** 0.8637 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 3.42 **Volatility** v.p. 1.82 mmHg at 20°C ; v.den. 4.1
Solubility Water: 20 mg l^{-1}. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 20 pppm (100 mg m^{-3})
FR-VME 25 ppm (125 mg m^{-3})
JP-OEL 25 ppm (120 mg m^{-3})
SE-LEVL 25 ppm (120 mg m^{-3}) **SE-STEL** 35 ppm (170 mg m^{-3})
UK-LTEL 25 ppm (125 mg m^{-3})
US-TWA 25 ppm (123 mg m^{-3})

UN No. 2325 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification irritant, dangerous for the environment
Risk phrases Flammable – Irritating to the respiratory system – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R10, R37, R51/53)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S61)

Ecotoxicity

Fish toxicity
LC_{Lo} (96 hr) goldfish 13 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (24 hr) *Daphnia magna* ~50 mg l^{-1}. NOEC (21 day) *Daphnia* reproduction test 0.4 mg l^{-1} (minimum value); 2 mg l^{-1} (nominal value) (2).
EC_{50} (48 hr) *Scenedesmus subspicatus* 25-53 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) inhalation rat 24 mg m^{-3} (4).
LD_{Lo} intraperitoneal guinea pig 1-3 mg kg^{-1} (5).

Metabolism and toxicokinetics
Eight volunteers aged 20-39, with no history of exposure to trimethylbenzene, were exposed in 8 hr inhalation tests to mesitylene at concentrations ranging from 5 to 150 mg m^{-3}. Pulmonary ventilation in the volunteers ranged from 0.56 to 1.0 m^3 hr^{-1}. The retention of mesitylene in the lungs was 67%. The highest rates of metabolite excretion and the highest quantities of dimethylbenzoic acids in urine during 24-hr intervals were observed on day-5 of exposure (6).

Irritancy
Skin and respiratory irritant (species unspecified) (7).

Other comments

Ground, air and water pollutant. Detected in gasoline and in diesel exhaust. Occurs in the aroma of some cooked foods.

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M91 mesityl oxide

$$(CH_3)_2C{=}CHC(O)CH_3$$

$C_6H_{10}O$ **Mol. Wt.** 98.14 **CAS Registry No.** 141-79-7

Synonyms 4-methylpent-3-en-2-one; isobutenyl methyl ketone; isopropylidene acetone; methyl 2,2-dimethylvinyl ketone; methyl isobutenyl ketone

EINECS No. 205-502-5 **RTECS No.** SB 4200000

Uses Solvent for nitrocellulose, gums and resins. In lacquers, varnishes and enamels. In methyl isobutyl ketone synthesis.

Physical properties

M. Pt. -59°C **B. Pt.** 130°C **Flash point** 30.5°C **Specific gravity** 0.8539 at 20°C with respect to water at 4°C
Volatility v.p. 10 mmHg at 20°C ; v.den. 3.38
Solubility Water: 28 g l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 25 ppm (100 mg m^{-3})
FR-VME 15 ppm (60 mg m^{-3})
UK-LTEL 15 ppm (61 mg m^{-3}) **UK-STEL** 25 ppm (102 mg m^{-3})
US-TWA 15 ppm (60 mg m^{-3}) **US-STEL** 25 ppm (100 mg m^{-3})

UN No. 1229 **HAZCHEM Code** 3W **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation, in contact with skin and if swallowed (R10, R20/21/22)
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} goldfish 540 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1120 mg kg^{-1} (2).
LD_{50} oral mouse 710 mg kg^{-1} (3).
LD_{50} oral rabbit 1000 mg kg^{-1} (4).
LC_{50} inhalation (4 hr) rat 9 g m^{-3} (3).
LC_{50} inhalation (2 hr) mouse 10 g m^{-3} (3).
LD_{50} dermal rabbit 5150 mg kg^{-1} (5).
LD_{50} intraperitoneal mouse 354 mg kg^{-1} (6).

Irritancy
Dermal rabbit 430 mg, open to atmosphere, caused mild irritation (7).
Eye rabbit 4325 µg caused severe irritation (duration unspecified) (8).
In humans eye, irritation was observed at 25 ppm and nasal irritation at 50 ppm (9).

Other effects

Other adverse effects (human)
Body temperature effects, effects on heart rate and convulsions have been reported (10,11).

Any other adverse effects

Inhalation (4 hr) rats (dose unspecified), leucopenia without any change in differential or red blood cell counts was observed. Leucopenia was caused when exposure reached irritant level (12).

Injury to lungs, liver and kidney were observed in animal experiments (13).

Inhalation studies in rats revealed hypertrophy of the liver, changes to the kidney and spleen, and anaemia and other changes to the blood (14).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

Other comments

Hazardous properties reviewed (16).

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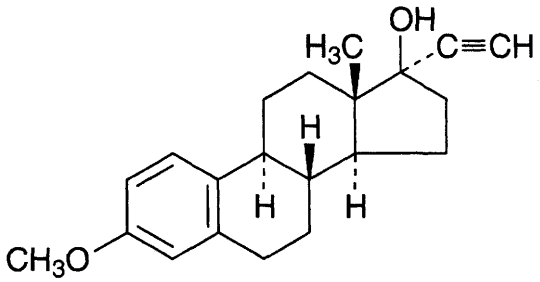
M92 mestranol



$C_{21}H_{26}O_2$ **Mol. Wt.** 310.44 **CAS Registry No.** 72-33-3

Synonyms 19-norpregna-1,3,5(10)-trien-20-yn-17-ol, 3-methoxy-, (17α)-; 17α-ethynylestradiol 3-methyl ether; 17α-ethynyl-3-methoxy-1,3,5(10)-estratriene-17β-ol; Menophase; Norquen

EINECS No. 200-777-8 **RTECS No.** RC 8960000

Uses Oestrogen in oral contraceptives and for oestrogen deficiency conditions, active by oral route.

Physical properties

M. Pt. 150-151°C
Solubility Organic solvents: acetone, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral blackbird 1 g kg^{-1} (1).
LD_{50} oral coturnix 1 g kg^{-1} (1).
LD_{50} intraperitoneal mouse 3.5 g kg^{-1} (2).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (3).
♀ mice given 20 mg kg^{-1} diet for their lifespan showed an increased incidence of chromophobe adenomas and an increase in some non-metastasising epithelial tumorous lesions (4).
Castrated ♂ mice receiving 0.1 or 1.0 mg kg^{-1} diet developed an increased incidence of mammary tumours (5).
♀ rats given 3 mg orally on 6 days of the wk for 50 wk developed no mammary tumours (6).
♀ monkeys receiving up to 50 times the human dose orally for 7 yr developed some slight ductal epithelial hyperplasia in mammary glands and some palpable nodules (7).
No significant increase in mammary tumour occurrence was seen in dogs dosed orally with mestranol (8,9).
Mice receiving 0.1 mg subcutaneously twice wkly from 1 to 21 months of age showed a significant increase in incidence of mammary tumours (10).

Teratogenicity and reproductive effects
Oral administration of 0.05-0.2 mg kg^{-1} to mice on days 4-8 increased the number of resorptions, while on days 7-11, abortions but no teratogenic effects were seen (11).
In rats, subcutaneous administration of 0.1 mg kg^{-1} on days 2-4 terminated pregnancy (12).
Prenatal administration to rats by oral administration to mothers of 0.1 mg kg^{-1} on days 14.5-19.5 influenced testosterone production of ♂ offspring both in foetal and adult stages (13).

Metabolism and toxicokinetics
Readily absorbed from gastro-intestinal tract of animals and humans with $t_{1/2}$ 50 hr. Enterohepatic circulation of metabolites is a significant feature of metabolism, with several metabolites being eliminated in urine (14-16).
In humans, 54% of dose can be demethylated to ethynylestradiol, with this proportion varying in other species (17).
The demethylated product then follows the pathways for ethynylestradiol metabolism (14,18).
Mestranol is well distributed within the body and is thought able to cross into the placenta (13,19).
Found in secretions such as breast milk. The main compound found in plasma after intravenous administration is ethynylestradiol 3-sulfate (14,19,20).

Genotoxicity

Salmonella typhimurium TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (21).
Drosophila melanogaster lethal mutagenicity negative (22).
In vivo mouse bone marrow cells chromosomal aberrations negative (23).
Effects on cell proliferation *in vitro* at 10^{-6} M have been found using hepatocarcinoma HepG2 cells (24).

Other comments

Toxicology and genotoxicity reviewed (25,26).

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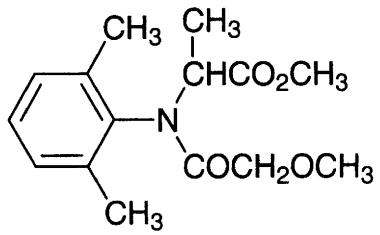
M93 metalaxyl



$C_{15}H_{21}NO_4$ **Mol. Wt.** 279.34 **CAS Registry No.** 57837-19-1

Synonyms methyl *N*-(methoxyacetyl)-*N*-(2,6-xylyl)-DL-alaninate; methyl *N*-(2-methoxyacetyl)-*N*-(2,6-xylyl)-DL-alaninate; Ridomil; Subdue; Metaxanin

EINECS No. 260-979-7 **RTECS No.** AY 6910000

Uses Fungicide.

Physical properties

M. Pt. 71.8-72.3°C **Specific gravity** 1.20 at 20°C **Volatility** v.p. 2.2×10^{-6} mmHg at 20°C
Solubility Water: 7.1 g l^{-1} at 20°C. Organic solvents: benzene, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, carp, bluegill sunfish >100 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 119 ppm Microtox test (2).

Non-toxic to bees (1).

Environmental fate

Degradation studies

Residual activity in soil can be detected for 70-90 days (3).

Abiotic removal

Many products were found in a study of the degradation of metalaxyl in soil in the presence of natural sunlight. Three of these compounds were identified and characterised: 2,6-dimethylaniline, 2,6-dimethyl-*N*-ethylacetanilide and *N*-(2,6-dimethylphenyl)alanine methyl ester (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 566 mg kg^{-1} (5).

LD_{50} dermal rat >3100 mg kg^{-1} (6).

Sub-acute and sub-chronic data

90-day feeding trial rats, NOEC 17 mg kg^{-1} (diet) (6).

6-month feeding trial dogs, NOEC 7.6 mg kg^{-1} (diet) (6).

Metabolism and toxicokinetics

In mammals, after oral administration, the ester bond is hydrolysed and the methyl ether bond oxidatively cleaved (1).

Irritancy

Slight irritant to rabbit eyes and skin (dose/duration unspecified) (6).

Sensitisation

No skin sensitisation in guinea pigs (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (7).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

ADI 0.03 mg kg^{-1} (6).

WHO Toxicity Class III (9).

EPA Toxicity Class III (6).

Other comments

Contaminant of food and water (3,10).

Transformation in soil and water has been reviewed (11).

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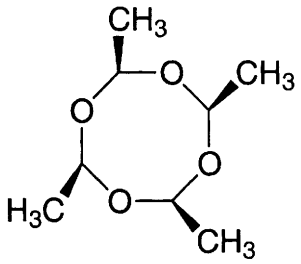
M94 metaldehyde



$C_8H_{16}O_4$ **Mol. Wt.** 176.21 **CAS Registry No.** 108-62-3

Synonyms 2,4,6,8-tetramethyl-1,3,5,7-tetroxocane; metacetaldehyde; 1'-2,C-4,C-6,C-8-tetramethyl-1,3,5,7-tetroxocane; acetaldehyde tetramer

EINECS No. 203-600-2 **RTECS No.** XF 9900000

Uses Molluscicide. In compressed form as a fuel.

Physical properties

M. Pt. 246°C (sealed tube) **B. Pt.** 112-115°C (sublimes with partial depolymerisation) **Flash point** 36-40°C
Solubility Water: 200 mg l^{-1} at 17°C. Organic solvents: benzene, chloroform

Occupational exposure

UN No. 1332 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid
Supply classification harmful
Risk phrases Flammable – Harmful if swallowed (R10, R22)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Avoid contact with the eyes – If swallowed seek medical advice immediately and show this container or label (S2, S13, S25, S46)

Ecotoxicity

Fish toxicity
Non-toxic to fish (1).

Invertebrate toxicity
Metaldehyde is orally active in molluscs on land and water and is thought to affect nervous system activity (2,3).

Environmental fate

Abiotic removal
Gradual degradation by depolymerisation to acetaldehyde is seen in the environment, followed by oxidation to acetic acid (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, dog, rat 600-630 mg kg^{-1} (1,4).
LD_{50} oral dog 1000 mg kg^{-1} (4).
LD_{Lo} oral child 100 mg kg^{-1} (5).
LD_{Lo} oral adult human 43 mg kg^{-1} (6).
LD_{50} dermal rat >5 g kg^{-1} (1).

Sensitisation

No significant dermatitis has been seen in patch tests (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (8).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).
WHO Toxicity Class III (10).
EPA Toxicity Class III (formulation) (1).
ADI 0.025 mg kg^{-1} body weight (4).

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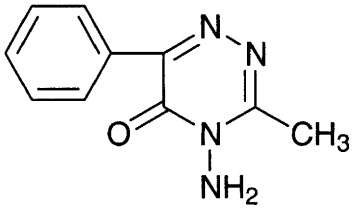
M95 metamitron



$C_{10}H_{10}N_4O$ **Mol. Wt.** 202.22 **CAS Registry No.** 41394-05-2

Synonyms 4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one; 4-amino-4,5-dihydro-3-methyl-6-phenyl-1,2,4-triazin-5-one; BAY DRW1139; methiamitron; Metamitrone

EINECS No. 255-349-3 **RTECS No.** XZ 3015000

Uses Herbicide.

Physical properties

M. Pt. 166.6°C **Specific gravity** 1.35 g cm^{-3} **Partition coefficient** log P_{ow} 0.833 **Volatility** v.p. 9.8×10^{-5} mmHg
Solubility Water: 1.82 g l^{-1} at 20°C. Organic solvents: cyclohexanone, dichloromethane

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 data sheet (S2, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) goldfish 400-500 mg l^{-1} (70% wettable powder formulation) (1).
LC_{50} (96 hr) carp 500 mg l^{-1} (1).
LC_{50} (96 hr) orfe 240-300 mg l^{-1} (70% wettable powder formulation) (1).

Invertebrate toxicity
Metamitron is toxic to starfish at concentrations >10 ppm. Exposure to light increases toxicity (2).

Environmental fate

Degradation studies
In soil, 20% of compound applied may be detectable after 4-6 wk, but can be as low as 4% by 8 wk (1,3).
The major metabolite is the active desamino-metamitron, but neither this nor the parent compound appear to leach below the top 20 cm of soil (3).

Adsorption and retention
Formation of bound residues occurs (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral canary >1 g kg^{-1} (5).
LD_{50} oral ♂, ♀ rat 3343, 1832 mg kg^{-1}, respectively (5).
LD_{50} oral mouse 1450-1463 mg kg^{-1} (5).
LD_{50} dermal rat >1 g kg^{-1} (5).

Sub-acute and sub-chronic data
A 90-day feeding trial in dogs established NOEC 500 mg kg^{-1} diet (5).

Carcinogenicity and chronic effects
A 2-yr feeding trial in rats established NOEC 250 mg kg^{-1} diet (5).

Metabolism and toxicokinetics
After oral administration to mammals, 50% of dose is eliminated in urine and 50% in faeces within 48 hr (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).
WHO Toxicity Class III (8).
EPA Toxicity Class III (formulation) (5).
ADI 0.025 mg kg^{-1} body weight (5).

Other comments

Metabolic pathways reviewed (9).

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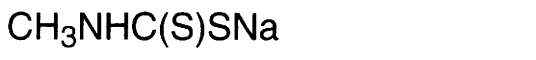
M96 metam-sodium



$C_2H_4NNaS_2$ **Mol. Wt.** 129.18 **CAS Registry No.** 137-42-8

Synonyms sodium methyldithiocarbamate; metham sodium; methylcarbamodithioic acid, sodium salt; methyldithiocarbamic acid, sodium salt; *N*-methylaminodithioformic acid, sodium salt; Vapam

EINECS No. 205-293-0 **RTECS No.** FC 2100000

Uses Soil fumigant.

Physical properties

M. Pt. 482°C (decomp.) **Partition coefficient** log P_{ow} <1.0 at 25°C

Solubility Water: 722 g l^{-1} at 20°C. Organic solvents: acetone, ethanol, kerosene, xylene

Occupational exposure

Supply classification harmful

Risk phrases Harmful in contact with skin and if swallowed – Contact with acids liberates toxic gas – Risk of serious damage to eyes (R21/22, R31, R41)

Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection (S2, S26, S36/37/39)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) guppy, bluegill sunfish, rainbow trout 4.2, 0.39, 0.079 mg l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rabbit, guinea pig, rat 50, 320, 815, 1700 mg kg^{-1}, respectively (2-4).

LD_{50} dermal rat, rabbit 636, 800 mg kg^{-1}, respectively (5,6).

Sub-acute and sub-chronic data

LC_{50} (5-day) mallard duck and Japanese quail >5000 mg kg^{-1} in diet (1).

Teratogenicity and reproductive effects

Foetal death, delayed ossification, but no external deformities reported in rats administered 90 mg kg^{-1} (route unspecified) during pregnancy (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).
WHO Toxicity Class II (9).
EPA Toxicity Class II (formulation) (1).

Other comments

Hazards reviewed (10).

References

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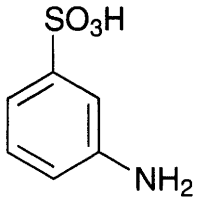
M97 metanilic acid



$C_6H_7NO_3S$ **Mol. Wt.** 173.19 **CAS Registry No.** 121-47-1

Synonyms 3-aminobenzenesulfonic acid; 1-aminobenzene-3-sulfonic acid; *m*-sulfanilic acid; aniline-*m*-sulfonic acid

EINECS No. 204-473-6 **RTECS No.** OY 2300000

Uses Synthesis of azo dyes and certain sulfa drugs.

Physical properties

M. Pt. decomposes without melting at ~288°C **Specific gravity** 1.69
Solubility Water: 10.8 g l^{-1} at 20°C. Organic solvents: hot methanol

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) – Avoid contact with the eyes – After contact with skin, wash immediately with plenty of water (S2, S25, S28)

Ecotoxicity

Bioaccumulation
Non-accumulative or low accumulative (1).

Environmental fate

Degradation studies
Decomposition by soil microflora in >64 days (2).
An adapted activated sludge utilises metanilic acid as sole carbon source at 20°C. 95% COD, 4 mg COD g^{-1} dry inoculum hr^{-1} (3).
BOD_5 1.1 mg l^{-1} standard diluting sewage (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 12 g kg^{-1} (5).

Metabolism and toxicokinetics
Metanilic acid interacts with rat liver glutathione-*S*-transferase by direct binding (6).

Irritancy
500 mg instilled in rabbit eye for 24 hr caused mild irritation (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (7).

Other comments

Reviews on physico-chemical properties, experimental toxicology, human health effects and ecotoxicology listed (8).

References

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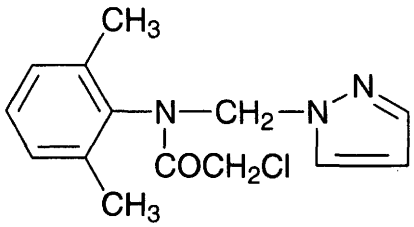
M98 metazachlor



$C_{14}H_{16}ClN_3O$ **Mol. Wt.** 277.75 **CAS Registry No.** 67129-08-2

Synonyms 2-chloro-*N*-(2,6-dimethylphenyl)-*N*-(1*H*-pyrazol-1-ylmethyl)acetamide; 2-chloro-*N*-(pyrazol-1-ylmethyl)acet-2′,6′-xylidide; BAS47900H; Butisan S

EINECS No. 266-583-0 **RTECS No.** AB 5442000

Uses Herbicide.

Physical properties

M. Pt. ~85°C **Specific gravity** ~1.31 at 20°C **Partition coefficient** log P_{ow} 2.13 at pH 7 and 22°C
Volatility v.p. 7.0×10^{-7} mmHg at 20°C
Solubility Water: 430 mg l^{-1} at 20°C. Organic solvents: acetone, chloroform, ethanol, ethyl acetate

Ecotoxicity

Fish toxicity
Toxic to trout, moderately toxic to carp (1).

Environmental fate

Degradation studies
Degradation in soil is reduced or inhibited by antimicrobial agents and protein synthesis inhibitors (2).
Degradation products in soil include: 2-hydroxy-*N*-(2,6-dimethylphenyl)-*N*-(1*H*-pyrazol-1-yl methyl)acetamide, 2-chloro-*N*-(2,6-dimethylphenyl)acetamide, and 4,4′-methylenebis(2,6-dimethylbenzeneamine). The latter product is seen only in low concentrations. Metazachlor $t_{1/2}$ 2 months and the metabolites $t_{1/2}$ 3-3.5 months (3).

Adsorption and retention
Does not show competitive adsorption with humic substances during water treatment with activated carbon, but does show carbon fouling through pre-adsorption (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2.15 g kg^{-1} (5).
LD_{50} dermal rat >6.8 g kg^{-1} (5).

Irritancy
Non-irritant to mucous membrane of rabbit (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).
WHO Toxicity Class Table 5 (8).
ADI 0.036 mg kg^{-1} body weight (5).

Other comments

Water pollutant. Food contaminant.
Non-toxic to bees (1).
Metabolic pathways reviewed (9).

References

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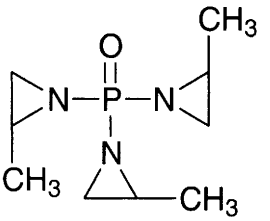
M99 metepa



$C_9H_{18}N_3OP$ **Mol. Wt.** 215.24 **CAS Registry No.** 57-39-6

Synonyms 1,1',1'-phosphinylidynetris(2-methylaziridine); tris(2-methyl-1-azirinyl)phosphine oxide; methylapoxide

Uses Chemosterilant. Also used in crease proofing and flameproofing textiles.

Physical properties

B. Pt. 90-92°C (0.15-0.3 mmHg) **Specific gravity** 1.079 at 25°C with respect to water at 25°C
Solubility Water: miscible. Organic solvents: miscible with chloroform, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

Pupae of mosquito flies exposed to ≤10,000 ppm for 2 hr or ♀ flies fed ≤0.5% in diet yielded no-effect levels of 1000 ppm and 0.05%, respectively. Higher doses to pupae and adults caused deaths (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂ rat 136 mg kg^{-1}; ♀ rat 213 mg kg^{-1} (2).
LD_{50} oral mouse 292 mg kg^{-1} (3).
LD_{50} dermal mouse 375 mg kg^{-1} (3).
LD_{50} subcutaneous mouse 140 mg kg^{-1} (3).

Carcinogenicity and chronic effects

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

Rats administered 0.625 mg kg^{-1} orally for ≤422 days did not develop tumours. Lymphatic leukaemias were seen at a low incidence in animals given ≥2.5 mg kg^{-1}, but not in a dose-related manner (5).

Teratogenicity and reproductive effects

Rats ♀ injected intraperitoneally with 30 mg kg^{-1} on day-12 of pregnancy showed teratogenic and embryotoxic effects. All neonates had malformations including ectrodactyly. Daily injections of 1.25 mg kg^{-1} on days 7-13 of pregnancy caused reduction in foetal and placental weight. In ♂ rats a sterilising effect was seen (5).

Metabolism and toxicokinetics

♂ mice injected intraperitoneally with 100 mg kg^{-1} [^{32}P]-metepa eliminated 50% of the dose in urine within 12 hr, mostly in unchanged form or as phosphoric acid. Unchanged metepa was the major radioactive substance in blood at 2 hr, but had almost disappeared by 6 hr (6).

Genotoxicity

Salmonella typhimurium G-46 host mediated assay positive (7).

Mice dominant lethal assay positive (8).

Chronic treatment of ♂ mice 40 mg kg^{-1} orally or intraperitoneally induced micronuclei in bone marrow cells and chromosomal aberrations in testicular germ cells (9).

Other comments

Toxicology reviewed (10).

References

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M100 metformin hydrochloride

$$(H_3C)_2NC(=NH)NHC(=NH)NH_2 \cdot HCl$$

$C_4H_{12}ClN_5$ **Mol. Wt.** 165.63 **CAS Registry No.** 1115-70-4

Synonyms 1,1-dimethylbiguanide hydrochloride; *N,N*-dimethylimidodicarbonimidic diamide monohydrochloride; Glucophage; Diabefagos; Meguan; metformin HCl

EINECS No. 214-230-6 **RTECS No.** DU 1800000

Uses Hypoglycaemic drug used in oral treatment of maturity onset diabetes.

Physical properties

M. Pt. 232°C

Solubility Water: 500 g l^{-1}. Organic solvents: 95% ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1000, 1450 mg kg^{-1}, respectively (1).
LD_{50} intraperitoneal mouse 420 mg kg^{-1} (1).
LD_{50} subcutaneous rat 300 mg kg^{-1} (1).

Metabolism and toxicokinetics

After oral administration to humans, there is incomplete absorption from the gastro-intestinal tract, but that part which is absorbed is excreted unchanged in urine (2,3).
There is no binding to plasma protein and $t_{1/2}$ is 1.5-3 hr (3,4).
There is little or no effect on blood sugar of normal human subjects, rats, guinea pigs or rabbits, but dogs are more sensitive, with an oral dose of 100 mg kg^{-1} reducing blood sugar significantly (5,6).

Irritancy

100 mg instilled into rabbit eye for 2 sec caused mild irritation and 500 mg applied to rabbit skin caused mild irritation (7,8).

Other effects

Other adverse effects (human)

The compound can cause lactic acid acidosis, and care has to be taken when using the compound in conditions where such acidosis might result. Other side-effects include anorexia, nausea, vomiting and diarrhoea (4).
Some drug interactions occur, including that with verapamil (4,9).

Other comments

The compound has been shown to be of use in treatment of ischaemia and anoxia (10).
Some circulating insulin must be present for the hypoglycaemic effect (2).

References

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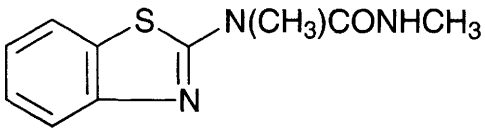
M101 methabenzthiazuron



$C_{10}H_{11}N_3OS$ **Mol. Wt.** 221.28 **CAS Registry No.** 18691-97-9

Synonyms 1-(1,3-benzothiazol-2-yl)-1,3-dimethylurea; 1-benzothiazol-2-yl-1,3-dimethylurea; *N*-2-benzothiazolyl-*N*,*N*'-dimethylurea; 1-(2-benzothiazolyl)-1,3-dimethylurea; methibenzuron; Tribunil

EINECS No. 242-505-0 **RTECS No.** YR 8980000

Uses Herbicide.

Physical properties

M. Pt. 119-121°C **Partition coefficient** log P_{ow} 2.640 (1) **Volatility** v.p. 4.4×10^{-6} mmHg at 20°C
Solubility Water: 59 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, dimethylformamide, hexane, isopropanol, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, golden orfe 16-29 mg l^{-1} (1).

Environmental fate

Degradation studies
60% loss from soil after 127 days (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit, cat, dog >1000 mg kg^{-1} (1,3).
LD_{50} oral guinea pig >2500 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >500 mg m^{-3} (1).
LD_{50} dermal rat >500 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 315-540 mg kg^{-1} (3).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 150 mg kg^{-1} diet (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
WHO Toxicity Class Table 5 (5).
EPA Toxicity Class IV (formulation) (6).

Other comments

In plants, metabolised to *N*-hydroxymethyl-*N*-(2-benzothiazolyl)urea and *N*-methyl-*N*-(2-benzothiazolyl)urea as the water-soluble glucosides (1).
Metabolic pathways reviewed (7).

References

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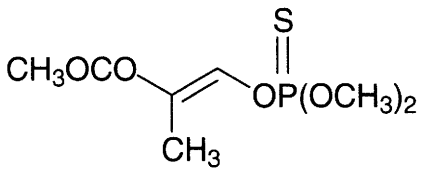
7. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

M102 methacrifos



$C_7H_{13}O_5PS$ **Mol. Wt.** 240.22 **CAS Registry No.** 62610-77-9

Synonyms methyl (*E*)-3-(dimethoxyphosphinothioyloxy)-2-methylacrylate; (*E*)-*O*-2-methoxycarbonylprop-1-enyl *O*,*O*-dimethyl phosphorothioate; (*E*)-methyl 3-[(dimethoxyphosphinothioyl)oxy]-2-methyl-2-propenoate; OMS 2005; Damfin

RTECS No. UD 3335000

Uses Acaricide. Insecticide.

Physical properties

B. Pt. 90°C at 0.01 mmHg **Specific gravity** 1.225 at 20°C **Partition coefficient** log P_{ow} ≥3.0
Volatility v.p. 1.2×10^{-3} mmHg at 20°C
Solubility Water: 400 mg l^{-1} at 20°C. Organic solvents: benzene, dichloromethane, diethyl ether, ethanol, hexane, methanol

Environmental fate

Abiotic removal
Calculated hydrolysis $t_{1/2}$ 66 days at pH 1, 29 days at pH 7 and 9.5 days at pH 9 (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 680 mg kg^{-1} (1,2).
LC_{50} (6 hr) inhalation rat 2200 mg m^{-3} (1,2).
LD_{50} dermal rat >3100 mg kg^{-1} (1-3).

Carcinogenicity and chronic effects
Oral ♀ rat (100 wk) 1-100 mg l^{-1} in drinking water for up to 30 wk for the higher concentrations, and for life at the lower concentrations. There was a dose-related incidence of tumours of the upper gastro-intestinal tract. The highest dose induced liver tumours (1).

Irritancy
Reported to be a mild skin irritant, but not irritating to the eyes of rabbits (1).

Genotoxicity

CASE structure-activity methodology predicted positive mutagenicity to *Salmonella typhimurium* (2).
Drosophila melanogaster sex-linked recessive lethal assay positive (3).

Other effects

Any other adverse effects
Inhibits cholinesterase activity (1,2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (4).
WHO Toxicity Class II (5).
ADI 0.006 mg kg^{-1} body weight (1).

References

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M103 methacrolein

$$CH_2=C(CH_3)CHO$$

C_4H_6O **Mol. Wt.** 70.09 **CAS Registry No.** 78-85-3

Synonyms isobutenal; methenylaldehyde; 2-methylacrolein; 2-methylpropenal; 2-methyl-2-propenal; methacrylaldehyde

EINECS No. 201-150-1 **RTECS No.** OZ 2625000

Uses Manufacture of copolymers and resins.

Physical properties

M. Pt. –81°C **B. Pt.** 69°C **Flash point** –15°C **Specific gravity** 0.847 at 20°C with respect to water at 4°C
Volatility v.p. 120 mmHg at 20°C ; v.den. 2.42
Solubility Water: 64 g l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2396 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic

Ecotoxicity

Fish toxicity

Fatal to brown trout, bluegill sunfish, yellow perch and goldfish after 22 hr at 5 ppm. Test conditions: pH 7.0; dissolved oxygen content 7.5 ppm; total hardness (soap method) 300 ppm; methyl orange alkalinity 310 ppm; free carbon dioxide 5 ppm; temperature 12.8°C (1).

Environmental fate

Degradation studies

65% ThOD removed by acclimatised sewage in 10 days at 20°C (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 110-140 mg kg^{-1} (3).

LC_{Lo} (4 hr) inhalation rat 125 ppm (4).

LD_{50} dermal rabbit 360 mg kg^{-1} (5).

Irritancy

Dermal rabbit (24 hr) 500 mg caused severe irritation. 50 μg instilled into rabbit eye caused severe irritation (3).

Genotoxicity

Salmonella typhimurium TA104 without metabolic activation positive (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

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M104 methacrolein diacetate

$$CH_2=C(CH_3)CH(O_2CCH_3)_2$$

$C_8H_{12}O_4$ **Mol. Wt.** 172.18 **CAS Registry No.** 10476-95-6

Synonyms acetic acid, 2-methyl-2-propene-1,1-diol diester; methallylidene diacetate

EINECS No. 233-974-2 **RTECS No.** UC 9800000

Physical properties

M. Pt. –15°C **B. Pt.** 191°C **Flash point** 83°C **Specific gravity** 1.039 at 20°C with respect to water at 20°C
Volatility v.p. 760 mmHg at 191°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 440 mg kg^{-1} (1).
LC_{Lo} (1 hr) inhalation rat 62 ppm (1).
LD_{50} dermal rabbit 44 mg kg^{-1} (1).
LD_{Lo} intraperitoneal mouse 250 mg kg^{-1} (2).

Irritancy

Causes severe irritation. High concentrations are extremely destructive to tissues of the mucous membranes, upper respiratory tract, eyes and skin (species unspecified) (3).
Rabbit eye studies demonstrated severe irritation and corneal damage, being rated 9 on a scale of 10 (4).

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M105 methacrylamide

$$CH_2=C(CH_3)C(O)NH_2$$

C_4H_7NO **Mol. Wt.** 85.11 **CAS Registry No.** 79-39-0
Synonyms 2-methylacrylamide; 2-methyl-2-propenamide; methacrylic acid amide; 2-methylpropenamide
EINECS No. 201-202-3 **RTECS No.** UC 6475000

Physical properties

M. Pt. 108-109°C **B. Pt.** 215°C **Flash point** 103°C **Specific gravity** 1.053 at 20°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 451, 459 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (3).

References

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M106 methacrylic acid

$$CH_2=C(CH_3)CO_2H$$

$C_4H_6O_2$ **Mol. Wt.** 86.09 **CAS Registry No.** 79-41-4

Synonyms α-methacrylic acid; 2-methylpropenoic acid; 2-methyl-2-propenoic acid

EINECS No. 201-204-4 **RTECS No.** OZ 2975000

Uses Manufacture of methacrylate resins and plastics.
Occurrence In oil from Roman chamomile.

Physical properties

M. Pt. 16°C **B. Pt.** 163°C **Flash point** 77°C (open cup) **Specific gravity** 1.0153 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.93 **Volatility** v.p. 1.0 mmHg at 25.5°C ; v.den. 2.97
Solubility Water: 89 g l^{-1} at 25°C. Organic solvents: diethyl ether, ethanol, methanol

Occupational exposure

FR-VME 20 ppm (70 mg m^{-3})
SE-LEVL 20 ppm (70 mg m^{-3}) **SE-STEL** 30 ppm (100 mg m^{-3})
UK-LTEL 20 ppm (72 mg m^{-3}) **UK-STEL** 40 ppm (143 mg m^{-3})
US-TWA 20 ppm (70 mg m^{-3})

UN No. 2531 (inhibited) **HAZCHEM Code** 3X (inhibited) **Conveyance classification** corrosive substance (inhibited)
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) – Keep away from heat – 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, S15, S26, S45)

Ecotoxicity

Fish toxicity
No toxic effects to stickleback and rainbow trout at 1 mg l^{-1} for 24 hr (1).

Bioaccumulation
Calculated bioconcentration factor of 3.0 indicates that environmental accumulation is unlikely (2).

Environmental fate

Degradation studies
ThOD 1.67 mg l^{-1} O_2; BOD_5 0.89 mg l^{-1} O_2 in standard dilute sewage (3,4).

Abiotic removal
Methacrylic acid may undergo photolysis, based upon its slight absorption of light at wavelengths >290 nm in methanol (5).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 6.12 hr (6).
Volatilisation $t_{1/2}$ 27.5 days in model river water and 300 days in model pond water (2,7).

Adsorption and retention
Calculated K_{oc} of 76 indicates that adsorption to soil and sediments would be insignificant (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >100 mg kg^{-1} (8).
LD_{50} oral rat, mouse 60, 1600 mg kg^{-1}, respectively (9,10).
LD_{50} dermal rabbit 500 mg kg^{-1} (11).
LD_{50} intraperitoneal mouse 48 mg kg^{-1} (12).

Sub-acute and sub-chronic data

Gavage rat (10 days) 5 or 10 mg kg^{-1} day^{-1} caused slight to moderate alveolar haemorrhage and lipid granuloma in the lungs and moderate to severe granularity of liver cytoplasm (13).
Gavage rat (5 days) 50, 100 or 1000 mg kg^{-1} day^{-1} caused sufficient reduction in feed intake and weight loss to terminate the study (14).
Inhalation rat (20 days) 300 ppm 6 hr day^{-1} caused no clinical symptoms. Histopathological examination revealed slight renal congestion (15).

Irritancy

Dermal guinea pig (24 hr) 1 ml caused severe irritation. Application for 10 days caused necrosis (13).

Sensitisation

Did not cause sensitisation in guinea pig skin tests (13).

Genotoxicity

Escherichia coli DNA-cell-binding assay positive (16).

Other comments

Physical properties, mammalian toxicity and health hazards reviewed (17,18).

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M107 methacrylic anhydride

$$[CH_2=C(CH_3)C(O)]_2O$$

$C_8H_{10}O_3$ **Mol. Wt.** 154.17 **CAS Registry No.** 760-93-0

Synonyms methacrolyl anhydride; 2-methyl-2-propenoic acid anhydride

EINECS No. 212-084-8 **RTECS No.** OZ 5700000

Uses Manufacture of polymers.

Physical properties

B. Pt. 87°C at 13 mmHg **Flash point** 84°C **Specific gravity** 1.035 at 20°C
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LC_{50} (2 hr) inhalation mouse 450 mg m^{-3} (1).

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 (2).

References

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M108 methacrylonitrile

$$CH_2=C(CH_3)CN$$

C_4H_5N **Mol. Wt.** 67.09 **CAS Registry No.** 126-98-7

Synonyms 2-cyano-1-propene; isopropene cyanide; isopropenylnitrile; α-methacrylonitrile; 2-methylpropenenitrile

EINECS No. 204-817-5 **RTECS No.** UD 1400000

Uses Manufacture of homo- and copolymers. Chemical intermediate.

Physical properties

M. Pt. -35.8°C **B. Pt.** 90-92°C **Flash point** 12°C (open cup) **Specific gravity** 0.80 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.68 **Volatility** v.p. 40 mmHg at 12.8°C ; v.den. 2.31
Solubility Water: 2.57 g 100 ml^{-1} at 20°C. Organic solvents: miscible with acetone, octane, toluene; soluble in diethyl ether, ethanol, petroleum ether

Occupational exposure

FR-VME 1 ppm (3 mg m^{-3})
UK-LTEL 1 ppm (2.8 mg m^{-3})
US-TWA 1 ppm (2.7 mg m^{-3})

UN No. 1992 **HAZCHEM Code** 3WE (inhibited) **Conveyance classification** flammable liquid, toxic (inhibited)
Supply classification highly flammable, toxic
Risk phrases Highly flammable – Toxic by inhalation, in contact with skin and if swallowed – May cause sensitisation by skin contact (R11, R23/24/25, R43)
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 – Handle and open container with care – Do not empty into drains – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S16, S18, S29, S45)

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor of 2 indicates that environmental accumulation is unlikely (1).

Environmental fate

Degradation studies
Utilised as sole nitrogen source by *Klebsiella pneumoniae* culture isolated from sewage sludge. Metabolites included ammonia and acrylamide, which was further hydrolysed to acrylic acid. Optimum pH 8.0 and temperature 40-55°C (2).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ ~2 days (3).
Estimated volatilisation $t_{1/2}$ 5.3 hr from model river water and 60 hr from model pond water (1,4).

Adsorption and retention
Calculated K_{oc} of 18 indicates that adsorption to soil and sediments would be insignificant (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 17, 250 mg kg^{-1}, respectively (5,6).
LD_{Lo} oral mouse 15 mg kg^{-1} (7).
LC_{50} (4 hr) inhalation rat 330 ppm (8).
LC_{50} (4 hr) inhalation mouse, rabbit 36-37 ppm (8).
LD_{50} dermal rabbit 320 mg kg^{-1} (8).
LD_{Lo} intraperitoneal mouse 15 mg kg^{-1} (9).

Sub-acute and sub-chronic data
Inhalation rat (9 days) 20, 50 or 100 ppm 7 hr day^{-1} 5 days wk^{-1} induced sickness by day-1 and a 20% weight loss by day-8. No gross or microscopic lesions were observed (10).
Inhalation rat (91 days) 50 or 100 ppm. Some ♂ rats died by day-1 in the high-dose group. Weight gains were decreased and liver weight increased in all groups (10).
Inhalation dog (90 days) 9 or 14 ppm 7 hr day^{-1} 5 days wk^{-1}. Central nervous system effects were observed, manifested by convulsions and loss of motor control in the hind limbs in the high-dose group. Microscopic brain lesions were also observed. Elevated serum transaminase values were recorded on day-21 (10).

Teratogenicity and reproductive effects
Oral rat, 50 mg kg^{-1} day^{-1} during the first or second wk of gestation and 100 mg kg^{-1} day^{-1} only during the second wk of gestation caused a dose-dependent reduction in maternal body-weight gain. All treated rats aborted and were found to have developed dose-dependent oedema in the Fallopian tubes (11).

Metabolism and toxicokinetics

Following oral administration to rats of 100 mg kg^{-1} ^{14}C-labelled methacrylonitrile, 43% of ^{14}C was excreted in the urine, 15% in the faeces and 2% expired as CO_2 in 5 days. Hydrogen cyanide was not detectable. The red blood cells retained significant levels of radioactivity for more than 5 days after administration, whereas plasma levels declined sharply. >50% of the radioactivity in erythrocytes was detected covalently bound to cytoplasmic haemoglobin and membrane proteins. ~13% of the administered dose was recovered as thiocyanate in the plasma and urine. The authors concluded that toxicity of methacrylonitrile may be attributable to the whole molecule and not to *in vivo* liberation of cyanide (12).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation. 500 mg instilled into rabbit eye for 24 hr caused mild irritation (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (14).
Drosophila melanogaster sex-linked recessive lethal assay negative (15).
Genotoxicity in HepG2 cells was investigated using the LSC-based assay for unscheduled DNA synthesis. Methacrylonitrile may be a mutagen/carcinogen at lower doses (20 nmol $plate^{-1}$), but at higher doses (40 nmol $plate^{-1}$) it is cytotoxic (16).

Other effects

Other adverse effects (human)

Whole body exposure to 24 ppm for 1 min caused nose, throat and eye irritation among 6-22% of exposed subjects. Concentrations of ≤14 ppm caused no effects (17).

Any other adverse effects

Inhalation exposure of laboratory animals to 0.2-22.5 mg m^{-3} was toxic to the kidney and central nervous system (18). 100 mg kg^{-1} body $weight^{-1}$ day^{-1} (species and route unspecified) resulted in a decrease in red cell count and haemoglobin. Fluidity of erythrocyte membranes was altered by increased membrane cholesterol and unchanged phospholipid levels. A decrease in erythrocyte-membrane-bound enzymes was also observed (19).

Other comments

Physical properties, use, mammalian toxicity and health precautions reviewed (20-21).

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M109 methacryloyl chloride

$$CH_2=C(CH_3)C(O)Cl$$

C_4H_5ClO **Mol. Wt.** 104.54 **CAS Registry No.** 920-46-7

Synonyms methacrylic chloride; 2-methyl-2-propenoyl chloride

EINECS No. 213-058-9 **RTECS No.** OZ 5791000

Uses Acylating agent. Organic synthesis. Manufacture of polymers used for contact lenses.

Physical properties

B. Pt. 95-96°C **Flash point** 2°C **Specific gravity** 1.0871 at 20°C with respect to water at 4°C
Volatility v.p. 78 mmHg at 20°C
Solubility Organic solvents: acetone, chloroform, diethyl ether

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) inhalation rat 60 mg m^{-3} (1).
LC_{50} (2 hr) inhalation mouse 115 mg m^{-3} (1).

Other effects

Other adverse effects (human)
Extremely destructive to tissue of 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 oedema (2).

References

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M110 methacryloyloxyethyl isocyanate

$$CH_2=C(CH_3)CO_2CH_2CH_2NCO$$

$C_7H_9NO_3$ **Mol. Wt.** 155.15 **CAS Registry No.** 30674-80-7

Synonyms 2-isocyanatoethyl methacrylate

RTECS No. OZ 4950000

Uses Preparation of polymers.

Physical properties

B. Pt. 87-89°C at 10 mmHg

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)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 670 mg kg^{-1} (1).
LC_{50} (6 hr) inhalation rat 4 ppm (1).

Sub-acute and sub-chronic data

Inhalation guinea pig (2 wk) 0.01-0.6 ppm caused a significant increase in respiratory rate at 0.1-0.4 ppm; 0.5-0.6 ppm caused irritation responses (2).

Teratogenicity and reproductive effects

Inhalation ♂ rat, lowest toxic concentration, 80 ppb for 6 hr day^{-1} for 49 days, reproductive effects (1).

Genotoxicity

In vivo rat, dominant lethal assay negative (1).

References

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M111 methamidophos

$$H_2NP(O)(OCH_3)SCH_3$$

$C_2H_8NO_2PS$ **Mol. Wt.** 141.13 **CAS Registry No.** 10265-92-6

Synonyms *O,S*-dimethyl phosphoramidothioate; methyl phosphoramidothioate; Acephate-met; Filitox; Monitor; Tamaron; Prodex; Multiphos; Afitox; Hamidop; Methaphos; Orthotox; Patrol

EINECS No. 233-606-0 **RTECS No.** TB 4970000

Uses Insecticide.

Physical properties

M. Pt. 46.1°C **Flash point** 66°C (EU A.9/ASTN-D56) **Specific gravity** 1.31 at 44.5°C
Partition coefficient log P_{ow} –0.8 at 20°C **Volatility** v.p. 1.7×10^{-5} mmHg at 20°C
Solubility Water: >200 g l^{-1}. Organic solvents: benzene, dichloromethane, ethanol, diethyl ether, n-hexane, isopropanol, kerosene, xylene

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Toxic in contact with skin – Very toxic if swallowed – Irritating to the eyes – Very toxic to aquatic organisms (R24, R28, R36, R50)

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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S22, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) guppy, rainbow trout, carp, goldfish 46-100 mg l^{-1} (1).

Invertebrate toxicity

IC_{50} (24 hr) *Daphnia magna* 1.88 mg l^{-1}; LC_{50} (24 hr) *Daphnia magna* 56 mg l^{-1} (2).

Environmental fate

Abiotic removal

Hydrolysis $t_{1/2}$ 120 hr at 37°C, pH 9.0; 140 hr at 40°C, pH 2.0 (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail 10-11 mg kg^{-1} (3).
LD_{50} oral rat, mouse, rabbit, dog 7.5, 10, 14, 60 mg kg^{-1}, respectively (1,4-6).
LC_{50} (4 hr) inhalation rat 200 mg m^{-3} (aerosol) (1).
LD_{50} dermal rat, rabbit 118-130 mg kg^{-1} (1,7).
LD_{50} dermal rat 50 mg kg^{-1} (8).
LD_{50} intraperitoneal rat 15 mg kg^{-1} (9).

Sub-acute and sub-chronic data

Oral rat (12 wk) the maximal dose which did not inhibit blood cholinesterase activity was 0.17 mg kg^{-1} day^{-1} (10).

Carcinogenicity and chronic effects

Oral rat and dog (2 yr) no-adverse-effect level 2 mg kg^{-1} diet (1).

Teratogenicity and reproductive effects

Oral, single dose of 1 or 2 mg kg^{-1} to pregnant rats caused embryolethality, growth retardation, encephaly and anotia. Visceral organs were not affected. The high dose caused cyanosis (time of administration not specified) (4).
Gavage ♂ mouse, 0.2, 0.8 or 3.2 mg kg^{-1} day^{-1} for 5 days. On day-35 sperm motility decreased and abnormal sperm rate increased markedly, the structure of mitochondria and smooth endoplasmic reticulum in Leydig cells changed, cells in convoluted tubules degenerated and interstitial tissue in the testes appeared oedematous. These effects were observed only in the mid- and high-dose groups (11).
Chick embryo 0.125-2.0 mg egg^{-1} on day-4 incubation caused embryo lethality, growth retardation and a low incidence of developmental anomalies, open umbilicus and thin debilitated toes and feet (12).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (13).
In vivo mouse bone marrow cells, micronucleus test and chromosomal aberrations positive (14).
Vicia faba root tip cells, mitotic index significantly decreased and chromosomal aberrations induced (15).

Other effects

Other adverse effects (human)

Occupational exposure to ≤0.13 mg m^{-3} during greenhouse spraying caused an 11% decrease in erythrocyte acetylcholinesterase activity (16).

Legislation

EEC maximum residue limits for pome, stone and citrus fruit 0.3 ppm (1).
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).
WHO Toxicity Class Ib (19).
EPA Toxicity Class I (formulation) (3).
ADI 0.004 mg kg^{-1} body weight (3).

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M112 methane

CH_4

CH_4 **Mol. Wt.** 16.04 **CAS Registry No.** 74-82-8

Synonyms fire damp; marsh gas; methyl hydride

EINECS No. 200-812-7 **RTECS No.** PA 1490000

Uses Fuel. Organic synthesis.

Occurrence Found during anaerobic degradation of organic matter. Principal constituent of natural gas.

Physical properties

M. Pt. –183°C **B. Pt.** –161°C **Flash point** –183.2°C **Specific gravity** 0.7168 g l^{-1} at 25°C and 760 mmHg
Partition coefficient log P_{ow} 1.09 (1) **Volatility** v.p. 40 mmHg at –86.3°C ; v.den. 0.55
Solubility Water: 25 mg l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1971 (compressed); 1972 (refrigerated liquid) **HAZCHEM Code** 2**S**E (compressed)
HAZCHEM Code 2WE (refrigerated liquid) **Conveyance classification** flammable gas
Supply classification extremely flammable
Risk phrases Extremely flammable (R12)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Environmental fate

Degradation studies
ThOD 3.99 mg l^{-1} O_2; BOD_{35} 3.04 mg l^{-1} at 25°C (2).
Utilised as sole carbon source by *Methylococcus* spp. (3,4).
Microbial degradation in soils, estimated $t_{1/2}$ 70 days (3).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 1900 days (5).
Estimated volatilisation $t_{1/2}$ 1.17 hr for model river water and 14 hr for model pond water (6,7).

Adsorption and retention
Calculated K_{oc} of 753 indicates that adsorption to soil may occur (6).

Mammalian & avian toxicity

Teratogenicity and reproductive effects
Inhalation mouse, 5-8% fuel gas (containing 85% methane with small amounts of ethane, propane and butane) for 1 hr on day-8 of gestation. Abnormalities in the foetal brain were found to result in brain hernia and hydrocephalus (8).

Metabolism and toxicokinetics
Absorbed via the lungs in mammals. When inhaled, the major proportion is exhaled unchanged. A small amount is metabolised to methanol (1,3).

Other effects

Other adverse effects (human)
Acts as a simple asphyxiant (1).
Liquefied methane gas causes frostbite on skin contact (1).

Other comments

Physical properties, use, mammalian toxicity and health hazards reviewed (1,9,10).
Autoignition temperature 650°C.

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M113 methanesulfonic acid

CH_3SO_3H

CH_4O_3S **Mol. Wt.** 96.11 **CAS Registry No.** 75-75-2

Synonyms methylsulfonic acid

EINECS No. 200-898-6 **RTECS No.** PB 1140000

Uses Catalyst. Organic synthesis. Solvent.

Physical properties

M. Pt. 20°C **B. Pt.** 167°C at 10 mmHg **Flash point** >110°C **Specific gravity** 1.4812 at 10°C with respect to water at 4°C

Solubility Water: miscible. Organic solvents: benzene, chlorotoluene, diethyl ether, ethanol, ethyl disulfide, toluene

Occupational exposure

Supply classification corrosive

Risk phrases Causes burns (R34)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – 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 quail 1000 mg kg^{-1} (1).

LD_{Lo} oral rat 200 mg kg^{-1} (2).

LD_{Lo} intraperitoneal rat 50 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation negative (3).

Other effects

Other adverse effects (human)

Extremely destructive to tissues 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 (4).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

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M114 methanesulfonyl fluoride

CH_3SO_2F

CH_3FO_2S **Mol. Wt.** 98.10 **CAS Registry No.** 558-25-8

Synonyms mesyl fluoride; MSF; fluoromethyl sulfone

EINECS No. 209-192-2 **RTECS No.** PB 2975000

Uses Formerly used as a fumigant insecticide.

Physical properties

B. Pt. 123-124°C **Specific gravity** 1.4805 at 18°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 2.5 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. 2927

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2 mg kg^{-1} (1).
LD_{Lo} subcutaneous rat, mouse, dog, rabbit 3.5 mg kg^{-1} (2,3).
LD_{50} intraperitoneal rat 3 mg kg^{-1} (4).
LD_{50} intravenous mouse, rabbit, dog 0.3-1.0 mg kg^{-1} (1).

Other effects

Other adverse effects (human)
Extremely destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (5).

Any other adverse effects
Inhibited central nervous system cholinesterase activity selectively in monkeys (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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M115 methanethiol

CH_3SH

CH_4S **Mol. Wt.** 48.11 **CAS Registry No.** 74-93-1

Synonyms mercaptomethane; methyl mercaptan; methyl sulfhydrate; thiomethyl alcohol

EINECS No. 200-822-1 **RTECS No.** PB 4375000

Uses Organic synthesis. Odourant for hazardous gases.

Occurrence Aroma component of cooked meat, fish and cheeses. Degradation product in spoilt foods. Food metabolite in mammals. Occurs in fossil fuels.

Physical properties

M. Pt. –123°C **B. Pt.** 6°C **Flash point** –18°C (open cup) **Specific gravity** 0.8665 at 20°C with respect to water at 4°C **Volatility** v.p. 1520 mmHg at 26.1°C ; v.den. 1.66

Solubility Water: 23.3 g l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 0.5 ppm (1 mg m^{-3})
FR-VME 0.5 ppm (1 mg m^{-3})
SE-LEVL 1 ppm
UK-LTEL 0.5 ppm (1.0 mg m^{-3})
US-TWA 0.5 ppm (0.98 mg m^{-3})

UN No. 1064 **HAZCHEM Code** 2WE **Conveyance classification** toxic gas, danger of fire (flammable gas)
Supply classification extremely flammable, harmful
Risk phrases Extremely flammable – Harmful by inhalation (R12, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Avoid contact with the eyes (S2, S16, S25)

Environmental fate

Degradation studies
Degraded by *Thiobacillus thioparus* when isolated from peat (1).
Readily metabolised in estuarine and fresh water sediments (2).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 11.6 hr (3).

Reaction under photochemical smog conditions, forming formaldehyde, sulfur dioxide, methyl nitrate and inorganic sulfate, $t_{1/2}$ 2 hr (4,5).
Estimated volatilisation $t_{1/2}$ 2 hr in model river water (6).

Mammalian & avian toxicity

Acute data
LC_{50} (2 hr) inhalation mouse 6.5 mg m^{-3} (7).

Sub-acute and sub-chronic data
Inhalation rat (3 month) 2, 20 or 60 ppm. Histopathological examination revealed liver damage. A dose-related reduction in body weight was reported (8).

Metabolism and toxicokinetics
Metabolised in rats to carbon dioxide and sulfate. The sulfate was excreted in the urine and 94% of the sulfur from methanethiol was eliminated in 24 hr (9).

Other effects

Other adverse effects (human)
Extremely destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema (10).

Any other adverse effects
Methanethiol strongly inhibited rat liver mitochondrial respiration, apparently by reacting with cytochrome c oxidase (11).

Other comments

Physical properties, use, mammalian toxicity and health precautions reviewed (12,13).

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M116 methanol

CH_3OH

CH_4O **Mol. Wt.** 32.04 **CAS Registry No.** 67-56-1

Synonyms carbinol; colonial spirit; methyl alcohol; methyl hydroxide; methylol; pyroxylic spirit; wood naphtha; wood spirit; wood alcohol

EINECS No. 200-659-6 **RTECS No.** PC 1400000

Uses Solvent. Antifreeze. Fuel and fuel additive. Organic synthesis.

Occurrence Occurs naturally in some woods.

Physical properties

M. Pt. -98°C **B. Pt.** 64.6°C **Flash point** 12°C (closed cup) **Specific gravity** 0.7915 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} -0.77 (1) **Volatility** v.p. 100 mmHg at 21.2°C ; v.den. 1.11

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

Occupational exposure

DE-MAK 200 ppm (270 mg m^{-3})

FR-VME 200 ppm (260 mg m^{-3}) **FR-VLE** 1000 ppm (1300 mg m^{-3})

JP-OEL 200 ppm (260 mg m^{-3})

SE-LEVL 200 ppm (250 mg m^{-3}) **SE-STEL** 250 ppm (350 mg m^{-3})

UK-LTEL 200 ppm (266 mg m^{-3}) **UK-STEL** 250 ppm (333 mg m^{-3})

US-TWA 200 ppm (262 mg m^{-3}) **US-STEL** 250 ppm (328 mg m^{-3})

UN No. 1230 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, toxic

Supply classification highly flammable, toxic

Risk phrases Highly flammable – Toxic by inhalation and if swallowed (R11, R23/25)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed – Keep away from sources of ignition – No smoking – Avoid contact with the skin – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7, S16, S24, S45)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) trout 8000 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (24 hr) brine shrimp 10,000 mg l^{-1} (2).

EC_{50} (30 min) *Photobacterium phosphoreum* 51,000-320,000 ppm, Microtox test (3).

Bioaccumulation

Bioconcentration factor for golden ide <10 (4).

Environmental fate

Nitrification inhibition

IC_{50} ammonic oxidation by *Nitrosomonas* 160 mg l^{-1} (exposure not specified) (5).

Degradation studies

ThOD 1.5 mg l^{-1} O_2; BOD_5 76% O_2 of ThOD (3).

Under anaerobic conditions traces of carbon monoxide were formed together with methane by activated sludge inoculum (6).

Biodegradation in anaerobic groundwater systems was enhanced in the presence of nitrate at pH ≥7.0 (7).
Metabolised by the marine ammonia-oxidising bacterium *Nitrococcus oceanus* with the liberation of CO_2 (8).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, forming formaldehyde, estimated $t_{1/2}$ 18 days (9).
Volatilisation from model river water $t_{1/2}$ 5.3 hr, and from pond water $t_{1/2}$ 2.6 days (10,11).
Adsorption by activated carbon 7 mg g^{-1} carbon (12).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 5600, 7300 mg kg^{-1}, respectively (13,14).
LC_{50} (4 hr) inhalation rat 64,000 ppm (15).
LD_{50} intraperitoneal rat 7500 mg kg^{-1} (16).
LD_{50} intravenous rat, mouse 2100, 4700 mg kg^{-1}, respectively (16).

Carcinogenicity and chronic effects
Inhalation rat (24 months) 1300 mg m^{-3} and mouse (18 months) 13,000 mg m^{-3}. A preliminary report indicated no evidence of carcinogenicity (17).

Teratogenicity and reproductive effects
Inhalation rat, lowest toxic concentration 20,000 ppm for 7 hr day^{-1} on days 1-22 of gestation, teratogenic effects (musculoskeletal system, cardiovascular system and urogenital system) (18).
Inhalation rat, lowest toxic concentration 10,000 ppm for 7 hr day^{-1} on days 7-18 of gestation, foetotoxic effects (19).
Gavage rats (day-10 of gestation) 0, 1.3, 2.6 and 5.2 ml kg^{-1}. A >20% decrease in weight gain was observed in dams at day-20 of gestation, foetuses showed an 11-19.5% decrease in body weight. Internal and external examinations of the foetuses at 20 days showed a dose-dependent increase in anomalies such as undescended testes, exophthalmia and anophthalmia (20).
Exposure of pregnant CD-1 mice to methanol on gestation days 6-15 causes dose-related increases in foetal cleft palate, exencephaly and skeletal defects. Exposure to methanol (10,000 ppm, 7 hr day^{-1} once between gestation days 5-9 or on two consecutive days between gestation days 6-13) indicated that gastrulation and early organogenesis represent a period of increased embryonal sensitivity to methanol (21).

Metabolism and toxicokinetics
Readily absorbed from the gastro-intestinal tract. It may also be absorbed by inhalation and through the skin. Oxidation by alcohol dehydrogenase with the formation of formaldehyde and formic acid takes place mainly in the liver and in the kidneys. These metabolites may be excreted in the urine or further metabolised to carbon dioxide and exhaled by the lungs (22).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (23).
100 mg instilled into rabbit eye for 24 hr caused moderate irritation (24).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (25).
Escherichia coli WP2, WP67, CM871 with and without metabolic activation positive (25).
In vitro mouse lymphoma L5178Y, tk^+/tk^- forward mutation assay positive (26).
In vitro Chinese hamster V79 lung fibroblasts, induction of micronuclei negative (27).
In vivo mouse, increase in micronuclei in blood and lung cells, sister chromatid exchanges and chromosomal aberrations in lung cells, synaptinemal complex damage in spermatocytes negative (28).

Other effects

Other adverse effects (human)

The outstanding features of methanol poisoning are metabolic acidosis with rapid, shallow breathing, visual disturbances which may lead to irreversible blindness and severe abdominal pain. Ingestion of ~30 ml may be fatal (29).

Epidemiological studies have demonstrated no increased incidence of cancer among exposed workers (30).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (31).

Other comments

Environmental health criteria reviewed (32).

Traces have been identified in engine exhausts and cigarette smoke (33).

Environmental fate reviewed (33).

The metabolites of methanol (formaldehyde and formic acid) are believed to be responsible for the symptoms of poisoning (29).

Physical properties, use, mammalian toxicity and health precautions reviewed (34-39).

Autoignition temperature 470°C.

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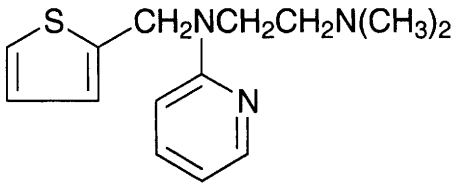
M117 methapyrilene



$C_{14}H_{19}N_3S$ **Mol. Wt.** 261.39 **CAS Registry No.** 91-80-5

Synonyms 2-[(2-dimethylaminoethyl)-2-thenylamino]pyridine; *N,N*-dimethyl-*N'*-2-pyridinyl-*N'*-(2-thienylmethyl)-1,2-ethanediamide; Dormin; Histadyl; Lullamin; paradormalene; pyrathin; pyrinistol; Restinyl; Semikon; Tenalin; thenylpyramine; Thionylan

EINECS No. 202-099-8 **RTECS No.** UT 1400000

Uses Antihistamine drug.

Physical properties

B. Pt. 173-175°C at 3 mmHg **Partition coefficient** log P_{ow} 2.74 (calc.) (1) **Volatility** v.p. 7.0×10^{-4} mmHg at 25°C

Ecotoxicity

Bioaccumulation

Calculated bioaccumulation factor of 71 (2).

Environmental fate

Adsorption and retention

Estimated K_{oc} of 740 indicates that adsorption to soil would be significant (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, guinea pig 180, 380 mg kg^{-1}, respectively (3).
LD_{50} intravenous mouse 20 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 77 mg kg^{-1} (4).
LD_{50} subcutaneous rat 150 mg kg^{-1} (5).

Metabolism and toxicokinetics

Following intravenous administration of 0.7 or 3.5 mg kg^{-1} to ♂ rats, 40 and 35% of the administered dose was excreted in the urine, respectively, and 38 and 44% was eliminated in the faeces, respectively, within 24 hr. The major urinary metabolites were methapyrilene *N*-oxide, mono-*N*-desmethylmethapyrilene, and unchanged methapyrilene (6).

The major urinary metabolite identified in rats was (5-hydroxypyridyl) methapyrilene. After 4 wk treatment rats also excreted the 3- and 6-isomers. *N'*-(2-pyridyl)-*N,N*-dimethylethylenediamine and its metabolite *N'*-2-(5-hydroxypyridyl)-*N,N*-dimethylethylenediamine were also identified (7).

Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation weakly positive (8).

In vitro Chinese hamster ovary cells HGPRT assay negative (9).

In vitro mouse lymphoma tk^+/tk^- forward mutation assay negative (10).

In vitro calf thymus, DNA binding occurred only after metabolic activation by rat liver microsomes and NADPH (11).

Other effects

Other adverse effects (human)

Overdoses produce excitement, convulsions, hyperpyrexia, cerebral oedema, depression and occasionally renal tubular necrosis. Death has been reported from an oral dose of 12 mg kg^{-1}, but others have survived 80 mg kg^{-1} (12).

Other comments

Administered as the fumarate and hydrochloride (13).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (14).

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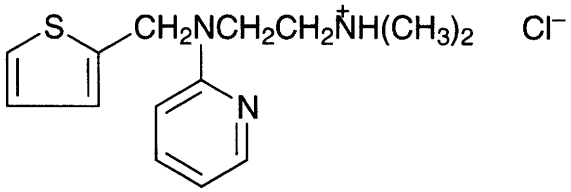
M118 methapyrilene hydrochloride



$C_{14}H_{20}ClN_3S$ **Mol. Wt.** 297.85 **CAS Registry No.** 135-23-9

Synonyms 2-[(2-(dimethylamino)ethyl)-2-thenylamino]pyridine hydrochloride; Barhist; Histidyl; Dozar; methacon; methoxylene; Semikon hydrochloride; thenylene hydrochloride; thenylpyramine hydrochloride

EINECS No. 205-184-8 **RTECS No.** UT 1750000

Uses Antihistamine drug.

Physical properties

M. Pt. 162°C

Solubility Water: 200% w/v. Organic solvents: chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 180, 520 mg kg^{-1}, respectively (1,2).

LD_{50} subcutaneous rat, mouse 75, 150 mg kg^{-1}, respectively (2,3).

LD_{50} intravenous mouse, guinea pig 15-18 mg kg^{-1} (3,4).

Carcinogenicity and chronic effects

Gavage rat single dose of 30, 100, 200 or 300 mg kg^{-1}. Rats were then fed 0.05% phenobarbital in diet for 3, 6 or 9 months. The number of altered hepatic foci was increased 2- to 4-fold for the highest dose, indicating that methapyrilene hydrochloride may act as a weak initiator of hepatocarcinogenesis (5).

Oral rat, 125 or 250 mg kg^{-1} diet (exposure unspecified). The high dose induced liver carcinomas or neoplastic nodules in almost all rats, whereas the low dose induced neoplastic nodules in the liver of 4% of animals (6).

Metabolism and toxicokinetics

Metabolites identified in mouse hepatocytes were methapyrilene glucuronide and desmethylmethapyrilene glucuronide (7).

Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation weakly positive (8).

In vitro mouse lymphoma L5178Y tk^+/tk^- with metabolic activation positive (9).

Other comments

Human health effects, experimental toxicology, physico-chemical properties reviewed (10).

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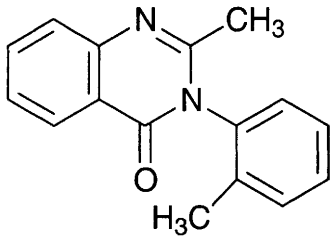
M119 methaqualone



$C_{16}H_{14}N_2O$ **Mol. Wt.** 250.30 **CAS Registry No.** 72-44-6

Synonyms citexal; 3,4-dihydro-2-methyl-4-oxo-3-*o*-tolylquinazoline; 2-methyl-3-(2-methylphenyl)-4-quinazolinone; 2-methyl-3-(2-methylphenyl)-4(3*H*)-quinazolinone; Metolquizalone; Orthonal; Revonal; Tuazole; Quaalude; Melsed; Dormigan; Halodorm; Hyminal; Mequin

EINECS No. 200-780-4 **RTECS No.** VA 3850000

Uses Sedative. Hypnotic.

Physical properties

M. Pt. 114-116°C
Solubility Organic solvents: chloroform, diethyl ether, ethanol

Environmental fate

Abiotic removal
Adsorption capacity of activated carbon 183 mg g^{-1} carbon (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral man 114 mg kg^{-1} (2).
LD_{50} oral rat, mouse 230, 420 mg kg^{-1}, respectively (3-5).
LD_{50} intraperitoneal rat, mouse 125, 180 mg kg^{-1}, respectively (4,6).
LD_{50} intravenous mouse 100 mg kg^{-1} (2).

Teratogenicity and reproductive effects
Oral rabbit, lowest toxic dose, 900 mg kg^{-1} day^{-1} on days 8-16 of gestation, teratogenic effects (foetal death and musculoskeletal abnormalities) (7).

Metabolism and toxicokinetics
Major metabolite of the drug is 2-methyl-3-(2′-hydroxymethylphenyl)-4(3*H*)-quinazolinone (species unspecified) (8).

Other effects

Other adverse effects (human)

Administration of 2.9 or 5.9 mg kg^{-1} increased mean reaction time to stimuli (9).

Coma has occurred after taking 2.4 g, and death after 8 g (10).

Any other adverse effects

Oral rat (6 days) 100 mg kg^{-1} day^{-1} evoked a 2.5-fold increase in *p*-nitrophenol glucuronidation by hepatic microsomes (11).

Studies in rats indicated that physical dependence on the drug may be similar in nature to that of benzodiazepines rather than barbiturates and alcohol (12).

Legislation

Listed as a Controlled Substance (Depressant) in US Code of Federal Regulations (13).

References

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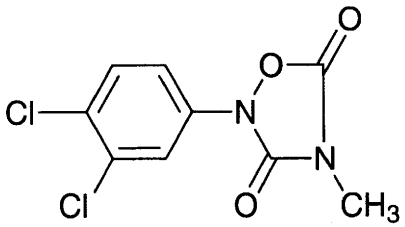
M120 methazole



$C_9H_6Cl_2N_2O_3$ **Mol. Wt.** 261.06 **CAS Registry No.** 20354-26-1

Synonyms bioxone; 2-(3,4-dichlorophenyl)-4-methyl-1,2,4-oxadiazolidine-3,5-dione; Oxydiazol; Mezapur; Paxilon; Probe; Tunic

EINECS No. 243-761-6 **RTECS No.** RO 0835000

Uses Superseded herbicide.

Physical properties

M. Pt. 123-124°C **B. Pt.** 163°C at 747 mmHg **Specific gravity** 1.24 at 25°C

Partition coefficient log P_{ow} 2.587 at 25°C (1) **Volatility** v.p. 1.0×10^{-6} mmHg at 25°C

Solubility Water: 1.5 mg l^{-1} at 25°C. Organic solvents: acetone, cyclohexanone, dichloromethane, dimethylformamide, methanol, xylene

Occupational exposure

Supply classification harmful
Risk phrases Harmful in contact with skin and if swallowed – Irritating to eyes and skin (R21/22, R36/38)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout 4-5 mg l^{-1} (1).

Environmental fate

Degradation studies
Microbial degradation in soil $t_{1/2}$ <30 days. Degradation product for plants and microbes, 3,4-dichloroaniline (1).

Abiotic removal
Decomposed by UV light in methanol, but suspension in water exposed to sunlight is more stable (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 780-2500 mg kg^{-1} (1,3,4).
LC_{50} (4 hr) inhalation rat >200 g m^{-3} (dust) (1).
LD_{50} dermal rabbit >12,500 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 600 mg kg^{-1} (2).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail, mallard duck 1800, 11,200 mg kg^{-1}, respectively, in diet (1).

Carcinogenicity and chronic effects
Oral rat, mouse (2 yr) a yellow/brown pigmentation of liver or spleen tissue occurred at >100 mg kg^{-1} diet (1).

Teratogenicity and reproductive effects
Not mutagenic and not teratogenic in rabbits at ≤60 mg kg^{-1} day^{-1}, but foetotoxic at ≥30 mg kg^{-1} day^{-1} (route of administration and exposure not specified) (5).
Oral rat, 50 mg kg^{-1} diet for three generations, cataracts were observed at ≥100 mg kg^{-1} diet. No other adverse effect was observed (5).

Metabolism and toxicokinetics
Metabolism in mammals involves decarboxylation to 1-(3,4-dichlorophenyl)-3-methylurea which undergoes *N*-demethylation to 3,4-dichlorophenylurea and then to 3,4-dichloroaniline (1).

Irritancy
Mild skin and eye irritant (species unspecified) (4).

Sensitisation
Negative in skin sensitisation test on guinea pigs (4).

Genotoxicity

In vitro Chinese hamster V79 cells positive in presence of hepatocytes, negative in absence of hepatocytes (6).
In vitro initiator tRNA acceptance assay with metabolic activation positive (7).

Other effects

Any other adverse effects

Chloracne has been reported in rabbits in studies and among some exposed workers at manufacturing plants (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (8).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

Occurs in some nitrite-treated processed foods. In tobacco smoke. In waste material (1).

Occurs in the atmosphere at some foundries (2).

Reviews on human health effects, expérimental toxicology, physico-chemical properties listed (10).

In situ formation and atmospheric removal have been reviewed (1).

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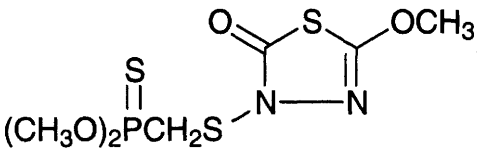
M121 methidathion



$C_6H_{11}N_2O_4PS_3$ **Mol. Wt.** 302.34 **CAS Registry No.** 950-37-8

Synonyms *S*-2,3-dihydro-5-methoxy-2-oxo-1,3,4-thiadiazol-3-ylmethyl *O,O*-dimethyl phosphorodithioate; 3-dimethoxyphosphinothioylthiomethyl-5-methoxy-1,3,4-thiadiazol-2(3*H*)-one; *S*-[(5-methoxy-2-oxo-1,3,4-thiadiazol-3(2*H*)-yl)methyl] *O,O*-dimethyl phosphorodithioate; supracide; suprathim; ultracide

EINECS No. 213-449-4 **RTECS No.** TE 2100000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 39-40°C **Partition coefficient** log P_{ow} 2.22 (1) **Volatility** v.p. 1.4×10^{-3} mmHg at 20°C

Solubility Water: 240 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, cyclohexanone, ethanol, methanol, octanol, xylene

Occupational exposure

Supply classification very toxic, dangerous for the environment
Risk phrases Harmful in contact with skin – Very toxic if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21, R28, 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) – 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, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout 2-10 μg l^{-1} (2).

Environmental fate

Degradation studies
Metabolised by the soil bacterium *Bacillus coagulans*. The major metabolite is desmethyl methidathion (3).

Abiotic removal
Hydrolysis $t_{1/2}$ 30 min at pH 13, 25°C (4).
~20% loss by evaporation from glass beads and in field trials after 24 hr (5).

Adsorption and retention
Sorption coefficient for organic matter (K_{oc}) 19.5. Sorption coefficient for pond sediments (K_d) 0.63-3.45 (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, guinea pig, rabbit 20-80 mg kg^{-1} (2,6,7).
LC_{50} (4 hr) inhalation rat 50 mg m^{-3} (8).
LD_{50} dermal rat 25 mg kg^{-1} (6).
LD_{50} dermal rabbit 200 mg kg^{-1} (8).

Carcinogenicity and chronic effects
Oral rat, dog (2 yr) no-adverse-effect level 0.15 mg kg^{-1} day^{-1} for rats, 0.25 mg kg^{-1} day^{-1} for dogs (2).

Metabolism and toxicokinetics
Following oral administration to rats of radiolabelled methidathion, 48% of radiolabel was excreted in the urine and 38% in expired air within 24 hr (9).
Readily absorbed from the lumen of lactating cows. Milk contained the sulfone and sulfoxide (10).

Irritancy
34 mg instilled into rabbit eye caused severe irritation (exposure not specified) (11).

Genotoxicity

In vitro hamster cells, sister chromatid exchanges negative (12).

Other effects

Other adverse effects (human)
Reduced serum cholinesterase activity in exposed agricultural workers (13).
Human volunteers tolerated oral doses of 0.11 mg kg^{-1} day^{-1} for >42 days without reaction (4).

Legislation

EEC maximum residue levels: citrus fruit 2 ppm, pome fruit 0.5 ppm, other fruit and vegetables 0.2 ppm (2).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (14).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).
WHO Toxicity Class Ib (16).
EPA Toxicity Class Ib (formulation) (4).
ADI 0.001 mg kg^{-1} body weight (4).

Other comments

In a study of accumulation in the Mediterranean mussel *Mytilis galloprovincialis*, bioconcentration factors were determined experimentally. The authors concluded that the bioaccumulation ability in living tissues represents a potential environmental risk to marine organisms and humans (17).

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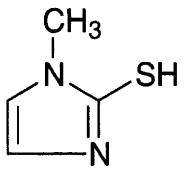
M122 methimazole



$C_4H_6N_2S$ **Mol. Wt.** 114.17 **CAS Registry No.** 60-56-0

Synonyms 1,3-dihydro-1-methyl-2*H*-imidazole-2-thione; methyl mercaptoimidazole; 1-methylimidazole-2-thiol; mercaptazole; 2-mercapto-1-methylimidazole; Danantizal; Favistan; Mercazolyl; Thiamazole; Thymidazole; Tapazole

EINECS No. 200-482-4 **RTECS No.** NI 8615000

Uses Antithyroid agent.

Physical properties

M. Pt. 146-148°C **B. Pt.** 280°C (decomp.)
Solubility Water: ~20%. Organic solvents: benzene, chloroform, diethyl ether, ethanol, petroleum ether

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 240-550 ppm, Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2250 mg kg^{-1} (2).
LD_{50} oral mouse 860 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 345 mg kg^{-1} (2).
LD_{50} subcutaneous rat 1050 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 500 mg kg^{-1} (4).

Teratogenicity and reproductive effects
Oral mouse, 0.1 mg ml^{-1} in drinking water from day-16 of gestation to postpartum day-10. Mean body weight of exposed offspring was reduced and development of behaviour patterns was delayed (5).

Metabolism and toxicokinetics
In rats, biliary excretion accounted for 80-90% of injected dose. The metabolites were not glucuronides but labile conjugates (6).

Genotoxicity

In vivo mouse bone marrow induction of micronuclei and chromosomal aberrations negative, mouse spermatocytes and spermatogonia, chromosomal aberrations negative (7).

Other effects

Any other adverse effects
In vitro studies indicate that the immunosuppressive activity of methimazole does not involve the B- or T-lymphocytes (8,9).

Other comments

Methimazole is a potent scavenger of free oxygen radicals. This could explain the suppression of the inflammatory response to skin exposed to UV irradiation. Use as a radioprotectant during radiotherapy has been suggested (10).

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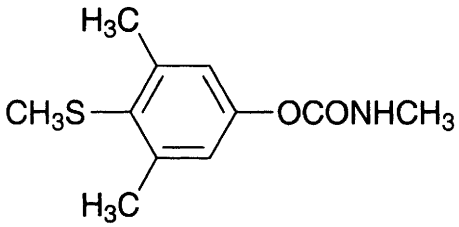
M123 methiocarb



$C_{11}H_{15}NO_2S$ **Mol. Wt.** 225.31 **CAS Registry No.** 2032-65-7

Synonyms methylcarbamic acid, 4-(methylthio)-3,5-xylyl ester; Bay 37344; Mercaptodimethur; Mesurol; Mesurol phenol; 3,5-dimethyl-4-(methylthio)phenyl methylcarbamate; Metmercapturon

EINECS No. 217-991-2 **RTECS No.** FC 5775000

Uses Insecticide. Molluscicide. Acaricide. Bird repellent.

Physical properties

M. Pt. 119°C **Specific gravity** 1.236 at 20°C **Partition coefficient** log P_{ow} 2.92 (1) **Volatility** v.p. 1.1×10^{-5} mmHg at 20°C

Solubility Water: 27 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, diethyl ether, ethanol, n-hexane, propan-2-ol

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) bluegill sunfish, golden orfe, carp and rainbow trout 0.21-3.8 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (24 hr) crayfish and grass shrimp 0.4-3.7 mg l^{-1} (3).

Bioaccumulation

Calculated bioconcentration factors of 91-98 indicate that significant environmental accumulation is unlikely (1).

Environmental fate

Abiotic removal

Effectively removed from wastewaters in bench-scale powdered activated carbon tests (4).

$t_{1/2}$ for hydrolysis at 20°C is >1 yr at pH 4, <35 day at pH 7 and 6 hr at pH 9. The hydrolysis product 4-methylthio-3,5-dimethylphenol (2,5).

$t_{1/2}$ for reactions with photochemically produced hydroxyl radicals in the atmosphere 7.92 hr (6).

Adsorption and retention

K_{oc} in silt loam soil 70 (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling, Japanese quail 5-50 mg kg^{-1} (2,8).
LD_{50} oral chicken 175-190 mg kg^{-1} (2).
LD_{50} oral rat, mouse, guinea pig 15, 34, 40 mg kg^{-1}, respectively (9-11).
LC_{50} (4 hr) inhalation rat >0.3 mg l^{-1} air (aerosol) (9).
LD_{50} dermal rat 350 mg kg^{-1} (12).
LD_{50} intraperitoneal mouse 16 mg kg^{-1} (13).

Carcinogenicity and chronic effects

Oral rat (2 yr) no-adverse-effect level 67 mg kg^{-1} diet (2).

Metabolism and toxicokinetics

Following oral administration to dogs and mice (unspecified dose and duration), rapid absorption and excretion occurs. Metabolised via hydrolysis, oxidation, hydroxylation, with principal excretion in urine in free or conjugated form. Only minor amounts excreted in faeces (2).

Other effects

Any other adverse effects

Inhibits cholinesterase activity (2).
When applied at the recommended application rate of 3 kg ha^{-1} (for slug control) or at an excess rate of 30 kg ha^{-1} caused a reduction in the number of surface-dwelling fauna (staphylinids and carabid beetles) (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (14).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).
EEC maximum admissible residue levels – salad 0.2 ppm; other vegetables and berries 0.1 ppm (2).
WHO Toxicity Class II (16).
EPA Toxicity Class I (formulation) (17).
ADI 0.001 mg kg^{-1} body weight (17).

Other comments

Residues have been isolated from crops (18).
Toxicity and environmental impact reviewed (19,20).

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M124 D-methionine

$$CH_3SCH_2CH_2CH(NH_2)CO_2H$$

$C_5H_{11}NO_2S$ **Mol. Wt.** 149.21 **CAS Registry No.** 348-67-4

Synonyms (*R*)-(–)-methionine

EINECS No. 206-483-6 **RTECS No.** PD 0455000

Uses Lipotropic agent.

Occurrence Formed by *Candida, Pseudomonas, Hansenula* and *Rhodococcus* species.

Physical properties

M. Pt. 273°C (decomp.)

Solubility Water: miscible

Environmental fate

Degradation studies

Metabolised by *Halobacterium halobium* by conversion into the L-form, possibly via keto acids (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 5200 mg kg^{-1} (2).

Metabolism and toxicokinetics

Metabolised in the rat liver to form methyl sarcosine via oxidative deamination and reamination to give the L-form (3).

Readily absorbed through the skin (species unspecified) (4).

Irritancy

Causes skin and eye irritation (species unspecified) (4).

Other effects

Any other adverse effects

Intraluminal administration to rabbits initially enhanced intestinal myoelectric activity, followed by a dose-dependent inhibitory phase (5).

Dietary administration reduced body weight gain in rats. Hepatic methionine transsulfuration enzymes activities, spleen weight, Fe content and methionine levels were all increased (6).

Other comments

Essential amino acid for protein synthesis (7).

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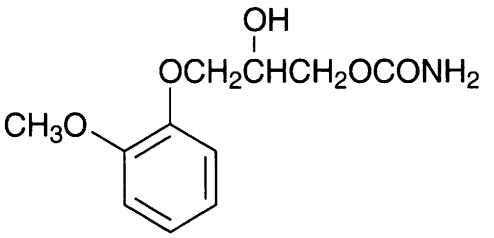
M125 *methocarbamol*



$C_{11}H_{15}NO_5$ **Mol. Wt.** 241.24 **CAS Registry No.** 532-03-6

Synonyms glycerylguaiacolate carbamate; guaiacol glyceryl ether carbamate; 2-hydroxy-3-(*o*-methoxyphenoxy)propyl 1-carbamate; 3-(2-methoxyphenoxy)-1-glyceryl carbamate; 3-(*o*-methoxyphenoxy)-1,2-propanediol 1-carbamate

EINECS No. 208-524-3 **RTECS No.** TY 8750000

Uses Muscle relaxant. Antispasmodic drug.

Physical properties

M. Pt. 92-94°C

Solubility Water: ~2.5% at 20°C. Organic solvents: benzene, chloroform, ethanol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, dog, hamster 1410-2000 mg kg^{-1} (1,2).

LD_{50} subcutaneous mouse 780 mg kg^{-1} (3).

LD_{50} intraperitoneal rat, mouse, hamster 820-1050 mg kg^{-1} (1,4).

LD_{50} intravenous rabbit 680 mg kg^{-1} (5).

Metabolism and toxicokinetics

Following an oral dose of 150 mg kg^{-1} to rats, peak plasma levels were reached after 150 min. It is excreted in the urine primarily as the glucuronide and sulfate conjugates. A small amount is excreted in faeces (6,7).

Other effects

Other adverse effects (human)

Adverse effects include drowsiness, dizziness, blurred vision, gastro-intestinal effects and hypersensitivity reactions including rashes, pruritus, urticaria, and conjunctivitis with nasal congestion (7).

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M126 methomyl

$$CH_3C(SCH_3)=NOC(=O)NHCH_3$$

$C_5H_{10}N_2O_2S$ **Mol. Wt.** 162.21 **CAS Registry No.** 16752-77-5

Synonyms *N*-[[(methylamino)carbonyl]oxy]ethanimidothioic acid, methyl ester; *S*-methyl *N*-[(methylcarbamoyl)oxy]thioacetimidate; *N*-[(methylcarbamoyl)oxy]thioacetimidic acid, methyl ester; DuPont 1179; lannate; nudrin

EINECS No. 240-815-0 **RTECS No.** AK 2975000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 78-79°C **Specific gravity** 1.29 at 24°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.09 (1) **Volatility** v.p. 5×10^{-5} mmHg at 25°C

Solubility Water: 57.9 g l^{-1}. Organic solvents: acetone, ethanol, methanol, propan-2-ol, toluene

Occupational exposure

FR-VME 2.5 mg m^{-3}

UK-LTEL 2.5 mg m^{-3}

US-TWA 2.5 mg m^{-3}

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) – 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) bluegill sunfish, rainbow trout 0.9, 3.4 mg l^{-1}, respectively (2,3).

LC_{50} (48 hr) carp, goldfish, killifish, guppy 0.9-2.8 mg l^{-1} (4).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 9 μg l^{-1} (3).

Bioaccumulation

Calculated bioconcentration factors of 1.3-1.7 indicate that the potential for environmental accumulation is unlikely (5).

Environmental fate

Nitrification inhibition

Nitrogen fixation ability of some bacteria was reduced by up to 80% when methomyl was applied at 20-160 mg kg^{-1} soil (6).

Degradation studies

Degraded by the soil fungi *Alternaria brassicola, Penicillium notatum, Aspergillus* and *Helminthosporium* species and *Verticillium agaricinum* (7,8).

Degradation $t_{1/2}$ 30-42 days in soil. Major degradation product was carbon dioxide. A minor degradation product, *S*-methyl-*N*-hydroxythioacetimidate, was a possible hydrolysis product (9).

Hydrolysis $t_{1/2}$ 56 wk at pH 8.0; 54 wk at pH 7.0; 38 wk at pH 6.0; 20 wk at pH 4.5, in sterile 1% ethanol (10).

Abiotic removal

Degrades rapidly in chlorinated water. Rate increases with decreasing pH, increasing temperature and increasing chlorine concentration. Reaction rate is 1000 × faster with free chlorine than with chloramine. Methomyl sulfoxide and *N*-chloromethomyl are formed before degrading to acetic acid, methanesulfonic acid and dichloromethylamine (11).

Adsorption and retention

Calculated K_{oc} 10-500 indicates low to moderate adsorption to soil and sediments is likely (5,12).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, mallard duck, pheasant, quail, starling 10-35 mg kg^{-1} (2,13-16).

LC_{50} (4 hr) inhalation rat 300 mg m^{-3}. Animals showed characteristic signs of cholinesterase inhibition, including salivation, lachrymation and tremors (17).

LD_{50} dermal rabbit 5800 mg kg^{-1} (18).

Sub-acute and sub-chronic data

Inhalation ♂ rat, 15 mg m^{-3} 4 hr day^{-1} 5 days wk^{-1} for 3 months caused no change in plasma and red cell cholinesterase activity, histopathology or lipid concentration (19).

LC_{50} (5 day) bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck 1100-2900 mg kg^{-1} diet (20).

Oral rat (13 wk) 0, 1, 3, 10 or 30 mg kg^{-1} day^{-1} caused no fatality or clinical signs of toxicity. Body-weight gain was reduced in treated ♀ but not ♂ at all dose levels. Kidney body weight ratio, but not absolute kidney weights were increased at the two high-dose levels. Red blood cell cholinesterase activity was elevated at the high-dose levels, but plasma and brain cholinesterase levels were unaffected (20).

Carcinogenicity and chronic effects

Oral rat (22 month) 1, 2.5, 5, 10 or 20 mg kg^{-1} day^{-1}. Autopsy revealed kidney tubular hypertrophy, vacuolation of epithelial cells of the proximal convoluted tubules and histological alterations in the spleen at the high-dose level. No effects were seen on plasma or red blood cell cholinesterase levels (13).

Oral rat (2 yr) 0, 2.5, 5 or 20 mg kg^{-1} day^{-1}. Effects observed in the high-dose group were reduced weight gain in both sexes, and, in ♀ rats, lower erythrocyte counts, haemoglobin values and haemotocrits. Blood and brain cholinesterase activity levels and other clinical chemistry parameters were not significantly altered (21).

Teratogenicity and reproductive effects

Oral rat 0, 2.5 or 5.0 mg kg^{-1} day^{-1} for three generations. No adverse effects were reported on reproduction or lactation and no pathological changes were found in the weanling pups of the F_3 generation (13).

Oral rabbit 0, 2, 6 or 16 mg kg^{-1} day^{-1} on days 7-19 of gestation. 1/5 animals in the high-dose group died, exhibiting characteristic signs of cholinesterase inhibition. No teratogenic or embryotoxic effects were observed (1).

Metabolism and toxicokinetics

Almost completely absorbed from the gastro-intestinal tract following oral administration to rats. After 72 hr, 15-25% of the dose was expired as carbon dioxide, 33-50% was expired as acetonitrile, and ~25% as metabolites in the urine. Metabolism was believed to involve partial isomerisation followed by hydrolysis of the two isomeric forms to yield two isomeric oximes that then break down to carbon dioxide and acetonitrile at different rates. No other metabolites were identified (22,23).

Irritancy

Eye irritant in rabbits. No irritation occurred after application to guinea pig skin (dose and duration unspecified) (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (24,25).

Drosophila melanogaster sex-linked recessive lethal assay positive (26).

In vivo mouse sperm morphological abnormalities and chromosomal aberrations positive (27).

In vitro Chinese hamster ovary cells induction of micronuclei dose and sample time-dependent (28).

In vivo mouse bone marrow erythrocytes induction of micronuclei dose and sample time-dependent (28).

Other effects

Other adverse effects (human)

Accidental doses of 12-15 mg kg^{-1} have been fatal to man (29,30).

Any other adverse effects

Attributed endocrine disruption effects in wildlife. Avian reproduction impaired (31).

Oral ♂ rat, single dose of 5, 10 or 15 mg kg^{-1}. Serum cholinesterase activity was inhibited in all treated groups. No haematological changes were observed. Biochemical studies revealed disorders of liver and kidney function in rats receiving the low dose. Histopathological alterations were seen in the lungs at all doses and in the liver and kidneys at the high dose. All treated rats showed a decrease in superoxide dismutase activity, an increase in serum lipoperoxide level and a decrease in serum α-tocopherol level (32).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (33).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (34).

US maximum residue on hops 12 ppm (35).

EC maximum residue levels: vegetables, citrus fruit 0.5 ppm; pome and stone fruit, grapes 1 ppm; salads 2 ppm (2).

Tolerable daily intake (TDI) human 0.001 mg kg^{-1} (36).

WHO Toxicity Class Ib (37).

EPA Toxicity Class II (2).

Other comments

Traces have been isolated from natural waters and on crops (1,38).

Physical properties, uses, occurrence, analysis, environmental fate, metabolism, mammalian toxicity, teratogenicity, mutagenicity, carcinogenicity and health advice reviewed (1,38,39,40).

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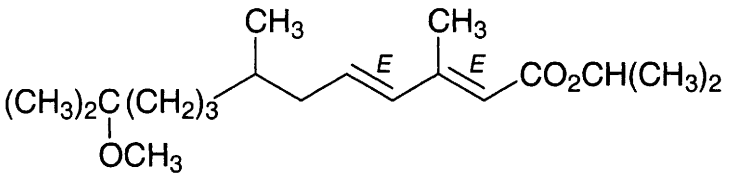
M127 methoprene



$C_{19}H_{34}O_3$ **Mol. Wt.** 310.48 **CAS Registry No.** 40596-69-8

Synonyms isopropyl (*E,E*)-(*RS*)-11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate; (*E,E*)-1-methylethyl 11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate

EINECS No. 254-993-2 **RTECS No.** JR 1685000

Uses Insect growth regulator.

Physical properties

B. Pt. 100°C at 0.05 mmHg **Flash point** 187°C (open cup) **Specific gravity** 0.926 at 20°C **Partition coefficient** log P_{ow} 5.21 **Volatility** v.p. 2.4×10^{-5} mmHg at 25°C
Solubility Water: 1.4 mg l^{-1}. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, trout 4.4-4.6 mg l^{-1} (1).
LC_{50} (96 hr) mummichog 125 mg l^{-1} (2).

Invertebrate toxicity
Non-toxic to adult bees. LD_{50} (oral and topical) >1000 μg bee^{-1} (3).
LC_{50} (24 hr) *Moina macrocopa* 0.51 mg l^{-1} (4).
LC_{50} (48 hr) *Moina macrocopa* 0.34 mg l^{-1} (4).

Toxicity to other species
Addition of 1 μl l^{-1} of methoprene degradates to the environment of developing frogs results in deformation of the juveniles (5).

Environmental fate

Abiotic removal
Degraded by UV irradiation. Rapidly degraded in soil, DT_{50} ~ 10 days (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >34,600 mg kg^{-1}, dog >5000 mg kg^{-1} (1,6).
LD_{50} dermal rabbit 3000-3500 mg kg^{-1} (1,6).

Sub-acute and sub-chronic data
LD_{50} (8 day) oral chicken >4640 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Oral (2 yr) rats receiving 5000 mg kg^{-1} diet and mice receiving 2500 mg kg^{-1} diet showed no ill-effects (1).

Teratogenicity and reproductive effects
Oral rat, three-generation study, 2500 mg kg^{-1} diet caused no reproductive adverse effects (1).

Metabolism and toxicokinetics
In mammals, the secondary metabolite cholesterol has been identified (1).

Genotoxicity

Drosophila melanogaster wing spot test weakly positive (7).

Other effects

Any other adverse effects
Acts as an insect growth regulator by mimicking the action of insect juvenile hormones, causing death by preventing the transformation of larva to pupa (8).
Investigators at the Center for Water and the Environment, Natural Resources Research Institute, in Duluth, MN 55811, USA found no convincing evidence that reproduction, growth, or foraging behaviour was negatively affected by anti-mosquito treatments of wetlands with methoprene (applied as Altosid sand granules). The numbers of aquatic insects were depressed in wetlands treated with methoprene in July and August, but it was thought unlikely that food available to avian species in the wetlands was lower during the breeding reason (May and June). The impact of the treatment on the dispersal of young birds within or to these sites and on individuals that use wetlands during migration was not addressed (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (10).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
WHO Toxicity Class Table 5 (12).
EPA Toxicity Class IV (3).
ADI 0.1 mg kg^{-1} body weight (3).

Other comments

Possible endocrine disrupting effects in non-target species (13).

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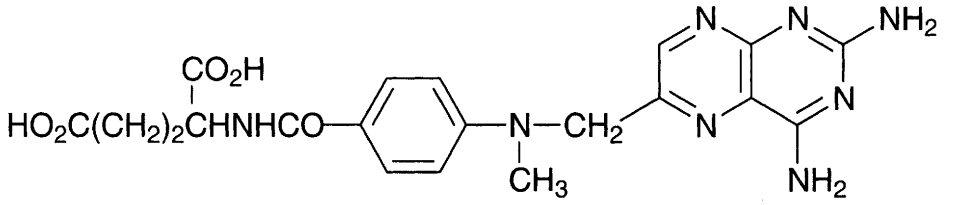
M128 methotrexate



$C_{20}H_{22}N_8O_5$ **Mol. Wt.** 454.45 **CAS Registry No.** 59-05-2

Synonyms L-(+)-amethopterin; *N*-4-[[(2,4-diamino-6-pteridinyl)methyl]methylamino]benzoyl-L-glutamic acid; amethopterin; 4-amino-10-methylfolic acid; 4-amino-*N*-methylpteroylglutamic acid; α-methopterin; methylaminopterin

EINECS No. 200-413-8 **RTECS No.** MA 1225000

Uses Antineoplastic agent. Antifungal agent. Treatment of psoriasis.

Physical properties

M. Pt. 108-204°C (monohydrate, yellow crystals from dil. HCl, decomp.)
Solubility dilute alkaline hydroxides and carbonates, dilute hydrochloric acid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 135, 180 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal rat, mouse 6 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 250 mg kg^{-1} (3).
LD_{50} intravenous rat, mouse 14, 65 mg kg^{-1}, respectively (2,4).
LD_{50} (5 day) intraperitoneal rat, mouse 1.1-2.0 mg kg^{-1} day^{-1} (1).

Sub-acute and sub-chronic data

Oral rat (6 wk) 100, 150, 200 or 300 μg kg^{-1} day^{-1}. The high dose caused systemic toxicity, although hepatotoxicity was not observed. The lower doses were tolerated for longer periods and were associated with hepatotoxicity, ranging from focal to confluent necrosis (5).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (6).
Oral hamster (2 yr) 5, 10 or 20 mg kg^{-1} diet for life. Median survival time for the high-dose group was 40-50 wk. Survival in the other treated groups was similar to that of controls. There was no significant difference in the incidence of tumours compared with controls (7).
Oral mouse (120 wk) 5, 8 or 10 mg kg^{-1} diet wk^{-1} on alternate wk for life. Median survival time was 80-90 wk. The incidence of tumours was not significantly different from that in controls (7).
Oral mouse, 0.1 mg kg^{-1} day^{-1} in drinking water for 18 months. 5/32 treated animals developed lung adenomas and 16/32 developed lung carcinomas (overall incidence 66%). This compared with incidence of 5.1% lung tumours in controls. One treated mouse developed a hepatoma (8).
Intraperitoneal rat, mouse (22 month) 0.15-1.0 mg kg^{-1} 3 × wk^{-1} for 6 months. The incidence of tumours was not significantly different from controls. Median survival times were significantly reduced in all treated groups (9).
Intravenous rat (2 yr) 1 mg kg^{-1} wk^{-1} for 52 wk. The incidence of tumours was not significantly different from that of controls. Survival rates were ~40% those of controls (4).

Teratogenicity and reproductive effects

Intraperitoneal mouse 20 mg kg^{-1} on day-9 of gestation induced a high incidence of median facial clefts in offspring (10).
Oral cat, 0.5 mg kg^{-1} day^{-1} on days 11-14, 14-17 or 17-20 of gestation. Maternal toxicity was observed in ~18% treated animals. Visceral abnormalities were seen only in some offspring of cats treated on days 17-20 of gestation (umbilical hernia, cleft palate, hydrocephalus, spina bifida and malformed limbs) (11).
Intraperitoneal rat, 0.2 and 0.3 mg kg^{-1} on day-9 of gestation was teratogenic to 35 and 75% of foetuses and lethal to 63 and 84% of embryos, respectively. Malformations were also induced by 0.25 mg kg^{-1} administered on day-5. This dose was lethal to all embryos when administered on days 6-9 of gestation (12).

Metabolism and toxicokinetics

Methotrexate was detected in the plasma after 4 hr following dermal application to shaved mice (13).
Following infusion in rats, metabolised in the liver to 7-hydroxymethotrexate, which was excreted in the bile.
Plasma $t_{1/2}$ 15 hr for methotrexate and 7-hydroxymethotrexate (14,15).
Other metabolites formed in rats and mice are 4-amino-4-deoxy-N^{10}-methylpteroic acid and various free pteridines which may be formed by the intestinal flora (16,17).
Methotrexate is retained in the liver, to a degree which is in part dependent upon the dose. It was excreted in the urine and bile. Partial reabsorption occurred in the gut. Within 24-48 hr after administration 67-91% of the dose was eliminated by dogs and monkeys (18).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation marginally positive (19).
Drosophila melanogaster wing spot test positive (20).
In vitro human fibroblasts, sister chromatid exchanges negative (21).
In vitro mouse lymphoma L5178Y, tk^+/tk^- mutation assay positive (22).

In vitro human bone marrow cells, sister chromatid exchanges positive (23).
In vitro hamster A(T^1)C1-3 cells, chromosomal damage positive (24).
In vivo mouse bone marrow micronucleus test positive (25).
In vivo mouse, dominant lethal assay positive (26).

Other effects

Other adverse effects (human)

A woman who took 2.5 mg day^{-1} for 5 days during the 9th wk of pregnancy in an attempt to abort, gave birth to an infant with no frontal bone, craniosynostosis of the coronal and lambdoid sutures, limb reduction defects, hypertelorism and a flat nasal bridge. A similar case was reported in a woman who took 5 mg day^{-1} for the first 2 months of pregnancy for the treatment of psoriasis (27,28).
Women treated with methotrexate prior to pregnancy do not appear to have an increased risk for spontaneous abortion or for offspring with congenital malformations (29,30).
Chromosomal damage was seen in bone marrow cells, but not in peripheral lymphocytes in methotrexate-treated patients (31,32).
Case reports of malignancy in patients treated for psoriasis include skin cancers, cervical cancer, non-Hodgkin's lymphoma, leukaemia, breast cancer, renal cancer and nasopharyngeal cancer (33-41).
Adverse effects are mainly associated with tissues with a rapid cell turnover, particularly the bone marrow, the alimentary tract epithelium, the epidermis, foetal tissue and germinal cells (42).

Any other adverse effects

Intraperitoneal rat 0.1-0.4 mg kg^{-1} day^{-1} and dog 1 mg kg^{-1} day^{-1} caused colonic ulceration, sometimes associated with an ileitis and/or intestinal haemorrhage (43).
Intraperitoneal rat, single dose of ≤50 mg kg^{-1}. The highest dose caused the bone marrow to become hypocellular within 15 hr, the reduction in the erythroid series being the most pronounced. Recticulocytopenia and panleucopenia were also evident in the peripheral blood. These effects progressed in severity up to 72 hr. Lower doses caused similar effects, with particularly significant anaemia and lymphocytopenia. In addition, the thymus, spleen and lymph nodes showed marked atrophy. Increased susceptibility to infection was also reported due to a decrease in the production of antibodies (1,43,44).
Administration into the cerebrospinal fluid of cats caused segmental axonal degeneration. None of the animals showed disseminated necrotising leukoencephalopathy. This suggested a direct toxic effect on the axon (45).

Other comments

Physical properties, use analysis, carcinogenicity, mammalian toxicity, metabolism, health effects and mutagenicity reviewed (46,47).

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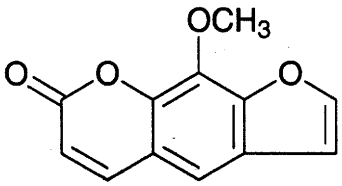
M129 methoxsalen



$C_{12}H_8O_4$ **Mol. Wt.** 216.19 **CAS Registry No.** 298-81-7

Synonyms 9-methoxy-7*H*-furo[3,2-*g*][1]benzopyran-7-one; 6-hydroxy-7-methoxy-5-benzofuranacrylic acid δ-lactone; 8-methoxypsoralen; oxypsoralen; Ammoidin; Meladinine; Meloxine; Puvalen; Puvamet; Xanthotoxin; Oxsoralen-Ultra

EINECS No. 206-066-9 **RTECS No.** LV 1400000

Uses Used with long-wave UV light in the treatment of vitiligo and psoriasis and as a pigmentation agent.

Occurrence Occurs in *Angelica* and *Ammi* species. It is also produced by the fungus *Sclerotinia sclerotiorum* which causes pink rot in celery.

Physical properties

M. Pt. 148-150°C

Solubility Organic solvents: acetic acid, acetone, benzene, chloroform, ethanol, petroleum ether, propylene glycol

Environmental fate

Degradation studies

Readily hydrolysed, whereby the lactone ring is opened (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 420, 790 mg kg^{-1}, respectively (2,3).

LD_{50} intraperitoneal rat, mouse 160, 470 mg kg^{-1}, respectively (2,3).

LD_{50} subcutaneous mouse 860 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (with UV irradiation) (5).

Intraperitoneal mouse 12 mg kg^{-1} day^{-1} for 1 yr induced no detectable toxic effects. However, administration of 4 mg kg^{-1} followed by exposure to UV irradiation at 320-400 nm resulted in severe toxic effects including erythema, burns and liver damage (3).

Oral mouse (12 months) 0.6-40 mg kg^{-1} day^{-1} caused a significant increase in skin tumours or tumours of internal organs either alone or in combination with UV radiation (PUVA) (6,7).

Dermal mouse, 115 applications of 15 μg cm^{-2} to the ear, followed by irradiation with 1.68×10^4 J m^{-2} of 365 nm UV light. 37/40 treated animals developed skin tumours compared with 0/20 irradiated controls (8).

Dermal mouse (60 wk) 5 μg $2 \times wk^{-1}$ with subsequent exposure to UV light (300-400 nm) for 15-60 min. Subcutaneous malignant tumours (mammary adenocarcinomas, skin carcinomas and carcino-mixo-sarcomas) and lymphomas were seen in 43/100 treated animals compared with 11/25 controls exposed to UV light alone (9).

Intraperitoneal mouse (11 month) 0.4 mg day^{-1} 6 days wk^{-1} for 10 months. In one group of 20 mice, each injection was followed 1 hr later by a 20-60 min UV exposure at 250 nm. A 3rd group was exposed to UV irradiation alone. No epidermal tumours were observed in the group that received methoxsalen alone. The epidermal tumour incidence in the two groups exposed to UV light with and without methoxsalen were 10-20% and 20%, respectively. In a concomitant experiment, mice were given intraperitoneal administration of 0.4 mg day^{-1} 6 days wk^{-1} for 6 wk 1 hr before 10 min exposure to UV light (>320 nm). All treated animals developed epidermal tumours (fibrosarcomas and squamous carcinomas of the ears and eye region), whereas none were observed in controls exposed only to UV light (10).

National Toxicology Program tested rats via gavage. No evidence of carcinogenicity in ♀ rats, clear evidence of carcinogenicity in ♂ rats (11).

Metabolism and toxicokinetics

Following oral administration of 10 mg kg^{-1} of ^{14}C-labelled methoxsalen to dogs, radioactivity recovered in urine represented 4-25% of the dose, and in the faeces 47-95% of the dose, within 4 days. In pigs 26-58% of the dose was recovered in urine indicating greater absorption (12).

Following intravenous administration of 2 mg kg^{-1} to dogs, plasma $t_{1/2}$ 2.17 hr (13).

Following intravenous administration to dogs <2% was excreted unchanged in the urine. Four urinary metabolites were isolated, three of which resulted from opening of the furan ring: 7-hydroxy-8-methoxy-2-oxo-2*H*-1-benzopyran-6-acetic acid; α,7-dihydroxy-8-methoxy-2-oxo-2*H*-1-benzopyran-6-acetic acid; and an unknown conjugate of the former at the 7-hydroxy position. The 4th metabolite, formed by opening of the pyrone ring, was an unknown conjugate of *Z*-3-(6-hydroxy-7-methoxybenzofuran-5-yl)-2-propenoic acid (14).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation marginally positive (15).

Saccharomyces cerevisiae forward mutation assay positive (16).
In vitro mouse lymphoma L5178Y cells, tk^+/tk^- positive (17).
In vitro human fibroblasts, DNA damage positive. Pre-treatment with UV light increased the rate of DNA damage by 50% (18).
In vivo rodent bone marrow, induction of chromosomal aberrations and micronuclei negative (PUVA) (19).
In vitro human lymphocytes, sister chromatid exchanges negative (20).

Other effects

Other adverse effects (human)

Basal and squamous cell skin cancers have been reported in patients treated with methoxsalen and long-wave UV light (PUVA) for psoriasis or mycosis fungoides (21-23).
Three cases of malignant melanoma of the skin have been reported in patients treated with methoxsalen and UV light (24,25).
In a follow-up study of 1380 PUVA-treated patients, the standardised incidence ratio for squamous cell carcinoma increased from 4.1 at low doses to 22.3 at medium doses and 56.8 at high doses. This effect was reported to be independent of possible confounding effects of therapy with ionising radiation and topical tar. The effect on basal-cell cancer incidence was much weaker (standardised incidence ratio 4.5 for high doses) (26).

Any other adverse effects

Intraperitoneal ♂ rat, single injection of 5 or 10 mg kg^{-1} at the end of a 14 hr light phase. After 2 hr when the normal nocturnal surge of *N*-acetyltransferase activity and melatonin content in the pineal gland had begun in controls, *N*-acetyltransferase was increased. Melatonin content was unaffected (27).
Methoxsalen forms cyclobutane mono- and di-adducts with pyrimide bases of DNA by photoaddition under UV irradiation. The regions with alternate sequence of A-T appear to be the best reception sites for the formation of mono-adducts, while the regions containing an alternate sequence of A-T and G-C appear to be the preferential sites for cross-linking (28).

Other comments

Use, occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (1,29,30).

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M130 methoxyacetic acid

$$CH_2(OCH_3)CO_2H$$

$C_3H_6O_3$ **Mol. Wt.** 90.08 **CAS Registry No.** 625-45-6

Synonyms 2-methoxyacetic acid; methylglycolic acid

EINECS No. 210-894-6 **RTECS No.** AI 8650000

Uses Catalyst.

Physical properties

B. Pt. 202-204°C **Flash point** >110°C **Specific gravity** 1.174 at 20°C with respect to water at 4°C
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (19 mg m^{-3})

Mammalian & avian toxicity

Acute data

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

Teratogenicity and reproductive effects

Intraperitoneal rat lowest toxic dose 225 mg kg^{-1} on day-8 of gestation, foetotoxic effects (2).
Oral rat, lowest toxic dose single dose of 590 mg kg^{-1} induced abnormal sperm (3).
Methoxyacetic acid and hCG (10 IU) treatment of cultured human luteal cells (0-5 mM, 6-48 hr) resulted in significantly elevated levels of progesterone after 24 hr incubation of ≥1 mM methoxyacetic acid. These results indicate that methoxyacetic acid has the potential to alter ovarian luteal function in women (4).
In vivo mouse exposed orally to 50, 100, 300, 600 or 900 mg kg^{-1} (single dose). Results were evaluated 2, 7, 14, 28 and 45 days after treatment. Induced cytotoxic damage on primary spermatocytes. Affected nucleic acid synthesis and spermatid morphology (5).

Metabolism and toxicokinetics

The elimination $t_{1/2}$ of methoxyacetic acid in rats following an intraperitoneal injection of 100 mg kg^{-1} 2-methoxyethanol was established to be 12.6 ± 1.3 hr in the ♂ and 14.1 ± 1.4 hr in the ♀ (6).

Genotoxicity

In vitro mouse embryo, inhibition of DNA synthesis (thymidine incorporation) positive (7).

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 (8).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).

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M131 methoxyacetone

$$CH_3C(O)CH_2OCH_3$$

$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 5878-19-3

Synonyms acetonyl methyl ether; 1-methoxy-2-propanone; 1-methoxyacetone

EINECS No. 227-549-0 **RTECS No.** UC 2988600

Uses Organic synthesis.

Physical properties

B. Pt. 118°C **Flash point** 25°C **Specific gravity** 0.957 at 20°C

Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 9 g kg^{-1} (1).

LD_{50} dermal rabbit >20 g kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation. 500 mg instilled into rabbit eye for 24 hr caused mild irritation (2).

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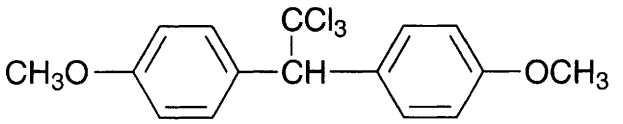
M132 methoxychlor



$C_{16}H_{15}Cl_3O_2$ **Mol. Wt.** 345.65 **CAS Registry No.** 72-43-5

Synonyms 1,1'-(2,2,2-trichloroethylidene)bis(4-methoxybenzene); 1,1-bis(*p*-methoxyphenyl)-2,2,2-trichloroethane; 2,2-bis(*p*-methoxyphenyl)-1,1,1-trichloroethane; dimethoxy-DDT; di(*p*-methoxyphenyl)trichloromethylmethane; DMDT; *p,p'*-DMDT; 1,1,1-trichloro-2,2-di(4-methoxyphenyl)ethane

EINECS No. 200-779-9 **RTECS No.** KJ 3675000

Uses Insecticide. Ectoparasiticide.

Physical properties

M. Pt. 89°C **Specific gravity** 1.41 at 25°C **Partition coefficient** log P_{ow} 4.68-5.08 (1)
Volatility v.p. 1.43×10^{-6} mmHg at 25°C
Solubility Water: 0.1 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, chloroform, ethanol, methanol, petroleum oils, toluene, xylene

Occupational exposure

DE-MAK 15 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 10 mg m^{-3}
UK-LTEL 10 mg m^{-3}
US-TWA 10 mg m^{-3}

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow, bluegill sunfish, rainbow trout, brown trout, coho salmon, king salmon, yellow perch 7.5-67 μg l^{-1} (1-5).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia* 0.8 μg l^{-1} (5).
LC_{50} (96 hr) *Asellus brevicaudus, Gammarus lacustris, Gammarus fasciatus, Palaemonetes kadiakensis, Orconectes nais* 0.5-3.2 μg l^{-1} (6,7).
EC_{50} (96 hr) *Chlorella vulgaris* 49 μg l^{-1} (8).

Toxicity to other species
Exposure of embryos and early larvae of the salamander *Ambystoma macrodactylum* to low, non-lethal levels of methoxychlor (at or above 0.1 mg l^{-1}) results in pronounced but variable effects including the precocial hatch of the embryos, probably a reduced likelihood of the larvae responding to a startle stimulus, and a significantly shorter distance travelled in response to the stimulus at 10 days after hatch. Transfer of larvae to clean water after methoxychlor exposure resulted in reversibility of at least some of these effects (9).

Bioaccumulation
Bioconcentration factor for fathead minnow 8300, sheepshead minnow 140 (10,11).

Environmental fate

Degradation studies
Biodegradation by estuarine sediment/water system, $t_{1/2}$ <2 wk. In aerobic sediments $t_{1/2}$ >100 days. Under anaerobic conditions the major degradation products are dechlorinated methoxychlor and mono- and dihydroxy derivatives (12,13).

Abiotic removal

Degraded in water by UV irradiation at 254 nm and hydrogen peroxide treatment (14).

Hydrolysis $t_{1/2}$ 367 days at pH 3-7 and 270 days at pH 9. At pH 7 2-hydroxy-1,2-bis(methoxyphenyl)ethanone and bis(methoxyphenyl)ethanedione are the major hydrolysis products. At pH 10 1,1-bis(*p*-methoxyphenyl)-2,2-dichloroethylene is the major product. This is also the major product of photolysis, with 4-methoxybenzaldehyde a minor photolysis product (15-17).

Volatilisation $t_{1/2}$ 4.5 days in model river water. This neglects the effect of adsorption which may increase the volatilisation $t_{1/2}$ to 2 yr (18,19).

Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 6.8 hr (20).

Adsorption and retention

Soil K_{oc} range from 9700 in clay soil to 100,000 in silt (21).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1000, 7000 mg kg^{-1}, respectively (22,23).

LD_{50} dermal rabbit >2000 mg kg^{-1} (5).

LD_{50} intraperitoneal hamster 500 mg kg^{-1} (24).

Sub-acute and sub-chronic data

LC_{50} (5 day) oral bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck >5000 mg kg^{-1} diet (25).

Dermal rabbit (13 wk) 2-3 ml of 30% solution 5 days wk^{-1} produced paralysis of the forelimbs, some fatty degeneration of the liver and lesions of the central nervous system (26).

Oral rat, monkey 400, 1000 or 2500 mg kg^{-1} day^{-1} for 3 or 6 months caused damage to the liver and small intestine (27).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (28).

Oral dog, pig (2 yr) 1000, 2000 or 4000 mg kg^{-1} diet. In dogs the two higher doses produced nervousness, apprehension, excess salivation, tremors and convulsions. Nephritis and mammary hyperplasia were observed in the pigs at autopsy (25).

Oral mouse (92 wk) 750-2800 mg kg^{-1} diet for 1 wk, when doses were increased to 1000-3500 mg kg^{-1} diet for 77 wk. There was no significant increase in the incidence of benign and malignant neoplasms compared with controls (29).

Oral rat (2 yr) 360-1500 mg kg^{-1} diet. Haemangiosarcomas of the spleen in ♂ rats were the only tumours that showed an increased incidence (29).

Dermal mouse, 0.1 or 10 mg $animal^{-1}$. The mean survival time ranged from 342 days for low-dose ♀ mice to 450 days in the other group. No skin tumours were observed (30).

Teratogenicity and reproductive effects

Methoxychlor injected into the yolk of eggs of Western and California gulls (20-100 ppm fresh egg wt) caused extensive feminisation of the embryos (31).

Gavage ♀ mouse (2-4 wk) 1.25, 2.5 or 5.0 mg $animal^{-1}$ day^{-1} 5 days wk^{-1}. A dose-related induction of persistent vaginal oestrus and an increase in the number of atretic large follicles, indicating potential loss in fertility, were observed. These effects were very similar to those induced by oestrogens (32).

Intraperitoneal ♂ mouse 0.1 or 1.0 mg $animal^{-1}$ day^{-1} on days 1-9 of age. Body weight and mortality were unaffected. Serum testosterone concentrations were reduced. The high dose significantly decreased DNA content of the seminal vesicles, bulbo-urethral glands and ventral prostate, but not of the testes, epididymides and efferent ductiles. The lower dose decreased DNA content only of the bulbo-urethral glands and seminal vesicles. These effects were similar to those induced by 17β-oestradiol (33).

Oral rat, single dose of 50, 100, 200 or 400 mg kg^{-1}. 200 and 400 mg kg^{-1} doses were foetotoxic. A dose-related increase in the incidence of wavy ribs was induced by doses of 100, 200 and 400 mg kg^{-1} (34).

♀ Rats treated with methoxychlor during the first week of pregnancy suffer reduced serum progesterone levels and impaired implantation (35).

Gavage pregnant ♀ rats 0, 5, 50 or 150 mg kg^{-1} during the weeks before and after birth. Pups were dosed from day-7 following birth until day-21 or day-42. Dose-dependent concentrations of methoxychlor and metabolites

were found in the milk and plasma of all animals, with litter size reduction of approximately 17% at high dosage. Vaginal opening was quicker in all treated groups, and ♂ prepuce separation delayed at middle and high dose. High-dose ♂s were more excitable. Antibody plaque-forming cell response decreased in ♂s only. In adult ♀s, oestrus cyclicity was disrupted, with reduced pregnancy and delivery rates and reduced uterine weights in all treated animals. Uterine displasias and reduced mammary alveolar development was also observed, with reduced oestrus levels of follicle stimulating hormone and progesterone and attributed to fewer corpora lutea secondary to ovulation defects. In adult ♂s, epididymal sperm count and testis weight were reduced at the higher doses and such ♂s impregnated fewer untreated ♀s. The primary adult effects of early exposure to methoxychlor are therefore reproductive, and 5 mg kg^{-1} day^{-1} is not a NO(A)EL in rats having this exposure paradigm. The sites of action are central and peripheral (36).

Metabolism and toxicokinetics

Metabolised by human and rat hepatic cytochrome P_{450} monooxygenases by sequential demethylations to mono- and bis-didemethylated phenolic derivatives and a trihydroxy derivative 1,1,1-trichloro-2-(4-hydroxyphenyl)-2-(3,4-dihydroxyphenyl)ethane (37).

In mice 98% of orally administered methoxychlor was eliminated in the urine as conjugated metabolites within 24 hr (38).

Weanling rats fed 500 mg kg^{-1} diet for 4-18 wk stored 14-36 mg kg^{-1} in fat. Equilibrium was reached within 4 wk and methoxychlor was cleared from the fatty tissue within 2 wk after the end of exposure. Rats fed 100 mg kg^{-1} diet stored 1-7 mg kg^{-1} fat. None was stored in rats fed 25 mg kg^{-1} diet. No sex differences were observed (39).

Residues were found in milk after cows were sprayed with aqueous suspensions of methoxychlor. A maximum level of 0.1 mg l^{-1} was found after 1 day, and detectable levels persisted for 1 wk (40).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (41).

Escherichia coli WP2, *Saccharomyces cerevisiae* D3 mutagenicity assays negative (42).

Drosophila melanogaster sex-linked recessive lethal assay negative (43).

In vitro mouse lymphoma L5178Y cells, tk^+/tk^- with metabolic activation positive (44).

In vitro Chinese hamster ovary cells, chromosomal aberrations negative, sister chromatid exchanges positive (metabolic activation unspecified) (44).

In vivo mouse bone marrow cells, chromosome damage negative (45).

In vivo mouse, a slight increase in chromosome breakage was observed in spermatogonia, but there was no increase in sperm abnormalities, and spermatocyte metaphases revealed no significant cytological damage (45).

In vivo mouse dominant lethal assay negative (45).

Other effects

Other adverse effects (human)

Oral man, 100 mg kg^{-1} diet for 2 yr produced no toxic symptoms. 500 mg kg^{-1} diet produced unspecified tissue changes (46).

Any other adverse effects

The binding of [3H]5α-DHT to rat androgen-binding protein was inhibited ~ 40% by methoxychlor (100 μM) (47).

Even at high concentrations (723.2 μmol kg^{-1}) methoxychlor administered intramuscularly to white leghorn roosters had neither oestrogenic nor antioestrogenic activity, as measured by its effect on oestrogen-related mRNA stabilising factor (48).

Legislation

EEC maximum residue limit for fruit and vegetables 10 ppm (5).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (49).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (50).

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (51).
WHO Guideline Value for drinking water 20 $\mu g\ l^{-1}$ (52).
UK Advisory Value for drinking water 20 $\mu g\ l^{-1}$ (53).
WHO Toxicity Class Table 5 (54).
ADI 0.1 mg kg^{-1} body weight (55).

Other comments

Attributed endocrine disruption effects in wildlife. Avian reproduction impaired; fish growth reduced, impaired hatching success (56).
Residues have been isolated from water, sediments, soil, crops and in animal tissues (57-59).
Environmental fate reviewed (59).
Use, occurrence, physical properties, analysis, carcinogenicity, mammalian toxicity, teratogenicity, metabolism and mutagenicity reviewed (57,60-64).

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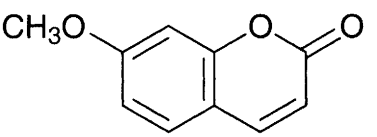
M133 7-methoxycoumarin



$C_{10}H_8O_3$ **Mol. Wt.** 176.17 **CAS Registry No.** 531-59-9

Synonyms herniarin; 7-methoxy-2*H*-1-benzopyran-2-one; ayapanin; methylumbelliferone

EINECS No. 208-513-3 **RTECS No.** DJ 3100380

Occurrence Present in citrus plant oils.

Physical properties

M. Pt. 118-120°C
Solubility Water: miscible. Organic solvents: methanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4300 mg kg^{-1} (1).
LD_{50} dermal guinea pig >5000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
A CASE study designated 7-methoxycoumarin as a marginal carcinogen (2).

Sensitisation
Negative when investigated by two different methods for identifying sensitising capacity (details unspecified) (3).

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M134 2-methoxyethanol

$$HOCH_2CH_2OCH_3$$

$C_3H_8O_2$ **Mol. Wt.** 76.10 **CAS Registry No.** 109-86-4

Synonyms ethylene glycol monomethyl ether; glycol methyl ether; methyl cellosolve; methyl ethoxol; EGME; EGMME

EINECS No. 203-713-7 **RTECS No.** KL 5775000

Uses Solvent. Antifreeze. Organic synthesis. Insect repellent. Analytical reagent.

Physical properties

M. Pt. -85°C **B. Pt.** 124-125°C **Flash point** 43°C (open cup) **Specific gravity** 0.9663 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} -0.77 (1) **Volatility** v.p. 6.2 mmHg at 20°C ; v.den. 2.62
Solubility Water: miscible. Organic solvents: acetone, diethyl ether, dimethylformamide, ethanol, glycerol

Occupational exposure

DE-MAK 5 ppm (16 mg m^{-3})
FR-VME 5 ppm (16 mg m^{-3})
JP-OEL 5 ppm (16 mg m^{-3})
SE-LEVL 5 ppm (16 mg m^{-3}) **SE-STEL** 10 ppm (30 mg m^{-3})
UK-LTEL MEL 5 ppm (16 mg m^{-3})
US-TWA 5 ppm (16 mg m^{-3})

UN No. 1188 **HAZCHEM Code** 2[redacted] **Conveyance classification** flammable liquid
Supply classification toxic
Risk phrases May impair fertility – May cause harm to the unborn child – Flammable – Harmful by inhalation, in contact with skin and if swallowed (R60, R61, R10, R20/21/22)

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

Ecotoxicity

Fish toxicity

LC_{50} (7 day) guppy 17,400 mg l^{-1} (2).

LC_{50} (96 hr) rainbow trout 15,520 mg l^{-1}(3)

Invertebrate toxicity

Toxicity threshold, cell multiplication inhibition *Pseudomonas putida* >10,000 mg l^{-1}, *Scenedesmus quadricauda* >10,000 mg l^{-1}, *Entosiphon sulcatum* 1715 mg l^{-1}(4).

Environmental fate

Anaerobic effects

Degraded anaerobically by the bacteria *Acetobacterium malicum* and *Pelobacter venetianus* isolated from freshwater sediments. Metabolites included methanol, ethanol and acetate (5).

Degradation studies

Biodegradation with filtered sewage seed in fresh water resulted in reduction of 30% of ThOD in 5 days and 88% in 20 days (6).

COD 1.69 mg l^{-1} O_2; BOD_5 0.12 mg l^{-1} O_2; BOD_{10} 1.10 mg l^{-1} O_2 (7,8).

Abiotic removal

Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ (estimated) 17.54 hr (9).

Evaporation from model river water, $t_{1/2}$ (calc.) 2.8 hr (10).

Adsorption by activated carbon 0.028 g g^{-1} carbon (11).

Adsorption and retention

Adsorption by activated carbon 0.028 g g^{-1} carbon (11).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, guinea pig, 890, 950 mg kg^{-1}, respectively (12,13).

LD_{50} oral rat, mouse 2460, 2560 mg kg^{-1}, respectively (14).

LC_{50}(7 hr) inhalation rat 1500 ppm (15).

LD_{50} dermal rabbit 1280 mg kg^{-1} (15).

LD_{50} intraperitoneal mouse, rat 2150, 2500 mg kg^{-1}, respectively (15,16).

LD_{50} intravenous rat 2140 mg kg^{-1} (13).

Sub-acute and sub-chronic data

Oral rat (10 day) 50-200 mg kg^{-1} day^{-1} in drinking water decreased testicular and thymus weight but not body weight. Toxicity to the immune system was also observed (17).

Dermal rat (4 day) 150, 300, 600, 900, or 1200 mg kg^{-1} daily. Reduced thymus weight was noted at 600 mg kg^{-1} body weight day^{-1}, while at 900 and 1200 mg kg^{-1} body weight day^{-1}, there was a reduction in spleen weight. Immunotoxicity was indicated by enhanced lymphoproliferative activity to certain antigens at 900 mg kg^{-1} body weight day^{-1} and a decreased ability to produce primary antibodies at 300 and 600 mg kg^{-1} body weight. day^{-1} (18).

Teratogenicity and reproductive effects

Oral mouse, 0-300 mg kg^{-1} day^{-1} on days 7-18 of gestation. Dosages >73 mg kg^{-1} produced total embryo mortality. Dosages >16 mg kg^{-1} produced cardiovascular malformations (19).

Oral ♂ rat, mouse, single dose of 0, 500, 750, 1000 or 1500 mg kg^{-1} caused a dose-related severe depletion of spermatocytes in both species, principally pachytene cells. In the rat, morphological abnormalities were observed in sperm that had been exposed as spermatocytes, whereas in the mouse the sensitive cells were the late spermatocytes and early spermatids. A dose-related decrease in fertility was observed after 5 wk in the rat, but

complete sterility in all but the lowest dose after 6 wk. In contrast, the reproductive capacity of the mouse was unaffected (20).

Metabolism and toxicokinetics

Human ♂ volunteers were exposed by inhalation to 16 mg m^{-3} for 4 hr, corresponding to a total dose of 0.25 mg kg^{-1}. $t_{1/2}$ for elimination in the urine was 77.1 hr. The major urinary metabolite was methoxyacetic acid (21).
In vitro mouse hepatocytes have a greater capacity to metabolise ME to its immunosuppressive metabolites than do rat hepatocytes (22).
The elimination $t_{1/2}$ of 2-methoxyethanol in rats following intraperitoneal injection of 100 mg kg^{-1} was established to be 49 ± 10 min in the ♂ and 28 ± 5 min in the ♀ (23).

Irritancy

Dermal rabbit 480 mg caused mild irritation and 10 μg instilled into guinea pig eye (exposure unspecified) caused mild irritation (24,25).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (26).
Drosophila melanogaster sex-linked recessive lethal assay equivocal results (26).
In vitro mouse lymphoma L5178Y, tk^+/tk^- with metabolic activation negative (26).
In vivo mouse sperm motility test positive (26).
In vivo rat, mouse dominant lethal mutation and F_1 abnormalities negative (20).

Other effects

Other adverse effects (human)

Shipyard painters exposed to time-weighted average concentrations of 0-80.5 mg m^{-3} (mean 9.9 mg m^{-3}) and to 2-methoxyethanol at time-weighted average of 0-17.7 mg m^{-3} (mean 2.6 mg m^{-3}) had increased prevalence of oligospermia and azoospermia and an increased potential for a lower sperm count (27).

Any other adverse effects

Produces immunosuppression in the rat but not in the mouse. *In vitro* experiments indicate that rat lymphocytes are more sensitive to 2-methoxyacetic acid, a metabolite of ME. Another metabolite, 2-methoxyacetaldehyde, is more immunosuppressive than 2-methoxyacetic acid and it is suggested that this may be the proximate immunotoxicant (22).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (28).
Solvents and pesticides are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (29).

Other comments

Environmental fate reviewed (30).
Physical properties, safety precaution and toxicity reviewed (31).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (32).
Autoignition temperature 285°C.

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M135 2-(2-methoxyethoxy)ethanol

$$CH_3OCH_2CH_2OCH_2CH_2OH$$

$C_5H_{12}O_3$ **Mol. Wt.** 120.15 **CAS Registry No.** 111-77-3

Synonyms diethylene glycol monomethyl ether; diglycol monomethyl ether; Dowanol DM; Jeffosol DM; methoxydiglycol; methyl carbitol; Poly-solv DM

EINECS No. 203-906-6 **RTECS No.** KL 6125000

Uses Adsorbent for hydrogen sulfide from natural gas and coal gas. Corrosion inhibitor for fuels and lubricating oils. Insect repellent. Solvent.

Physical properties

M. Pt. –70°C **B. Pt.** 194.2°C **Flash point** 93°C (open cup) **Specific gravity** 1.0354 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.68 (calc.) (1) **Volatility** v.p. 0.2 mmHg at 20°C ; v.den. 4.14 **Solubility** Water: miscible. Organic solvents: acetone, diethyl ether, dimethylformamide, ethanol, glycerol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 7500 mg l^{-1} static bioassay at 23°C (2).

Bioaccumulation

Calculated bioconcentration factor of 6 indicates that environmental accumulation is unlikely (3).

Environmental fate

Degradation studies

BOD_5 5% of ThOD (4).

Abiotic removal

Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ ~6 hr (5).

Adsorption and retention

Calculated K_{oc} of 10 indicates that adsorption to soil and sediments is not significant (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, rat, mouse 4200, 5500, 9200 mg kg^{-1}, respectively (6,7).
LD_{50} dermal rabbit 6500 mg kg^{-1} (8).
LD_{Lo} intraperitoneal mouse, rat 2600, 3000 mg kg^{-1}, respectively (7,9).

Sub-acute and sub-chronic data

Oral ♂ rat (20 days) 500, 1000 or 2000 mg kg^{-1} for 1, 2, 5 or 20 days. The highest doses caused a reduction in liver weight. An increase in hepatic microsomal protein, and cytochrome P_{450} were induced. Cytochrome b_5 and the reduced form of NADP cytochrome c reductase were unaffected. The activity of cytosolic ADH was also unaffected (10).
Dermal guinea pig (13 wk) 0, 40, 200 or 1000 mg kg^{-1} day^{-1} 5 days wk^{-1}. The two highest doses caused a decrease in spleen weight. Testicular weight was unaffected. The highest dose induced an increase in lactate dehydrogenase activity, while all doses caused an increase in urinary calcium excretion (11).

Teratogenicity and reproductive effects

Oral mouse, 500 mg kg^{-1} on day-11 of gestation was embryotoxic (12).
Oral mouse, 720-5200 mg kg^{-1} day^{-1} on days 7-16 of gestation. At the highest dose 2/9 dams died, all litters were resorbed and maternal body-weight gain was reduced. At a dose of 3400 mg kg^{-1} day^{-1} 6/9 litters were resorbed. A dose-related increase in malformations, primarily of the ribs and cardiovascular system, was recorded (13).

Metabolism and toxicokinetics

An oral dose of 500 mg kg^{-1} to pregnant mice was metabolised predominantly by *O*-demethylation and subsequent oxidation to (2-methoxyethoxy)acetic acid. Urinary excretion of this metabolite over 48 hr accounted for 63% of the administered dose. A smaller percentage of the administered dose was metabolised at the central ether linkage to produce 2-methoxyethanol, which was further metabolised by alcohol dehydrogenase to methoxyacetic acid, a powerful developmental toxicant. Urinary excretion of this metabolite accounted for 26% of the administered dose within 48 hr. Unchanged 2-(2-methoxyethoxy)ethanol and methoxyacetic acid were detected in embryonic tissues (12).

Irritancy

500 mg instilled into rabbit eye for 24 hr caused moderate irritation (14).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

Other comments

Residues have been isolated from effluent and drinking waters (16).
Environmental fate reviewed (16).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (17).

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M136 2-methoxyethyl acetate

$$CH_3CO_2CH_2CH_2OCH_3$$

$C_5H_{10}O_3$ **Mol. Wt.** 118.13 **CAS Registry No.** 110-49-6

Synonyms 2-methoxyethanol acetate; ethylene glycol monomethyl ether acetate; methyl cellosolve acetate; methyl glycol acetate; methyl glycol monoacetate

EINECS No. 203-772-9 **RTECS No.** KL 5950000

Uses Solvent.

Physical properties

M. Pt. –65.1°C **B. Pt.** 144-145°C **Flash point** 55.6°C (open cup) **Specific gravity** 1.0067 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 0.121 (1) **Volatility** v.p. 7 mmHg at 20°C ; v.den. 4.1
Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (25 mg m^{-3})
FR-VME 5 ppm (24 mg m^{-3})
JP-OEL 5 ppm (24 mg m^{-3})
SE-LEVL 5 ppm (25 mg m^{-3}) **SE-STEL** 10 ppm (50 mg m^{-3})
UK-LTEL MEL 5 ppm (25 mg m^{-3})

US-TWA 5 ppm (24 mg m^{-3})

UN No. 1189 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Supply classification toxic

Risk phrases May impair fertility – May cause harm to the unborn child – Harmful by inhalation, in contact with skin and if swallowed (R60, R61, R20/21/22)

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

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) goldfish 190 mg l^{-1} (1).

LC_{50} (96 hr) bluegill sunfish, inland silverside 40-45 mg l^{-1} (2).

Environmental fate

Degradation studies

22% removal in 10 days from wastewater at 1000 mg l^{-1} in acclimated seed at 20°C (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, rat 1250, 3400 mg kg^{-1}, respectively (4,5).

LC_{Lo} (4 hr) inhalation rat 7000 ppm (5).

LD_{50} dermal rabbit 5250 mg kg^{-1} (6).

LD_{Lo} intraperitoneal rat 1200 mg kg^{-1} (7).

Irritancy

218 mg instilled into rabbit eye caused mild irritation (duration unspecified) (6).

Genotoxicity

Saccharomyces cerevisiae D61.M induction of aneuploidy positive, mitotic recombination and point mutation negative (8).

Drosophila melanogaster induction of aneuploidy positive (9).

In vitro Chinese hamster ovary cells sister chromatid exchanges and chromosomal aberrations with metabolic activation positive (10).

Legislation

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

Other comments

Reviews on physical properties, safety precautions and toxicity listed (12).

Human health effects, experimental toxicology, physico-chemical properties reviewed (13).

Autoignition temperature 392°C.

References

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13. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M137 2-methoxyethylmercury acetate

$$CH_3OCH_2CH_2HgOC(O)CH_3$$

$C_5H_{10}HgO_3$ **Mol. Wt.** 318.72 **CAS Registry No.** 151-38-2

Synonyms methoxyethylmercury(II) acetate; Landisan; Mema; Mercuran; Panogen; Radosan

EINECS No. 205-790-2 **RTECS No.** OV 6300000

Uses Superseded fungicide, used in seed dressings.

Physical properties

M. Pt. 40-42°C **Volatility** v.p. 1.3×10^{-5} mmHg at 20°C
Solubility Water: miscible. Organic solvents: ethylene glycol, methanol

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Hg) (total dust)
FR-VME 0.01 mg m^{-3} (as Hg)
JP-OEL 0.05 mg m^{-3} (as Hg)
SE-LEVL 0.03 mg m^{-3} (as Hg)
US-TWA 0.01 mg m^{-3} (as Hg) **US-STEL** 0.03 mg m^{-3} (as Hg)

UN No. 2024 (liquid)

UN No. 2025 (solid) **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R26/27/28, R33)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S13, S28, S36, S45)

Environmental fate

Degradation studies
In soil, degraded to inorganic mercury salts or metallic mercury. Metallic mercury is ultimately converted into mercury sulfide by the reaction with hydrogen sulfide liberated by soil microorganisms (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 25, 45 mg kg^{-1}, respectively (2,3).
LD_{50} intragastric mouse, rat 60-70 mg kg^{-1} (Radosan) (4).

Metabolism and toxicokinetics

In single doses alkoxyalkyl mercury compounds are rapidly converted into inorganic mercury and do not appear to cross the blood-brain barrier appreciably in mammals. Mercury accumulates principally in the kidneys and liver. With repeated exposure there is a slow but progressive increase in brain levels of mercury (5).

Other effects

Other adverse effects (human)

Symptoms of chronic organomercury compound toxicity include disorders of the central nervous system (general depression, weakness, disturbed coordination of movements, increased reflexes, excitability, tremors, paralysis, convulsions) and blood disorders (advancing anaemia, leucopenia, eosinopenia, declining lymphocyte count, onset of granules in neutrophils). The number of young cells and mitosis decline in the bone marrow (6).

Legislation

Limited under EC Directive on drinking water quality 80/778/EEC. Mercury: maximum admissible concentration 1 $\mu g\ l^{-1}$; individual pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (7).
Included in Schedule 5 (Release into Water: Prescribed Substances) and Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Organomercury compounds comprehensively reviewed (9).

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M138 methoxyfluorane

$$CH_3OCF_2CHCl_2$$

$C_3H_4Cl_2F_2O$ **Mol. Wt.** 164.97 **CAS Registry No.** 76-38-0

Synonyms 2,2-dichloro-1,1-difluoro-1-methoxyethane; 2,2-dichloro-1,1-difluoroethyl methyl ether; 1,1-difluoro-2,2-dichloroethyl methyl ether

Uses Human and veterinary anaesthetic.

Physical properties

M. Pt. -35°C **B. Pt.** 105°C **Specific gravity** 1.4262 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3600 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat 33.5 g m^{-3} (1).
LC_{50} (2 hr) inhalation mouse 118 g m^{-3} (2).
TC_{Lo} (1 hr) inhalation human 3500 ppm (3).

Sub-acute and sub-chronic data

Inhalation Swiss Webster mice (9 wk) 0.02-0.5% 4 hr day^{-1}, 5 days wk^{-1}. There were no significant differences in body weights among exposure groups. Organ weights, haematocrits, and SGOT activity levels were similar among all groups. No anaesthetic-related organ toxicity was revealed by histological examination. Cytochrome b5 and P_{450} levels were similar for exposed groups and between sexes (4).
Inhalation ♂ Fischer 344 rats (14 wk) air or 50 ppm methoxyfluorane. After 14 wk, half the rats in each group were killed and the remainder breathed air for a further 4 wk (recovery period) before being killed. Growth of the methoxyfluorane-exposed rats was markedly depressed during the exposure period, although food consumption was similar in both groups. Both water consumption and urine volume were increased by methoxyfluorane treatment. This may have been caused by the nephrotoxic effects of F^- which was found in the sera of all exposed rats at a concentration >50 μmolar. All of the exposed rats, but none of the controls, showed focal hepatocellular degeneration and necrosis, and prominent fatty change. During recovery, water consumption and urine volume returned to near-normal values. After 4 wk of recovery, focal hepatonecrosis was still seen but fatty change was no longer present. No histological abnormalities were seen in exposed or control rats (5).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (6).

Irritancy

100 mg instilled into rabbit eyes caused moderate irritation (7).

Other effects

Other adverse effects (human)

Can cause renal toxicity in man due to the release of fluoride acting on the distal tubules. May cause polyuric or oligouric renal failure. Depresses the cardiovascular system and hypotension may occur (8).

Any other adverse effects

Methoxyfluorane was extremely toxic when diffused into the brains of cats via silastic rubber semipermeable membrane implants (9).

Other comments

Toxicity and metabolism of methoxyfluorane reviewed (8).

References

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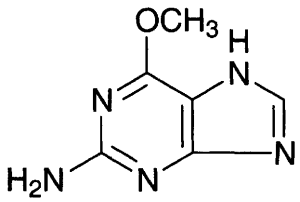
M139 6-methoxyguanine



$C_6H_7N_5O$ **Mol. Wt.** 165.15 **CAS Registry No.** 20535-83-5

Synonyms 2-amino-6-methoxypurine; 6-methoxy-1*H*-purin-2-amine; O^6-methylguanine

RTECS No. UO 7473000

Uses Alkylating agent. Antineoplastic agent.

Genotoxicity

M13mp8 phage, incorporation of a single residue of 6-methoxyguanine in the phage DNA induced G to A transitions (1).
In vitro human lymphocytes, chromosomal aberrations positive (metabolic activation unspecified) (2).
In vivo rat bone marrow, kidney, lung, spleen and intestine modulated the activity of the DNA repair enzyme O^6-alkylguanine-DNA alkyltransferase (3).

Other comments

In vitro Chinese hamster ovary and human cells, treatment with several alkylating agents indicated that the formation of 6-methoxyguanine is the major mutagenic lesion (4,5).

References

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M140 4-methoxy-4-methyl-2-pentanone

$$CH_3C(O)CH_2C(CH_3)(OCH_3)CH_3$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 107-70-0

Synonyms 4-methoxy-4-methylpentan-2-one; methoxyhexanone; Pentoxane; ME-6K

EINECS No. 203-512-4 **RTECS No.** SA 9185000

Uses Azeotropic agent. Solvent.

Physical properties

B. Pt. 159.1°C **Flash point** 60.5°C **Specific gravity** 0.899 at 25°C with respect to water at 25°C
Volatility v.p. 3.16 mmHg at 25°C
Solubility Water: 280 g l^{-1} at 25°C. Organic solvents: acetone, allyl alcohol, ethanol, n-hexane

Occupational exposure

UN No. 2293 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Risk phrases Flammable (R10)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 3800 mg l^{-1} (1).

Bioaccumulation
Calculated bioconcentration factor 0.5 indicates that environmental accumulation is unlikely (2).

Environmental fate

Degradation studies
BOD_5 0.11 mg l^{-1} O_2; COD 2.24 mg l^{-1} O_2 (1).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals, estimated $t_{1/2}$ 3.1 days (3).
Laboratory studies demonstrated direct photolysis occurs at 313 nm in hexane, ethanol and allyl alcohol.
Photolysis products included mesityl oxide, methanol, a hydroxyfuran derivative and small amounts of acetone and methyl isoprenyl ether (4).
Estimated volatilisation $t_{1/2}$ 22 days for model river water and 236 days for model pond water (2,5).

Adsorption and retention
Estimated K_{oc} of 4.4 indicates that adsorption to soil and sediments is unlikely (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 2100 mg kg^{-1} (1).
LC_{Lo} (15 hr) inhalation mouse 2300 ppm (1).
LD_{Lo} dermal rabbit 3000 mg kg^{-1} (1).

Irritancy
Dermal rabbit, 500 mg caused moderate irritation (exposure unspecified) (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).
Saccharomyces cerevisiae mitotic gene conversion negative (8).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

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

References

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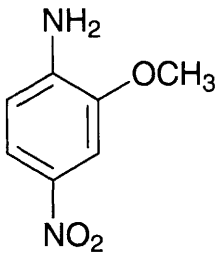
10. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M141 2-methoxy-4-nitroaniline



$C_7H_8N_2O_3$ **Mol. Wt.** 168.15 **CAS Registry No.** 97-52-9

Synonyms 2-methoxy-4-nitrobenzenamine; 4-nitro-o-anisidine; 2-amino-5-nitroanisole; Amorthol Fast Red B Base; C.I. 37125; Diazo Fast Red B; Naphthenil Red B Base; Sanyo Fast Red B Base

EINECS No. 202-588-6 **RTECS No.** BZ 7170000

Uses Organic synthesis. Manufacture of dyestuffs.

Physical properties

M. Pt. 140-142°C **Specific gravity** 1.211 at 156°C
Solubility Organic solvents: dimethyl sulfoxide

Mammalian & avian toxicity

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

Irritancy
Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (2).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation positive (3).

Other effects

Other adverse effects (human)
Absorption into the body leads to the formation of methaemoglobin, which in sufficient amounts causes cyanosis (2).

Other comments

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

References

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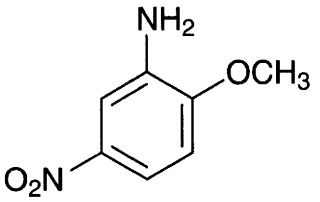
M142 2-methoxy-5-nitroaniline



$C_7H_8N_2O_3$ **Mol. Wt.** 168.15 **CAS Registry No.** 99-59-2

Synonyms 2-amino-1-methoxy-4-nitrobenzene; 3-amino-4-methoxynitrobenzene; 2-amino-4-nitroanisole; *o*-anisidine nitrate; C.I. 37130; 2-methoxy-5-nitrobenzenamine; 3-nitro-6-methoxyaniline; 5-nitro-*o*-anisidine

EINECS No. 202-770-5 **RTECS No.** BZ 7175000

Uses Intermediate in organic dye and pigment manufacture.

Physical properties

M. Pt. 117-119°C **Specific gravity** 1.207 at 156°C **Partition coefficient** log P_{ow} 0.97
Solubility Organic solvents: acetic acid, hot benzene, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 704 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral administration of 8000 mg kg^{-1} diet for 7 wk to rats caused liver and testicular degeneration and gastric mucosal sclerosis in ♂, and thyroid follicle pigmentation and haematopoiesis in the spleen of both sexes (1).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (2).
NTP tested rats and mice via feed. Clear evidence of carcinogenicity in rats and mice. Mice were fed 8000 mg kg^{-1} for 78 wk, or 16,000 mg kg^{-1} for 15 wk and then 4000 mg kg^{-1} for 63 wk; rats were fed 4000 or 8000 mg kg^{-1} for 78 wk (3).
Human carcinogen potency factor 0.0456 mg kg^{-1} day^{-1} orally (4).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation positive, TA100 without metabolic activation negative (5).
Did not induce sex-linked recessive lethal mutations in *Drosophila melanogaster* (6).

Legislation

A health and environmental effects profile has been prepared under section 3001 of the US Resource Conservation and Recovery Act (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

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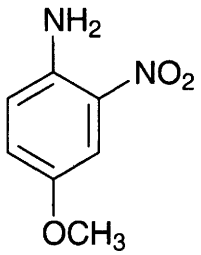
M143 4-methoxy-2-nitroaniline



$C_7H_8N_2O_3$ **Mol. Wt.** 168.15 **CAS Registry No.** 96-96-8

Synonyms 4-methoxy-2-nitrobenzenamine; 2-nitro-*p*-anisidine; 4-amino-3-nitroanisole

EINECS No. 202-547-2 **RTECS No.** BY 4415000

Uses Organic synthesis. Manufacture of dyestuffs.

Physical properties

M. Pt. 123-126°C

Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

Supply classification very toxic

Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R26/27/28, R33, R52/53)

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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Mammalian & avian toxicity

Acute data

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

LD_{50} oral rat 14,100 mg kg^{-1} (2).

Irritancy

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

Other effects

Other adverse effects (human)

Absorption into the body leads to the formation of methaemoglobin, which in sufficient amounts causes cyanosis (3).

Other comments

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

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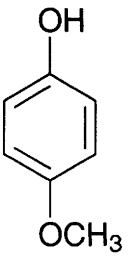
M144 4-methoxyphenol



$C_7H_8O_2$ **Mol. Wt.** 124.14 **CAS Registry No.** 150-76-5

Synonyms *p*-methoxyphenol; *p*-guaiacol; hydroquinone methyl ether; Leucobasal; Mequinol; PMF (antioxidant)

EINECS No. 205-769-8 **RTECS No.** SL 7700000

Uses Antioxidant. Corrosion inhibitor. Organic synthesis. Polymerisation inhibitor. Manufacture of photographic compounds. Treatment of skin hyperpigmentation.

Physical properties

M. Pt. 55-57°C **B. Pt.** 243°C **Flash point** 132°C (open cup) **Specific gravity** 1.55 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 1.34 (1)

Solubility Water: 40 g l^{-1} at 25°C. Organic solvents: acetone, benzene, diethyl ether, ethanol, ethyl acetate

Occupational exposure

FR-VME 5 mg m^{-3}
UK-LTEL 5 mg m^{-3}
US-TWA 5 mg m^{-3}

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) goldfish ~200 mg l^{-1} (2).
LC_{50} (96 hr) fathead minnow 140 mg l^{-1}, flow-through bioassay (3).

Environmental fate

Degradation studies
Complete degradation by soil microflora in 8 days (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1600 mg kg^{-1} (5).
LD_{50} intraperitoneal mouse 250 mg kg^{-1} (6).

Sub-acute and sub-chronic data
Oral rat (7 wk) 0.1-5% diet caused a dose-related decrease in body-weight gain (5).
Oral rat (duration not specified) 2% diet induced deep ulceration parallel to the limiting ridge of the forestomach mucosa, with hyperplasia and mild hyperkeratosis in the adjoining mucosa. These effects were similar to those caused by 3-*tert*-butyl-4-hydroxyanisole after two days administration (7).
Injection into the substantia nigra of rats led to a dose-related destruction of dopamine neurons, as indicated by a reduction in dopamine and its metabolites in the ipsilateral striatum and loss of tyrosine hydroxylase immunoreactivity (8).

Carcinogenicity and chronic effects
Oral ♂ F344 rats (2 yr) 2% 4-methoxyphenol in diet. Retardation of body weight and elevated relative liver weights were noted. Formalin-fixed and paraffin embedded liver tissues from rats killed terminally were cut and stained for glutathione S-transferase placental form (GST-P) and tumour growth factor α (TGFα) immunohistochemistry. Numbers and areas of GST-P +ve foci per unit area of liver section were measured and the treated/control proportional values were calculated to be 49% and 39%. Long-term inhibitory effects of phenolic compounds on liver carcinogenesis, predicted from the Ito test, were thus confirmed (9).

Irritancy
Dermal rabbit (12 days) 6000 mg day^{-1} caused mild irritation (10).

Genotoxicity

In vitro human peripheral lymphocytes inhibited DNA repair and semi-conservative DNA synthesis (11).

Other effects

Other adverse effects (human)
Severe reversible irregular hypopigmentation was reported in a West Indian woman (12).

Any other adverse effects
In vitro IC_{50} (4 hr) mouse hepatocytes 32 mg l^{-1} (13).

Other comments

Autoignition temperature 421°C.

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2. McKee, J. E. et al *Water Quality Criteria* 1963, Resources Agency of California, State Water Quality Control Board, USA.
3. Schultz, T. W. et al *Ecotoxicol. Environ. Saf.* 1986, **12**(2), 146-153.
4. Alexander, M. et al *J. Agric. Food Chem.* 1966, **14**, 410.
5. *Patty's Industrial Hygiene and Toxicology* 2nd ed., 1963, **2**, 1688, John Wiley & Sons, New York, USA.
6. *NTIS Report AD691-490*, Natl. Tech. Info. Serv., Springfield, VA, USA.
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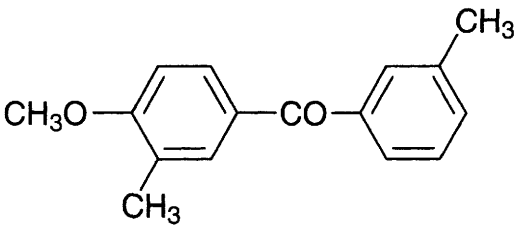
M145 methoxyphenone



$C_{16}H_{16}O_2$ **Mol. Wt.** 240.30 **CAS Registry No.** 41295-28-7

Synonyms (4-methoxy-3-methylphenyl)(3-methylphenyl)methanone; 4-methoxy-3,3'-dimethylbenzophenone; Kayametone; NK 049

EINECS No. 255-300-6 **RTECS No.** PC 4961000

Uses Catalyst. Superseded herbicide.

Physical properties

M. Pt. 62.0-62.5°C

Solubility Water: 2 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp, goldfish 3.21 mg l^{-1} (1).

Environmental fate

Abiotic removal

Slowly decomposed by sunlight (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse >4000 mg kg^{-1} (2).

LD_{50} dermal rat >4000 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rat, mouse (90 day) no-adverse-effect level 1000-1500 mg kg^{-1} (1).

References

1. *The Pesticide Manual* 8th ed., 1987, 556, British Crop Protection Council, Thornton Heath, UK.
2. *Jpn. Pestic. Inf.* 1976, **27**, 11

M146 methoxypropanol

$$CH_3CH(OH/CH_3)CH_2(OH/CH_3)$$

$C_4H_{10}O_2$ **Mol. Wt.** 90.12 **CAS Registry No.** 1320-67-8

Synonyms monopropylene glycol methyl ether; propanol, 1 (or 2)-methoxy-; Dowanol PM; methyl ether of propylene glycol; propylene glycol monomethyl ether

EINECS No. 215-306-1 **RTECS No.** TZ 0660000

Physical properties

M. Pt. –96.7°C **B. Pt.** 120°C **Flash point** 168.3°C **Specific gravity** 0.919 at 25°C with respect to water at 25°C

Occupational exposure

SE-LEVL 50 ppm (190 mg m^{-3}) **SE-STEL** 75 ppm (300 mg m^{-3})

Mammalian & avian toxicity

Metabolism and toxicokinetics

Inhalation (6 hr) rats 300 and 3000 ppm 1 or 10 × daily, blood levels failed to plateau, indicating that absorption was limited by respiration. Methoxypropanol blood levels were higher in ♂ than in ♀ rats receiving a single 3000 ppm exposure (1).

Irritancy

Eye rabbit 100 mg caused severe irritation (2).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Morgott, D. A. et al *Toxicol. Appl. Pharmacol.* 1987, **89**(1), 19-28.
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M147 1-methoxy-2-propanol

$$CH_3CH(OH)CH_2OCH_3$$

$C_4H_{10}O_2$ **Mol. Wt.** 90.12 **CAS Registry No.** 107-98-2

Synonyms 1-methoxypropan-2-ol; Dowtherm 209; (±)-1-methoxypropan-2-ol; monopropylene glycol methyl ether; Propasol; propylene glycol monomethyl ether; Solvent M

EINECS No. 203-539-1 **RTECS No.** UB 7700000

Uses Solvent.

Physical properties

M. Pt. –96.7°C **B. Pt.** 118-119°C **Flash point** 33°C **Specific gravity** 0.919 at 25°C with respect to water at 25°C **Volatility** v.p. 11.8 mmHg at 25°C ; v.den. 3.11

Solubility Water: miscible. Organic solvents: diethyl ether, methanol

Occupational exposure

DE-MAK 100 ppm (370 mg m^{-3})
FR-VME 100 ppm (360 mg m^{-3})
SE-LEVL 50 ppm (190 mg m^{-3}) **SE-STEL** 75 ppm (300 mg m^{-3})
UK-LTEL 100 ppm (375 mg m^{-3}) **UK-STEL** 300 ppm (1120 mg m^{-3})
US-TWA 100 ppm (369 mg m^{-3}) **US-STEL** 150 ppm (553 mg m^{-3})

UN No. 3092 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Risk phrases Flammable (R10)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin (S2, S24)

Ecotoxicity

Fish toxicity

Not toxic to brown trout, bluegill sunfish, yellow perch or goldfish at 5 ppm after 24 hr exposure (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 5700, 12,000 mg kg^{-1}, respectively (2,3).
LC_{Lo} (4 hr) inhalation rat 7000 ppm (4).
LD_{50} subcutaneous rat 7800 mg kg^{-1} (3).
LD_{50} intravenous rat, rabbit 4200, 8000 mg kg^{-1}, respectively (3,5).
LD_{50} intraperitoneal rat 3700 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Oral rat (13 wk) 0.5, 0.9, 1.8 or 3.6 mg kg^{-1} day^{-1} 5 days wk^{-1} caused dose-related central nervous system depression, reduced food intake and growth depression. Liver enlargement was accompanied by cell necrosis mainly in the peripheral parts of the lobules. The highest dose caused appreciable mortality. The high doses also caused kidney injury (3).

Oral rat (35 day) 3000 mg kg^{-1} day^{-1} on 26 days induced mild histopathological changes in the liver and kidneys (4).

Inhalation rat (13 wk) 300, 1000 or 3000 ppm 6 hr day^{-1}, 5 days wk^{-1}. The high-dose group appeared sedated during the first 2 wk. Pathological changes were observed in the liver of the high-dose group (6).

Dermal rabbit (3 month) 2, 4, 6 or 9 g kg^{-1} day^{-1}. All the high-dose and 8/9 of the 6 g kg^{-1} day^{-1} group died within 6 wk. Deaths were associated with loss of body weight and narcosis. The stomachs of these animals were distended with food indicating gastric retention. Renal necrosis or slight granular degeneration of the tubules was also observed (4).

Subcutaneous rat (4 wk) 0.5, 0.9, 1.8 or 3.7 g kg^{-1} day^{-1}. Some fatalities occurred in the high-dose group. Ataxia, prostration and liver lesions were seen at ≥1.8 g kg^{-1} day^{-1}, dyspnoea at ≥0.9 g kg^{-1} day^{-1}. Dose-related body weight loss and reduced urinary volume were observed (3).

Teratogenicity and reproductive effects

Oral and subcutaneous rat, mouse, rabbit 0.03-2.0 mg kg^{-1} day^{-1} on days 18-21 of gestation. Only rat foetuses showed any effect, a delayed ossification of the skull at the highest dose (0.7 mg kg^{-1}) (3).
Inhalation rat, lowest toxic concentration 3000 ppm 6 hr day^{-1} on days 6-15 of gestation, teratogenic effects (7).

Metabolism and toxicokinetics

Following oral administration of ^{14}C-labelled substance, 11-25% of the radioactivity was found in urine, 0.7-1.5% in faeces and 57-63% was exhaled as carbon dioxide after two days (8).
Six human volunteers were exposed to 100 ppm 1-methoxy-2-propanol (M2P) for 8 hr, including a 30 minute break. Post-exposure levels of free M2P in urine were found to reach up to 110 μmol l^{-1}. Levels of M2P were monitored in blood (maximum 103 μmol l^{-1}) and exhaled air samples (up to 252 nmol l^{-1}). M2P is rapidly excreted in urine, $t_{1/2}$ <2.6 hr (9).

Irritancy

Dermal rabbit 500 mg caused mild irritation. 230 mg instilled into rabbit eye caused mild irritation (exposure not specified) (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (10).
In vitro Chinese hamster ovary cells, chromosomal aberrations negative (10).
In vitro primary rat hepatocytes, unscheduled DNA synthesis negative (10).

Legislation

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

Other comments

Physical properties, mammalian toxicity, teratogenicity and mutagenicity reviewed (12,13).

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M148 1-methoxy-2-propanol acetate

$$CH_3CH(OC(O)CH_3)CH_2OCH_3$$

$C_6H_{12}O_3$ **Mol. Wt.** 132.16 **CAS Registry No.** 108-65-6

Synonyms 1-methoxypropan-2-ol acetate; propylene glycol methyl ether acetate; 2-acetoxy-1-methoxypropane

EINECS No. 203-603-9 **RTECS No.** AI 8925000

Uses Solvent.

Physical properties

B. Pt. 145-146°C **Flash point** 43°C **Specific gravity** 0.968

Occupational exposure

DE-MAK 50 ppm (270 mg m^{-3})

Ecotoxicity

Fish toxicity

Fatal to brown trout after 21 hr and to yellow perch after 24 hr at 5 ppm. Not toxic to bluegill sunfish or goldfish after 24 hr at 5 ppm. Test conditions: pH 7, dissolved oxygen content 7.5 ppm, total hardness (soap method) 300 ppm, methyl orange alkalinity 310 ppm, free carbon dioxide 5 ppm and temperature 12.8°C (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 8500 mg kg^{-1} (2).

LD_{50} dermal rat >5000 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 750 mg kg^{-1} (3).

Legislation

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

Other comments

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

References

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M149 2-methoxypropanol acetate

$$CH_3CH(OCH_3)CH_2OC(O)CH_3$$

$C_6H_{12}O_3$ **Mol. Wt.** 132.16 **CAS Registry No.** 70657-70-4

Synonyms 2-methoxypropyl acetate

EINECS No. 274-724-2 **RTECS No.** AI 8967450

Uses Solvent.

Occupational exposure

DE-MAK 20 ppm (110 mg m^{-3})

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Inhalation rat 0, 0.6, 3.0 or 15 mg l^{-1} for 6 hr day^{-1} on days 6-15 of gestation. The two high doses caused a degree of maternal toxicity. Skeletal anomalies of the thoracic vertebrae were observed in foetuses of the high-dose group (1).

Inhalation rabbit 0, 0.2, 0.8 or 3.0 mg l^{-1} for 6 hr day^{-1} on days 6-18 of gestation. Severe developmental malformations, without maternal toxicity, were observed in the high-dose group (1).

Dermal rabbit, 1000 or 2000 mg kg^{-1} day^{-1} on days 6-18 of gestation caused no maternal or foetal toxicity (1).

Legislation

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

Other comments

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

References

1. Merkle, J. et al *Fundam. Appl. Toxicol.* 1987, 8(1), 71-79.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M150 *N*-methylacetamide

$$CH_3C(O)NHCH_3$$

C_3H_7NO **Mol. Wt.** 73.09 **CAS Registry No.** 79-16-3

Synonyms methylacetamide; monomethylacetamide

EINECS No. 201-182-6 **RTECS No.** AC 5960000

Physical properties

M. Pt. 26-28°C **B. Pt.** 204-206°C **Flash point** >107°C (closed cup) **Specific gravity** 0.9571 at 25°C with respect to water at 4°C

Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5000 mg kg^{-1} (1).
LD_{50} subcutaneous rat 3600 mg kg^{-1} (2).
LD_{50} intraperitoneal rat, mouse 2750, 4380 mg kg^{-1}, respectively (1,3).
LD_{Lo} intravenous rabbit 16,940 mg kg^{-1} (4).
LD_{50} intravenous mouse 4015 mg kg^{-1} (3).

References

1. *J. Reprod. Fertil.* 1962, **4**, 219.
2. *C. R. Hebd. Seances Acad. Sci.* 1960, **251**, 1937.
3. *J. Pharm. Pharmacol.* 1964, **16**, 472.
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M151 methyl acetate

$$CH_3CO_2CH_3$$

$C_3H_6O_2$ **Mol. Wt.** 74.08 **CAS Registry No.** 79-20-9

Synonyms methyl ethanoate

EINECS No. 201-185-2 **RTECS No.** AI 9100000

Uses Solvent for resins and oils. Used in the manufacture of artificial leather.

Physical properties

M. Pt. -98°C **B. Pt.** 56.9°C **Flash point** -10°C (closed cup) **Specific gravity** 0.93 at 25°C with respect to water at 4°C **Volatility** v.p. 100 mmHg at 9°C ; v.den. 2.55
Solubility Organic solvents: miscible with ethanol, diethyl ether

Occupational exposure

DE-MAK 200 ppm (610 mg m^{-3})
FR-VME 200 ppm (610 mg m^{-3}) **FR-VLE** 250 ppm (760 mg m^{-3})
JP-OEL 200 ppm (610 mg m^{-3})
SE-LEVL 150 ppm (450 mg m^{-3}) **SE-STEL** 300 ppm (900 mg m^{-3})
UK-LTEL 200 ppm (616 mg m^{-3}) **UK-STEL** 250 ppm (770 mg m^{-3})
US-TWA 200 ppm (606 mg m^{-3}) **US-STEL** 250 ppm (757 mg m^{-3})

UN No. 1231 **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 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 320-399 mg l^{-1} (1,2).

Invertebrate toxicity
EC_{50} *Photobacterium phosphoreum* 162mM Microtox test (3).

Bioaccumulation
Calculated bioconcentration factors of 0.57-0.81 indicate that environmental accumulation is unlikely (4).

Environmental fate

Carbonaceous inhibition
0.2% (v/v) methyl acetate was hydrolysed to methanol and acetate within 24-36 hr by *Pseudomonas* sp. strains which possess non-specific inducible carboxyl esterase activity (5).

Anaerobic effects
>66% of methyl acetate was degraded to methane in 90 days using an anaerobic digester seed acclimated to acetic acid (6).

Degradation studies
Oxidised by *Alcaligenes faecalis* isolated from activated sludge (7).
BOD_5 26% reduction in dissolved oxygen using a sewage seed inoculum (8).
Calculated soil adsorption coefficients indicate that methyl acetate will be highly mobile in soil (9).

Abiotic removal
Generally alkyl esters were resistant to hydrolysis under acidic or neutral conditions typically found in the environment (10).
Evaporation was significant in the removal of methyl acetate from the environment (11).
Photochemical reactivity, $t_{1/2}$ 47-94 days at 19-30°C (12).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 3700 mg kg^{-1} (13).
LC_{50} (1 hr) inhalation cat 67 g m^{-3} (14).
LC_{Lo} (4 hr) inhalation mouse 34 g m^{-3} (14).
LD_{Lo} subcutaneous cat 3000 mg kg^{-1} (14).

Metabolism and toxicokinetics
Two-hr exposures twice daily (species unspecified) at concentration of 200 ppm for 3-4 days caused an increase in urinary excretion of methanol (15).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation, 100 mg instilled into rabbit eye in 24 hr caused severe irritation (16,17).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with metabolic activation negative (18). *Saccharomyces cerevisiae* induced sex chromosome loss and non-disjunction (19).

Other effects

Other adverse effects (human)
A 17-yr-old girl, who had sniffed a lacquer thinner for 3 months, suffered acute blindness followed by optic atrophy. A brain scan revealed symmetrical low attenuation areas in the bilateral putamen. Major components of the thinner in the vaporised state were methanol and methyl acetate (20).
Reported to be narcotic (21).

Other comments

Reviews on experimental toxicology, epidemiology and human health effects listed (22).

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M152 methyl acetoacetate

$$CH_3C(O)CH_2CO_2CH_3$$

$C_5H_8O_3$ **Mol. Wt.** 116.12 **CAS Registry No.** 105-45-3

Synonyms methyl acetylacetate; methyl 3-oxobutyrate

EINECS No. 203-299-8 **RTECS No.** AK 5775000

Uses Cross-linking catalyst. Chelating agent. Organic synthesis.

Physical properties

M. Pt. 27.5°C **B. Pt.** 204-206°C **Flash point** 108°C **Specific gravity** 1.0762 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.264 (calc.) (1) **Volatility** v.p. 0.7 mmHg at 20°C ; v.den. 4.00
Solubility Water: ~38%. Organic solvents: diethyl ether, ethanol

Occupational exposure

Supply classification irritant
Risk phrases Irritating to the eyes (R36)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S26)

Ecotoxicity

Bioaccumulation

Calculated bioconcentration factors of 0.37-0.48 indicate that environmental accumulation is unlikely (2).

Environmental fate

Adsorption and retention

Calculated K_{oc} of ~17 indicates that adsorption to soil and sediments will not be significant (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, rabbit 1250-3500 mg kg^{-1} (3,4).
Inhalation rat, 8 hr exposure to saturated vapour was not lethal (4).
LD_{50} dermal rabbit >10 ml kg^{-1} (4).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation (5).
2 mg instilled into rabbit eye caused severe irritation (exposure not specified) (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).
Autoignition temperature 280°C.

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M153 methyl acrylate

$$CH_2{=}CHCO_2CH_3$$

$C_4H_6O_2$ **Mol. Wt.** 86.09 **CAS Registry No.** 96-33-3

Synonyms acrylic acid, methyl ester; methoxycarbonylethylene; methyl 2-propenoate; methyl prop-2-enoate

EINECS No. 202-500-6 **RTECS No.** AT 2800000

Uses Used in production of acrylic and modacrylic fibres, thermoplastic coatings, adhesives and sealants, and amphoteric surfactants for shampoos.

Occurrence Has been identified in the extractable volatile components of fresh pineapple puree (1).

Physical properties

M. Pt. -75°C **B. Pt.** 80°C **Flash point** 6°C **Specific gravity** 0.9561 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.80 **Volatility** v.p. 70 mmHg at 20°C ; v.den. 3.0
Solubility Water: 0.06 g ml^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (18 mg m^{-3})
FR-VME 10 ppm (35 mg m^{-3}) **FR-VLE** 15 ppm (50 mg m^{-3})
SE-LEVL 10 ppm (35 mg m^{-3}) **SE-STEL** 15 ppm (50 mg m^{-3})
UK-LTEL 10 ppm (36 mg m^{-3})
US-TWA 2 ppm (7 mg m^{-3})

UN No. 1919 (inhibited) **HAZCHEM Code** 3WE (inhibited) **Conveyance classification** flammable liquid (inhibited)
Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful by inhalation, in contact with skin and if swallowed – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact (R11, R20/21/22, R36/37/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Avoid contact with eyes – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Take precautionary measures against static discharges – Wear suitable protective clothing and gloves – In case of fire use water (S2, S9, S25, S26, S33, S36/37, S43)

Ecotoxicity

Invertebrate toxicity
LOEC *Uronema parduczi* 64 mg l^{-1} (duration unspecified) (2).

Environmental fate

Degradation studies
Biodegradable (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 270 mg kg^{-1} (4).
LD_{50} oral mouse, rabbit, rat 200-826 mg kg^{-1} (1).
LC_{50} inhalation mouse, rat, rabbit 8800, 6400, 6800 mg m^{-3}, respectively (duration unspecified) (4).
LC_{50} inhalation mouse, rat 12,800, 7300 mg m^{-3}, respectively (duration unspecified) (1).
In inhalation studies 3/6 rats died after exposure for 4 hr to 3500 mg m^{-3} (1).
LD_{50} dermal rabbit 1240 mg kg^{-1} (1).
LD_{50} percutaneous rabbit 0.7 ml kg^{-1} (4).
LD_{50} intraperitoneal mouse, rat 254, 325 mg kg^{-1}, respectively (1).

Sub-acute and sub-chronic data
Inhalation rabbit, guinea pig, rat (2-7 day) 2000 mg m^{-3} 7 hr day^{-1} caused reduced body weight, salivation, laboured respiration and lethargy in all three species, distension of ear veins in rabbits and lachrymation in rabbits and guinea pigs (1).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).
Inhalation ♂, ♀ Sprague-Dawley rats (2 yr) 0, 15, 45 or 135 ppm 6 hr day^{-1}, 5 × wk^{-1}. No dose-related increase was seen in either the overall tumour incidence or for any of a variety of observed tumour types (1).

Metabolism and toxicokinetics
Following intraperitoneal and oral administration of methyl [2,3-^{14}C]acrylate to rats the majority of the ^{14}C was

found in the liver, kidneys and lungs. Loss of ^{14}C from these tissues was fairly rapid, with excretion in expired air (>50% of the dose) and urine (10-50% of the dose) (6).

Irritancy
Highly irritating to skin and mucous membranes of humans (1).

Sensitisation
Induced contact sensitivity in guinea pigs and dermal application to rabbits caused local irritation, erythema, oedema, vascular damage and dystrophic and necrotic effects (1).
The threshold value for irritation sensitisation in humans was 31 mg m^{-3} (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (1).
Escherichia coli WP2, WP2*uvr*A- with and without metabolic activation negative (1).
In vitro Chinese hamster lung cells without metabolic activation, 7.5-15 μg ml^{-1} caused an increase in chromosomal aberrations (1).
In vivo mouse bone marrow cells, two intraperitoneal injections (total dose 37.5-300 mg kg^{-1}) increased the number of micronuclei in polychromatic erythrocytes × 3; a single dose of 250 mg kg^{-1} or 4 doses of 125 mg kg^{-1} by gavage caused no increase (1).
L-5178Y mouse lymphoma cells without metabolic activation. Concentration-dependent increases in mutant frequency and gross chromosomal aberrations produced (7).

Other effects

Other adverse effects (human)
The frequency of disturbances in menstrual functions in 1044 women exposed to acrylonitrile and methyl acrylate was 2 × that seen in a control group (1).
Workers exposed to 1.9-83.0 mg m^{-3} for 6.9 yr reported irritation of the mucous membranes of the eyes, nose and upper respiratory tract, and effects on the central nervous system. The main complaints included dizziness, weakness, insomnia, amnesia, chest pain, breathlessness, sore throat, coughing and congestion of surrounding tissues. When subjects were X-rayed, more lung markings were seen than in controls (8).

Any other adverse effects
The threshold concentrations for temporal decrease of respiratory rate in rabbits was 80 mg m^{-3} (4).
In chronic toxicity tests, body weight was retarded and leukocyte and T-lymphocyte counts decreased (species not given) (4).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).
The threshold value for odour identification in humans was 1.5 mg m^{-3} (4).
Autoignition temperature 468°C.

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M154 methylamine

CH_3NH_2

CH_5N **Mol. Wt.** 31.06 **CAS Registry No.** 74-89-5

Synonyms aminomethane; methanamine; monomethylamine; carbinamine; mercurialin

EINECS No. 200-820-0 **RTECS No.** PF 6300000

Uses Used in tanning, organic synthesis, dyeing of acetate textiles, paint removers. Intermediate for accelerators, dyestuffs, pharmaceuticals, insecticides, fungicides and surface active agents.

Occurrence *f*Occurs in certain plants such as *Mentha aquatica*.

Physical properties

M. Pt. -93.5°C **B. Pt.** -6.3°C **Flash point** 0°C (closed cup) **Specific gravity** 0.662 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.77 **Volatility** v.p. 2650 mmHg at 25°C ; v.den. 1.07

Solubility Organic solvents: acetone, benzene, ethanol; miscible with diethyl ether

Occupational exposure

DE-MAK 10 ppm (13 mg m^{-3})

FR-VLE 10 ppm (12 mg m^{-3})

JP-OEL 10 ppm (13 mg m^{-3})

SE-LEVL 10 ppm (13 mg m^{-3}) **SE-STEL** 20 ppm (25 mg m^{-3})

UK-LTEL 10 ppm (13 mg m^{-3})

US-TWA 5 ppm (6.4 mg m^{-3}) **US-STEL** 15 ppm (19 mg m^{-3})

UN No. 1061 (anhydrous); 1235 (aqueous solution) **HAZCHEM Code** 2PE **Conveyance classification** flammable gas (anhydrous) **Conveyance classification** flammable liquid, corrosive (aqueous solution)

Supply classification extremely flammable

Supply classification corrosive

Risk phrases Extremely flammable – Harmful by inhalation and if swallowed – Causes burns (R12, R20/22, R34)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep in a cool 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 – Do not empty into drains – 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, S16, S26, S29, S36/37/39, S45)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) creek chub 10-30 mg l^{-1} (1).

Invertebrate toxicity

LD_{Lo} *Daphnia magna* 480 mg l^{-1} (2).

EC_{50} (5 min) *Photobacterium phosphoreum* 34.8 mg l^{-1} Microtox test (3).

Bioaccumulation

The estimated bioconcentration factor of 0.22 using a measured log K_{ow} of –0.57 indicates that environmental accumulation is unlikely (4).

Environmental fate

Nitrification inhibition

50% inhibition of NH_3 oxidation in *Nitrosomonas* at 310 mg l^{-1} (5).

Anaerobic effects

Anaerobic degradation occurred using mixed cultures from marine sediments and pure cultures of *Methanosarcina barkeri* (6,7).

Degradation studies

Pseudomonas sp. MA utilises methylamine as a sole source of carbon and nitrogen (8).
In the OECD screening test and closed bottle test, degradation was 96% and 107%, respectively (9).
BOD_{13} 67.8% reduction of dissolved oxygen concentration (10).

Abiotic removal

A rate constant for aqueous hydroxy radical reaction with methylamine in water is 1.1×10^7 molecules sec^{-1}. At a typical aqueous hydroxyl radical concentration of the methylamine $t_{1/2}$ would be 199 yr, suggesting aqueous hydrolytic degradation is insignificant (9,11,12).
Atmospheric $t_{1/2}$ from hydroxyl radicals is 3-22 hr (13).

Adsorption and retention

Estimated soil adsorption coefficient of 12 indicates that methylamine will not strongly adsorb to organic matter in soil or sediment and is expected to leach readily through most soils (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 100-200 mg kg^{-1} (10% solution) (14).
LC_{50} (2 hr) inhalation mouse 2.4 g m^{-3} (15).
LC_{50} inhalation rat 0.448 ml l^{-1} (16).
LD_{50} subcutaneous mouse 2.5 g kg^{-1} (17).

Sub-acute and sub-chronic data

Inhalation rat (2 wk) 6 hr day^{-1} 5 day wk^{-1} 0, 75, 250 or 750 ppm methylamine. The highest dose caused mortality or severe body-weight losses and clinical pathological changes suggestive of liver damage. Nasal degenerative changes and haematopoietic changes were observed during the recovery period of 14 days. Exposure to 250 ppm produced damage of the respiratory mucosa of the nasal turbinates, whilst mild irritation of the nasal turbinate occurred after 75 ppm (18).

Teratogenicity and reproductive effects

Intraperitoneal pregnant CD-1 mice (1-17 day gestation) 75 and 155 mg kg^{-1} day^{-1}, no obvious maternal or foetal effects. When administered to embryos in culture, caused dose-dependent decreases in size, DNA, RNA and protein content as well as survival, suggesting methylamine acts as an endogenous teratogen under certain conditions (19).

Metabolism and toxicokinetics

After ingesting fish containing methylamine, the major excretory route in humans was in the urine. A four-fold increase in excretion of dimethylamine and >eight-fold increase in excretion of trimethylamine was reported. There is potential for *in vivo* conversion of dimethylamine into nitrosodimethylamine, a carcinogen, although no studies have determined that the ingestion of fish increases the risk of cancer (20).
Inhalation rat, serum enzyme activities were not significantly different in animals exposed to ≤0.3 ml l^{-1}. Methylamine residues were not detected in muscles, but there was a significant increase in the lipid peroxidation values of the lungs indicating a toxic effect (16).

Other effects

Other adverse effects (human)

Workers at a plant processing dimethylamine where <36.7 mg m^{-3} of methylamine was present in ambient air from 0600 to 1800 hr had urinary concentrations of 1.3-2.48 mg l^{-1} methylamine during a 24-hr period (21).

Other comments

The utilisation of methylamine in yeast and bacteria has been reviewed (22).
Reviews on physico-chemical properties, human health effects, epidemiology, workplace experience and experimental toxicology listed (23).
Fire hazard, moderately explosive with nitromethane.

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M155 2-(methylamino)ethanol

$$CH_3NHCH_2CH_2OH$$

C_3H_9NO **Mol. Wt.** 75.11 **CAS Registry No.** 109-83-1

Synonyms (2-hydroxyethyl)methylamine; *N*-methylethanolamine; *N*-methyl-2-hydroxyethylamine; monomethylaminoethanol; *N*-methyl-2-aminoethanol

EINECS No. 203-710-0 **RTECS No.** KL 6650000

Uses Absorbent for removal of carbon dioxide from natural gas. Amidation reagent. Catalyst. Corrosion inhibitor. Organic synthesis.
Occurrence *In vivo* precursor of choline in mammals.

Physical properties

M. Pt. –4.5°C **B. Pt.** 159°C **Flash point** 72°C **Specific gravity** 0.9414 at 20°C with respect to water at 20°C
Volatility v.p. 0.7 mmHg at 20°C ; v.den. 2.9
Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

Supply classification corrosive
Risk phrases Causes burns.(R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – 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)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2300 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 1800 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 1300 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 125 mg kg^{-1} (4).

Teratogenicity and reproductive effects
Oral rat, choline-deficient diet supplemented with 1% for 15 days pre-delivery to 15 days post-partum. All pups died within 36 hr. Levels of choline and acetylcholine were elevated (5).

Irritancy
Dermal rabbit (24 hr) 10 mg caused mild irritation. 250 μg instilled into rabbit eye caused severe irritation (exposure unspecified) (1).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

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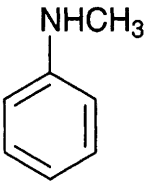
M156 *N*-methylaniline



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 100-61-8

Synonyms anilinomethane; (methylamino)benzene; *N*-methylbenzenamine; methylphenylamine; monomethylaniline; *N*-phenylmethylamine

EINECS No. 202-870-9 **RTECS No.** BY 4550000

Uses Organic synthesis. Solvent. Acid acceptor.

Physical properties

M. Pt. -57°C **B. Pt.** 196°C **Flash point** 79°C (closed cup) **Specific gravity** 0.989 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.66 (1) **Volatility** v.p. 0.3 mmHg at 20°C ; v.den. 3.70
Solubility Water: ~5 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 0.5 ppm (2.2 mg m^{-3})
FR-VME 0.5 ppm (2 mg m^{-3})
UK-LTEL 0.5 ppm (2.2 mg m^{-3})
US-TWA 0.5 ppm (2.2 mg m^{-3})

UN No. 2294 **HAZCHEM Code** 3X **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 – Danger of cumulative effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R33, 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} (30 min) *Photobacterium phosphoreum* 14 ppm, Microtox test (2).

Environmental fate

Nitrification inhibition
Inhibition of ammonia oxidation by *Nitrosomonas* 90% at 100 mg l^{-1}; 83% at 50 mg l^{-1}; 71% at 10 mg l^{-1}; 50% at 1 mg l^{-1} (1).

Degradation studies
Metabolised by *Mycobacterium* to yield *N,N*-dimethylaniline (3).
42% degradation by acclimated petrochemical plant wastewater at an initial concentration of 100 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rabbit, guinea pig 280, 1200 mg kg^{-1}, respectively (5,6).
LD_{Lo} intravenous rabbit, cat 24 mg kg^{-1} (5).
LD_{Lo} subcutaneous guinea pig 1200 mg kg^{-1} (6).

Carcinogenicity and chronic effects

Oral rat, mouse reported to induce cancer of the oesophagus when administered with sodium nitrite (details not given) (7,8).

Metabolism and toxicokinetics

Metabolised to aniline and 4-(methylamino)phenol in rabbits (9,10).

Irritancy

Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (11).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (12).
In vitro primary rat hepatocytes, DNA repair assay negative (13).

Other effects

Other adverse effects (human)

Absorption into the body leads to the formation of methaemoglobin, which in sufficient concentration causes cyanosis (11).

Legislation

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

Other comments

Physical properties, use, toxicity and safety precautions reviewed (15).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).

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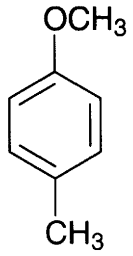
M157 4-methylanisole



$C_8H_{10}O$ **Mol. Wt.** 122.17 **CAS Registry No.** 104-93-8

Synonyms *p*-cresol methyl ether; *p*-methoxytoluene; 1-methoxy-4-methylbenzene; *p*-methylanisole; 4-methylphenol methyl ether; *p*-tolyl methyl ether

EINECS No. 203-253-7 **RTECS No.** BZ 8780000

Uses Organic synthesis. Flavour and fragrance agent.

Occurrence Aroma component of plant oils, cooked meats and dairy products.

Physical properties

M. Pt. -36°C **B. Pt.** 176.5°C **Flash point** 53°C **Specific gravity** 0.9689 at 25°C with respect to water at 25°C

Partition coefficient log P_{ow} 2.81 **Volatility** v.p. 6 mmHg at 25°C ; v.den. 5.79

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

FR-VME 1 ppm (7 mg m^{-3}) **FR-VLE** 5 ppm (35 mg m^{-3})

UN No. 1702 **HAZCHEM Code** 2XE **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 3.5 ppm, Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1920 mg kg^{-1} (2).

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

Metabolism and toxicokinetics

Metabolites identified in rabbits include 3-methyl-4-hydroxyanisole, anisic acid and *p*-cresol (4,5).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (2).

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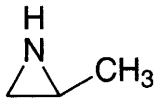
M158 2-methylaziridine



C_3H_7N **Mol. Wt.** 57.10 **CAS Registry No.** 75-55-8

Synonyms 2-methylethylenimine; propylenimine; 1,2-propylenimine; propylene imine

EINECS No. 200-878-7 **RTECS No.** CM 8050000

Uses Solvent. Intermediate in production of polymers, adhesives, coatings, paper finishes and textiles.

Physical properties

M. Pt. –65°C **B. Pt.** 66-67°C **Flash point** –15°C **Specific gravity** 0.812 at 16°C **Volatility** v.p. 112 mmHg at 20°C ; v.den. 2.0

Solubility Water: miscible. Organic solvents: ethanol

Occupational exposure

JP-OEL 2 ppm (4.7 mg m^{-3})

US-TWA 2 ppm (4.7 mg m^{-3})

UN No. 1921 (inhibited) **HAZCHEM Code** 2WE (inhibited) **Conveyance classification** flammable liquid (inhibited)

Supply classification highly flammable, very toxic

Risk phrases May cause cancer – Highly flammable – Very toxic by inhalation, in contact with skin and if swallowed – Risk of serious damage to eyes (R45, R11, R26/27/28, R41)

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

Not expected to bioaccumulate significantly in aquatic organisms based on the complete water solubility (1).

Environmental fate

Abiotic removal

Removed from soil by: chemical hydrolysis, $t_{1/2}$ 17.5 days at neutral pH; ring-opening reactions with naturally occurring chemical species; and volatilisation from dry soil surfaces. Water: chemical hydrolysis, $t_{1/2}$ 17.5 days at neutral pH; volatilisation, $t_{1/2}$ ≥5 days at depth of 1 m flowing at 1 m sec^{-1}; and ring-opening reactions with naturally occurring chemical species (2,3).

Not expected to photolyse or oxidise (4).

If released to the atmosphere predicted to exist as the vapour phase with removal by reaction with photochemically generated hydroxyl radicals, $t_{1/2}$ 1.6 days (1,5,6).

Adsorption and retention

Mobile in soil, but leaching to groundwater limited due to relatively rapid degradation (1,7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 19 mg kg^{-1} (8).

LD_{50} dermal guinea pig 43 mg kg^{-1} (8).

LC_{Lo} (4 hr) inhalation rat 500 ppm (9).

LC_{Lo} (1 hr) inhalation guinea pig 500 ppm (10).

Carcinogenicity and chronic effects

No adequate evidence of carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (11).

Gavage rat 20 mg kg^{-1} twice daily for 28 wk or 10 mg kg^{-1} for 60 wk. 22/52 of the high-dose group had tumours within 60 wk and 37/52 in the low-dose group. Paralysis occurred in both groups after 18 to 30 wk and the high-dose animals suffered significant mortality. Cancer occurred in a range of organs (12).

Irritancy

250 μg instilled in rabbit eye, exposed to the atmosphere, caused severe irritation (8).

Genotoxicity

Drosophila melanogaster uz zeste-white eye system positive (13).

Drosophila melanogaster white-ivory reversion system positive (14).

In vitro C3H/10T1/2 clone 8 mouse embryo cells negative for phenotypic transformation in standard assay, positive upon amplification (15).

Other effects

Any other adverse effects

Produces renal papillary necrosis following acute exposure (16).

Intraperitoneal ♂ Fischer rats 20 μl kg^{-1} caused complete necrosis of renal papilla after 48 hr. There was a rapid increase in urine volume with rapid decrease in urine osmolality. Levels of urinary trimethylamine *N*-oxide, acetic acid, dimethylamine and *N,N*-dimethylglycine were increased. Levels of osmolytes were high in the papilla (17).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Pollutant from plants which manufacture or use as surface coating resins to improve adhesion (2).

Hazards reviewed (19).

Reviews on experimental toxicology, human health effects, epidemiology, workplace experience and physico-chemical properties listed (20).

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17. Gartland, K. P. R. et al *Mol. Pharmacol.* 1989, **35**(2), 242-250.
18. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
19. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(4), 81-84.
20. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M159 methylazoxymethanol

$$CH_3N(O)=NCH_2OH$$

$C_2H_6N_2O_2$ **Mol. Wt.** 90.08 **CAS Registry No.** 590-96-5

Synonyms (methyl-*ONN*-azoxy)methanol; MAM

RTECS No. PC 2625000

Occurrence As a glucoside (cycasin) in seeds of Cycadaceae from Guam.

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (1).

Intraperitoneal (237-244 day) ♀ Fisher rats, 2 mg × 10 injections, 4 mg × 4-12 injections or 6 mg × 2 injections to give a total dose of 12-48 mg (a total of 6 rats were used, 1 for each injection regime). 4/6 rats developed tumours of the intestinal tract, with the duodenum being the primary site of mucinous adenocarcinomas in 3 rats. The rats without intestinal tumours developed neoplasms at other sites such as the liver and kidneys (2).

Teratogenicity and reproductive effects

Pregnant rats treated on gestation day-15 with 25 mg kg^{-1} gave birth to hyperactive offspring that showed clear impairments in acquisition of instrumental learning in mazes. Elevated levels of noradrenaline and dopamine were observed in several regions of the brain (3).

Crj:CD(SD) pregnant rats treated with 40 mg kg^{-1} on gestational days 12, 13, 14 or 15 had microencephalic offspring. Neurobehavioural ontogeny was retarded (4).

Single dose 25 mg kg^{-1} injected into pregnant rats did not affect gestational and litter parameters. Degrees of altered physical and behavioural development were dependent on the time of administration (5).

The histochemical reactivity of the enzyme $NADH_2$-tetrazolium reductase at the level of frontal and occipital cortex, neostriatum and hippocampus was reduced in the offspring of mice treated on gestational day-15. Cholinacetyltransferase immunoreactivity within nerve cell bodies of the pontine tegmentum was also decreased, but acetylcholinesterase reactivity was increased in most brain areas (6).

Metabolism and toxicokinetics

Metabolised by rat liver cytochrome P_{450} to methanol and formic acid (7).

Metabolised by F344 rat liver microsomes, in presence of an NADPH-generating system, to methanol and formic acid. Spontaneous decomposition yields methanol and formaldehyde. Different enzymes are responsible for activation of the carcinogen in the liver and the colon (8).

Genotoxicity

Salmonella typhimurium C50, D130, G46 reversion to histidine independence of histidine-requiring mutants without metabolic activation positive (9).

Drosophila melanogaster sex-linked recessive lethal mutations positive (10).

References

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8. Fiala, E. S. et al *J. Cancer Res. Clin. Oncol.* 1987, **113**(2), 145-150.
9. Smith, D. W. E. *Science (Washington, D. C. 1883-)* 1966, **152**, 1273-1274.
10. Teas, H. J. et al *Proc. Soc. Exp. Biol. Med.* 1967, **125**(3), 988-990

M160 methylazoxymethanol acetate

$$CH_3N(O)=NCH_2OC(O)CH_3$$

$C_4H_8N_2O_3$ **Mol. Wt.** 132.12 **CAS Registry No.** 592-62-1

Synonyms (methyl-*ONN*-azoxy)methanol, acetate (ester); methylazoxymethyl acetate; MAM acetate

EINECS No. 209-765-7 **RTECS No.** PC 2800000

Physical properties

B. Pt. 191°C **Flash point** 98°C **Specific gravity** 1.172

Occupational exposure

Supply classification toxic

Risk phrases May cause cancer – May cause harm to the unborn child (R45, R61)

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

Medaka 0.3 ppm for 3 days or 0.1 ppm for 2 wk caused liver cell adenomas and carcinomas. Morphological alterations appeared from the second wk in the first group and at the fourth or fifth wk in the second (1).

Guppy exposed to ≤100 mg l^{-1} for 2 hr developed pancreatic neoplasms in ~9% of animals. Neoplasms included adenomas, acinar cell carcinomas and adenocarcinomas (2).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral mouse 35 mg kg^{-1} (3,4).

LD_{50} intraperitoneal rat, mouse 90-105 mg kg^{-1} (5).

LD_{50} intravenous mouse 10 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).

Oral rat 100 mg kg^{-1} of diet for 2 wk, cumulative dose 13.4-13.7 mg $animal^{-1}$, produced 3 carcinomas of the colon, 31 kidney tumours, 4 liver-cell adenomas, 8 bile-duct adenomas and 1 hepatoma in the 26 tested animals (8).

Intravenous CD1 ♂ mice given single dose 1-25 mg kg^{-1} body weight showed no tumours within 14 months in 19 individuals (9).
Intravenous rat 35 mg kg^{-1} body weight single dose produced intestinal, liver and kidney tumours after 6-7 months (4,9,10).
Offspring of prenatally intraperitoneally or intravenously treated Fischer rats 20 mg kg^{-1} body weight developed a range of tumours within 356-637 days of birth (11).

Teratogenicity and reproductive effects
Intraperitoneal rat 30 mg kg^{-1} on gestation day-13 impaired motor behaviour of offspring, most severe in ♂ (12).
Intraperitoneal rat 1-25 mg kg^{-1} on gestation day-15 caused dose-dependent reductions in cerebral hemisphere basal ganglia, diencephalon and mesencephalon in the offspring. The larger doses elevated levels of noradrenaline, dopamine and 5-HT in parts of the brain of the young (13).
When 20 mg kg^{-1} was administered to rats on gestation days 14 and 16 massive reductions in brain weight of the offspring occurred when adult. The earlier application offspring included a small number of dwarves that had very small pituitary glands and an immature pattern of somatotrope distribution. This group generally had a significant, selective reduction in growth hormone releasing factor neurones, but an increased number of periventricular somatotropin release inhibiting factor neurones. Day-16 treated offspring showed accelerated post-natal growth which was significant in ♂. These animals had very large pituitary glands with some hypertrophy of somatotropes (14).
Young rats exposed prenatally showed a reduced ultrasonic vocalisation and in ♀ reduced locomotor activity (15).
Intraperitoneal rat 30 mg kg^{-1} on day-13 of gestation led to delays in cliff avoidance reflex and negative geotaxis, delays in achieving control of body in swimming and a prolonged time to complete a T-maze (16).

Genotoxicity

Salmonella typhimurium his G46 without metabolic activation positive. Mutagenicity was higher at lower pH. Lignin, pectin and hemicellulose inhibited mutagenicity, cellulose did not effectively inhibit mutagenicity (17).
Escherichia coli HV with metabolic activation positive (18).
In vivo $B6D2F_1$ mouse bone marrow, alveolar macrophages, liver, kidney sister chromatid exchange negative (19).

Other effects

Any other adverse effects
Reduced DNA synthesis in rat liver and kidney (4).
Inhibited nucleolar RNA synthesis in the rat liver (9).
Single strand breaks in the DNA from rat liver remained unrepaired after 14 days (20).

Other comments

The pattern of cell death in prentatlly treated rats described (21).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (22).

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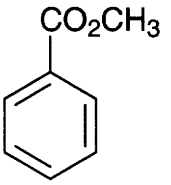
M161 methyl benzoate



$C_8H_8O_2$ **Mol. Wt.** 136.15 **CAS Registry No.** 93-58-3

Synonyms benzoic acid methyl ester; niobe oil; Oil of Niobe; FEMA 2683

EINECS No. 202-259-7 **RTECS No.** DH 3850000

Uses Perfume manufacture. Flavourings. Pesticides.

Occurrence In oils of cloves, ylang ylang and tuberose.

Physical properties

M. Pt. –12.5°C **B. Pt.** 199.6°C **Flash point** 82.8°C (closed cup) **Specific gravity** 1.0888 at 20°C with respect to water at 4°C

Solubility Organic solvents: miscible with diethyl ether, ethanol, methanol

Occupational exposure

UN No. 2938 **HAZCHEM Code** 3Z **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

Rainbow trout exposed to 5 mg l^{-1} experienced loss of equilibrium in 14-16 hr (1).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 4.61 mg l^{-1} Microtox test (2).

Environmental fate

Degradation studies

Non-biodegradable (qualified) (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1350, 3330 mg kg^{-1}, respectively (4).

Irritancy

Dermal (24 hr) rabbit 10 mg caused mild irritation (5).

Other comments

Methyl benzoate was slow to penetrate the skin of rats (6).
Reviews on human health effects and experimental toxicology listed (7).

References

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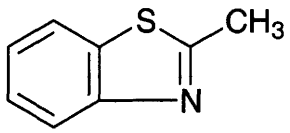
M162 2-methylbenzothiazole



C_8H_7NS **Mol. Wt.** 149.22 **CAS Registry No.** 120-75-2

Synonyms USAF EK-1853

EINECS No. 204-423-3 **RTECS No.** DL 5600000

Physical properties

M. Pt. 12-14°C **B. Pt.** 238°C **Flash point** 102°C **Specific gravity** 1.173

Mammalian & avian toxicity

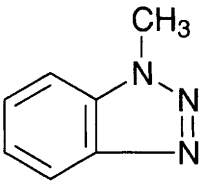
Acute data

LD_{50} intravenous mouse 105 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 300 mg kg^{-1} (2).

References

1. *J. Pharmacol. Exp. Ther.* 1952, **105**, 486.
2. *NTIS Report* AD277-689, Natl. Tech. Inf. Serv., Springfield, VA, USA

M163 1-methylbenzotriazole



$C_7H_7N_3$ **Mol. Wt.** 133.15 **CAS Registry No.** 13351-73-0

Synonyms 1-methyl-1*H*-benzotriazole

EINECS No. 236-401-4 **RTECS No.** DM 1330000

Uses Corrosion inhibitor.

Physical properties

M. Pt. 64-65°C **B. Pt.** 270-271°C

Solubility Organic solvents: benzene, petroleum ether

Mammalian & avian toxicity

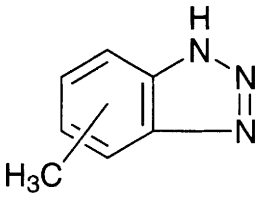
Acute data

LD_{50} intravenous mouse 375 mg kg^{-1} (1).

References

1. *J. Pharmacol. Exp. Ther.* 1952, **105**, 486

M164 4(*or* 5)-methylbenzotriazole



$C_7H_7N_3$ **Mol. Wt.** 133.15 **CAS Registry No.** 29385-43-1

Synonyms methyl-1*H*-benzotriazole; 4(*or* 5)-methyl-1*H*-benzotriazole; methylbenzotriazole; Cobratec TT100; tolyltriazole; TTZ

EINECS No. 249-596-6 **RTECS No.** DM 1300000

Uses Corrosion inhibitor. Antioxidant. In photographic developers.

Physical properties

M. Pt. 83°C **B. Pt.** 160°C at 2 mmHg **Flash point** 182.2°C **Specific gravity** 1.13 at 100°C with respect to water at 25°C **Volatility** v.p. 3.0×10^{-2} mmHg at 50°C ; v.den. 4.6

Solubility Water: <1 g l^{-1} at 18°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 680 mg kg^{-1} (1).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 without metabolic activation negative, with metabolic activation weakly positive (2).

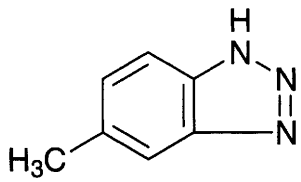
Other comments

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

References

1. *Huntingdon Research Centre Report* 1972.
2. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11**(Suppl. 12), 1-158.
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

M165 5-methylbenzotriazole



$C_7H_7N_3$ **Mol. Wt.** 133.15 **CAS Registry No.** 136-85-6

Synonyms 5-methyl-1*H*-benzotriazole; 5-methyl-1,2,3-benzotriazole

EINECS No. 205-265-8 **RTECS No.** DM 1400000

Uses Corrosion inhibitor. Preparation of antifogging photographic reagents.

Physical properties

M. Pt. 80-82°C **B. Pt.** 210-212°C at 12 mmHg

Solubility Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1600 mg kg^{-1} (1).

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (2).

References

1. *Kodak Company Report* 21 May, 1971.
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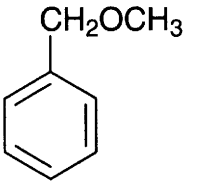
M166 methyl benzyl ether



$C_8H_{10}O$ **Mol. Wt.** 122.17 **CAS Registry No.** 538-86-3

Synonyms methoxymethylbenzene; benzyl methyl ether; α-methoxytoluene

EINECS No. 208-705-7

Occurrence Aroma and taste components in plants.

Physical properties

B. Pt. 174°C **Specific gravity** 0.987 at 20°C **Partition coefficient** log P_{ow} 1.35

Solubility Organic solvents: diethyl ether, ethanol, methanol

Mammalian & avian toxicity

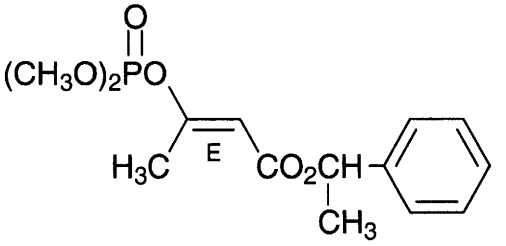
Acute data

LD_{50} oral rat 9800 mg kg^{-1} (1).

References

1. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470

M167 α-methylbenzyl 3-hydroxycrotonate, dimethyl phosphate



$C_{14}H_{19}O_6P$ **Mol. Wt.** 314.28 **CAS Registry No.** 7700-17-6

Synonyms 2-butenoic acid, 3-[(dimethoxyphosphinyl)oxy]-, 1-phenylethyl ester, (*E*)-; crotonic acid, 3-hydroxy-, α-methylbenzyl ester, dimethyl phosphate, (*E*)-; Ciodrin; Crotoxyphos; Cyodrin; Volfazol

EINECS No. 231-720-5 **RTECS No.** GQ 5075000

Uses Livestock insecticide (superseded).

Physical properties

B. Pt. 135°C at 0.03 mmHg **Flash point** 79.4°C **Specific gravity** 1.19 at 25°C **Partition coefficient** log P_{ow} 0.82 (1) **Volatility** v.p. 1.4×10^{-5} mmHg at 20°C

Solubility Water: 1200 mg l^{-1}. Organic solvents: acetone, chloroform, highly chlorinated hydrocarbons, ethanol, kerosene

Occupational exposure

Supply classification toxic
Risk phrases Toxic in contact with skin and if swallowed (R24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) largemouth bass, channel catfish 1100-2600 μg l^{-1} (2).
LC_{50} (96 hr) bluegill sunfish 152 μg l^{-1} (2).
LC_{50} (96 hr) fathead minnow 12 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (24 hr) *Gammarus lacustris* 49 μg l^{-1} at 15°C (2).
LC_{50} (96 hr) *Gammarus fasciatus* 11 μg l^{-1} (3).

Environmental fate

Degradation studies
$t_{1/2}$ ranged from 2 hr in silty clay loam soil to 71 hr in loamy sand. In aqueous systems at pH 9, 6 and 2, $t_{1/2}$ were respectively 180, 410 and 540 hr (4).
An enzyme isolated from clay loam hydrolysed the compound to dimethyl phosphate and α-methylbenzyl 3-hydroxycrotonate in 16 hr at 37°C (5).

Abiotic removal
Slowly hydrolysed by water. 50% decomposition occurs in 35 hr at pH 9 and 87 hr at pH 1 at 38°C (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken 111 mg kg^{-1} (7).
LD_{50} oral redwing blackbird 56.2 mg kg^{-1} (8).
LD_{50} oral rat, mouse 38-40 mg kg^{-1} (9).
LD_{50} oral ♂, ♀ rat 74, 110 mg kg^{-1}, respectively (10).
LD_{50} dermal rabbit 385 mg kg^{-1} (11).
LD_{50} dermal ♀, ♂ rat 202, 375 mg kg^{-1}, respectively (10).
LD_{50} intravenous mouse 4.5 mg kg^{-1} (12).
LD_{50} subcutaneous rat 47 mg kg^{-1} (13).

Sub-acute and sub-chronic data
Oral rat 300-900 mg kg^{-1} in diet for 90 days caused no effects to growth and no pathological changes. Blood cholinesterase activity was inhibited at oral doses of 20 mg kg^{-1} in feed (6).

Metabolism and toxicokinetics
Radiolabel studies showed in lactating ewes and goats that hydrolytic fission to the corresponding monomethyl phosphate and dimethyl phosphate occurred. Excretion in urine was the major eliminatory route. The very small amount of unmodified compound found in milk consisted solely of the β-isomer (14).
61-90% of radiolabel in the urine of orally administered ewe was associated with dimethyl phosphoric acid. There was rapid elimination with moderate absorption (4).
3-(Dimethoxyphosphinyloxy)crotonic acid was an important urinary metabolite appearing as 11% of metabolites after 3 hr and falling to 3% after 6 hr (15).

Genotoxicity

Saccharomyces cerevisiae with and without metabolic activation mitotic recombination negative, but toxic (16).
In vivo mouse bone marrow dose- and administration route (intragastrically and inhalation)-dependent increase in chromosomal aberrations (17).

Legislation

Regulated under the US Clean Water Act and Federal Insecticide, Fungicide and Rodenticide Act (18).
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).

References

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2. Johnson, W. W. et al *Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates* 1980, Fish and Wildlife Service, USDI, Washington, DC, USA.
3. Sanders, H. O. *The toxicities of some insecticides to four species of Malocostracan crustacea* 1972, Fish Pesticide Research Laboratory, Bureau of Sport Fisheries and Wildlife, Columbia, MO, USA.
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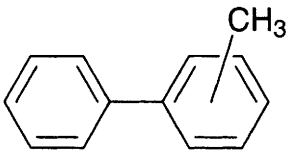
18. *Dangerous Prop. Ind. Mater. Rep.* 1993, **13**(1), Van Nostrand Reinhold, New York, USA.
19. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
20. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M168 methylbiphenyl



$C_{13}H_{12}$ **Mol. Wt.** 168.24 **CAS Registry No.** 28652-72-4

Synonyms methyl-1,1'-biphenyl; phenyltoluene

EINECS No. 249-124-9

Uses Solvent. Heat transfer fluid.

Occurrence In the essential oil of rue (*Ruta graveolens*). In fossil fuels. In diesel fumes. Residues have been isolated from sediments and natural waters and in fish tissues (1-6).

Physical properties

M. Pt. –2 to 50°C **B. Pt.** 255-272°C **Volatility** v.p. 0.3 mmHg at 20°C
Solubility Organic solvents: diethyl ether, dimethyl sulfoxide, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 1.5 mg l^{-1}, static bioassay (Sure-Sol 170) (7).

Bioaccumulation
Bioconcentration factor in *Rangia cuneata* and *Crassostrea virginica* 300-1700 (3).

Environmental fate

Degradation studies
Degraded by the marine bacteria *Alcaligenes* and *Acinetobacter* species to yield α-hydroxymuconic semialdehydes, which were further degraded (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (9).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

Methylbiphenyl is the major component of the solvent Sure-Sol. Other components include biphenyl and other aromatic hydrocarbons (11).

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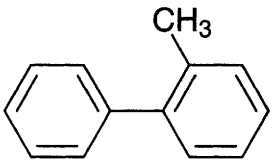
M169 2-methylbiphenyl



$C_{13}H_{12}$ **Mol. Wt.** 168.24 **CAS Registry No.** 643-58-3

Synonyms 2-methyl-1,1'-biphenyl; 2-phenyltoluene

EINECS No. 211-400-1

Physical properties

B. Pt. 255°C **Flash point** 137°C (open cup) (1) **Specific gravity** 1.011

Environmental fate

Degradation studies

Surfactants at low concentrations stimulate biodegradation of sorbed hydrocarbons in samples of aquifer sand and oil (2).

Other comments

Present in airborne coal tar emissions, coal tar and wood preservative sludge (3).
Biphenyls are formed by the anaerobic reduction of polychlorinated biphenyls (4).
Autoignition temperature: 495 and 502°C reported.

References

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2. Aronstein, B. N. et al *Environ. Toxicol. Chem.* 1992, **11**, 1227-1233.
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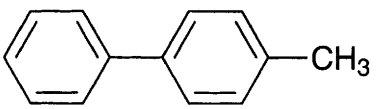
M170 4-methylbiphenyl



$C_{13}H_{12}$ **Mol. Wt.** 168.24 **CAS Registry No.** 644-08-6

Synonyms 4-methyl-1,1'-biphenyl; 4-methyldiphenyl; 4-phenyltoluene

EINECS No. 211-409-0 **RTECS No.** DV 5460000

Physical properties

M. Pt. 44-47°C **B. Pt.** 267-268°C **Flash point** >110°C **Partition coefficient** log P_{ow} 4.63

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 2.22 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} rat 2570 mg kg^{-1} (2).

Other comments

Pollutant of groundwater (3).

Present in airborne coal tar emissions, coal tar and wood preservative sludge (4).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. *Food Cosmet. Toxicol.* 1975, **13**, 487.
3. Tu, J. et al *Huanjing Huaxue* 1986, **5**(5), 60-74 (Ch.) (*Chem. Abstr.* **106**, 22946x).
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M171 methyl bromoacetate

$$BrCH_2CO_2CH_3$$

$C_3H_5BrO_2$ **Mol. Wt.** 152.98 **CAS Registry No.** 96-32-2

Synonyms bromoacetic acid, methyl ester

EINECS No. 202-499-2 **RTECS No.** AF 6300000

Uses Alkylating agent. Chemical intermediate.

Physical properties

B. Pt. 130-133°C at 750 mmHg **Flash point** 62°C **Specific gravity** 1.6350 at 20°C with respect to water at 4°C

Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2643 **HAZCHEM Code** 2W **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LD_{Lo} intravenous mouse 16 mg kg^{-1} (1).

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 (2).

References

1. *Summary Tables Biological Tests* 1954, **6**, 138.
2. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2304, Sigma-Aldrich, Milwaukee, WI, USA

M172 2-methylbutane

$$CH_3CH(CH_3)CH_2CH_3$$

C_5H_{12} **Mol. Wt.** 72.15 **CAS Registry No.** 78-78-4

Synonyms isopentane; ethyldimethylmethane; isoamyl hydride

EINECS No. 201-142-8 **RTECS No.** EK 4430000

Physical properties

M. Pt. -160.5°C **B. Pt.** 27.8°C **Flash point** <-50°C (closed cup) **Specific gravity** 0.62 at 19°C
Volatility v.p. 595 mmHg at 21.1°C ; v.den. 2.48
Solubility Water: 48 mg l^{-1} at 20°C

Occupational exposure

DE-MAK 1000 ppm (3000 mg m^{-3})
US-TWA 600 ppm

UN No. 1265 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not empty into drains – Take precautionary measures against static discharges (S2, S9, S16, S29, S33)

Environmental fate

Degradation studies
Zero biodegradation of an initial concentration of 3.29 µl l^{-1} after 192 hr at 13°C incubation with natural flora in groundwater in presence of other components of high octane petrol (1).

Other comments

Reviews on human health effects, environmental toxicity and physico-chemical properties listed (2).

References

1. Jamison, V. W. et al *Proc. Third Int. Biodeg. Symp.* 1976, Applied Science Publishers, New York, USA.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M173 2-methyl-2-butanol

$$CH_3CH_2(OH)C(CH_3)_2$$

$C_5H_{12}O$ **Mol. Wt.** 88.15 **CAS Registry No.** 75-85-4

Synonyms 2-methylbutan-2-ol; *tert*-pentyl alcohol; *tert*-amyl alcohol; amylene hydrate; dimethylethylcarbinol; ethyldimethylcarbinol; *tert*-pentanol

EINECS No. 200-908-9 **RTECS No.** SC 0175000

Uses Hypnotic.

Physical properties

M. Pt. –12°C **B. Pt.** 102.5°C at 765 mmHg **Flash point** 19°C (closed cup), 21°C (open cup)
Specific gravity 0.8084 at 20°C **Partition coefficient** log P_{ow} 0.89 **Volatility** v.p. 10 mmHg at 17.2°C ; v.den. 3.03
Solubility Water: 1 in 8 parts. Organic solvents: benzene, chloroform, diethyl ether; miscible with ethanol, glycerol

Occupational exposure

Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful by inhalation (R11, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Avoid contact with skin and eyes (S2, S9, S16, S24/25)

Ecotoxicity

Fish toxicity
NOEC (24 hr) Creek chub 1300 mg l^{-1} (1).
LC_{100} (24 hr) Creek chub 2000 mg l^{-1} (1).

Invertebrate toxicity
LOEC reproduction *Microcystis aeruginosa* 105 mg l^{-1} (2).
Cell multiplication inhibition test *Pseudomonas putida* 410 mg l^{-1}, *Scenedesmus quadricauda* 1250 mg l^{-1}, and *Entosiphon sulcatum* 680 mg l^{-1} (3).
Cell multiplication inhibition test *Uronema parduczi* Chatton-Lwoff 859 mg l^{-1} (4).

Environmental fate

Degradation studies
Using bench-scale activated sludge, fill and draw operations after 6, 12 and 24 hr, respectively, 1.3, 1.7 and 3.7% ThOD (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1-2 g kg^{-1} (6,7).
LD_{50} subcutaneous mouse 2100 mg kg^{-1} (8).
LD_{Lo} subcutaneous rat 1400 mg kg^{-1} (9).
LD_{Lo} intraperitoneal rat 1530 mg kg^{-1} (10).
LD_{Lo} rectal rat 1400 mg kg^{-1} (9).

Other comments

Hazards and properties reviewed (11).
Reviews on experimental toxicology, human health effects and physico-chemical properties listed (12).
Included in QSAR on toxicity and narcosis to the tadpole (13).
Autoignition temperature 435-437°C.

References

1. Gillette, L. A. et al *Sewage Ind. Wastes* 1952, **24**(11), 1397-1401.
2. Bringmann, G. et al *GWF: Gas, Wasserfach: Wasser/Abwasser* 1976, **117**(9), 410-413.
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4. Bringmann, G. et al *Z. Wasser/Abwasser Forsch.* 1980, (1), 26-31.
5. Gerhold, R. M. et al *J. Water Pollut. Control. Fed.* 1966, **38**(4), 562.
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M174 3-methyl-1-butanol

$$(CH_3)_2CHCH_2CH_2OH$$

$C_5H_{12}O$ **Mol. Wt.** 88.15 **CAS Registry No.** 123-51-3

Synonyms 3-methylbutan-1-ol; isopentyl alcohol; fermentation amyl alcohol; isoamyl alcohol; isoamylol; isobutylcarbinol; isopentanol

EINECS No. 204-633-5 **RTECS No.** EL 5425000

Uses Solvent for fats, alkaloids and resins. In microscopy. For determining fat in milk. In manufacture of isoamyl compounds, isovaleric acid, artificial silk, lacquers, mercury fulminate and pyroxylin.

Physical properties

M. Pt. -117.2°C **B. Pt.** 131-132°C **Flash point** 43°C (closed cup), 55°C (open cup) **Specific gravity** 0.813 at 15°C with respect to water at 4°C **Volatility** v.p. 2.3 mmHg at 20°C, 4.8 mmHg at 30°C ; v.den. 3.04
Solubility Water: 20 g l^{-1} at 14°C. Organic solvents: miscible with benzene, chloroform, diethyl ether, ethanol, glacial acetic acid and petroleum ether

Occupational exposure

DE-MAK 100 ppm (370 mg m^{-3})
FR-VME 100 ppm (360 mg m^{-3})
JP-OEL 100 ppm (360 mg m^{-3})
UK-LTEL 100 ppm (366 mg m^{-3}) **UK-STEL** 125 ppm (458 mg m^{-3})
US-TWA 100 ppm (361 mg m^{-3}) **US-STEL** 125 ppm (452 mg m^{-3})

Ecotoxicity

Invertebrate toxicity

Ratio of chemical water solubility to concentration causing immobilisation in 50% of marine barnacle larvae 0.038 (1).

Environmental fate

Degradation studies

BOD_5 determined using acclimated mixed microbial cultures 4.46 mg l^{-1} (2).

Waste water treatment; bench-scale activated sludge, fill and draw operations, 20°C, 1-5 days observed, feed 333 mg l^{-1}, 30 days acclimation, 79% removed (3).

BOD_5 0.162 mg l^{-1} O_2 with standard dilution technique with sewage as seed material (4,5).

BOD_5 59% ThOD; COD 77% ThOD (0.05N $K_2Cr_2O_7$) (6).

ThOD: 2.740 mg $l^{-1}O_2$ (5).

First-order biodegradation rate constants (per day) and $t_{1/2}$: ground water, 0.045 and 15 days; river water, 0.064 and 11 days; and fresh water-lake harbour water, 0.113 and 6 days (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1300 mg kg^{-1} (8).

LD_{Lo} oral rabbit 4250 mg kg^{-1} (9).

LD_{50} dermal rabbit 3212 mg kg^{-1} (10).

LD_{Lo} intraperitoneal mouse, rat 233, 813 mg kg^{-1}, respectively (11,12).

LD_{Lo} subcutaneous mouse 7480 mg kg^{-1} (11).

LD_{50} intravenous mouse 234 mg kg^{-1} (12).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate to severe erythema and moderate oedema and 20 mg instilled into rabbit eye (24 hr) caused moderate irritation (13).

Acute patch testing, 12/12 volunteers produced erythema. The reaction is provoked by the corresponding aldehyde (14).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

Other comments

Included in QSAR for upper respiratory tract irritation in mice (16).

Experimental toxicology and human health effects reviewed (17).

Reviews on experimental toxicology, human health effects, epidemiology and workplace experience listed (18).

Autoignition temperature 340-350°C.

References

1. Vaishnav, D. D. et al *Arch. Environ. Contam. Toxicol.* 1990, **19**, 624-628.
2. Baben, L. et al *J. Ind. Microbiol.* 1987, **2**, 107-115.
3. Ludzack, F. J. et al *J. Water Pollut. Control Fed.* 1960, **32**, 1173.
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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

M175 3-methyl-1-butene

$$(CH_3)_2CHCH=CH_2$$

C_5H_{10} **Mol. Wt.** 70.13 **CAS Registry No.** 563-45-1

Synonyms α-isoamylene; isopentene; isopropylethylene; 3-methylbut-1-ene

EINECS No. 209-249-1

Uses Organic synthesis. Manufacture of polymers.

Occurrence In fossil fuels. Detected in natural and drinking waters (1).

Physical properties

M. Pt. −168°C **B. Pt.** 20°C **Flash point** −62°C **Specific gravity** 0.6272 at 20°C with respect to water at 4°C

Volatility v.den. 2.4

Solubility Water: 130 mg l^{-1} at 20°C. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2561 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Environmental fate

Degradation studies

Degradation by activated sludge, 0.8% of ThOD after 12 hr (initial concentration not specified) (2).

Mammalian & avian toxicity

Irritancy

Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (3).

Other effects

Other adverse effects (human)

Symptoms of exposure include burning sensation, coughing, wheezing, laryngitis, shortness of breath, headache, nausea and vomiting (3).

Other comments

Autoignition temperature 365°C.

References

1. Smith, R. L. *Trace Subst. Environ. Health* 1989, **22**, 215-232.
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M176 3-methyl-2-buten-1-ol

$$(CH_3)_2C{=}CHCH_2OH$$

$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 556-82-1

Synonyms dimethylallyl alcohol; 3,3-dimethylallyl alcohol; 3-methylbut-2-en-1-ol; Prenol; prenyl alcohol

EINECS No. 209-141-4 **RTECS No.** EM 9472500

Uses Organic synthesis.

Occurrence In plant oils.

Physical properties

B. Pt. 140°C **Flash point** 43°C **Specific gravity** 0.848 at 20°C **Volatility** v.p. 1.4 mmHg at 20°C

Solubility Organic solvents: vegetable oils

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 810 mg kg^{-1} (1).

LD_{50} dermal rabbit 3900 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (1).

Irritating to the eyes, upper respiratory tract and mucous membranes (species unspecified) (2).

References

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2. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2311, Sigma-Aldrich, Milwaukee, WI, USA

M177 3-methyl-3-buten-1-ol

$$CH_2{=}C(CH_3)CH_2CH_2OH$$

$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 763-32-6

Synonyms isobutenylcarbinol; 3-isopentenyl alcohol; isopropenylethyl alcohol; methallylcarbinol

EINECS No. 212-110-8

Physical properties

B. Pt. 129.8°C at 760 mmHg **Flash point** 36°C **Specific gravity** 0.853 at 20°C

Occupational exposure

UN No. 1987

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (1).

Other comments

It is an attractant to houseflies and European engraver beetles (2,3).

References

1. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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M178 2-methyl-3-buten-2-ol

$$(CH_3)_2C(OH)CH{=}CH_2$$

$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 115-18-4

Synonyms α,α-dimethylallyl alcohol; dimethylvinylcarbinol; dimethylvinylmethanol

EINECS No. 204-068-4 **RTECS No.** EM 9472000

Physical properties

B. Pt. 98-99°C **Flash point** 13°C **Specific gravity** 0.824 at 20°C **Volatility** v.p. 517 mmHg at 25°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 810 mg kg^{-1} (1).

LD_{50} dermal rabbit 3900 mg kg^{-1} (1).

Irritancy

Dermal rabbit 500 mg caused moderate irritation (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

It is an attractant to engraver beetle, bark beetle and *Pityogenes chalcographus* (3-5).

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M179 3-methyl-3-buten-2-one

$$CH_3C(O)C(CH_3)=CH_2$$

C_5H_8O **Mol. Wt.** 84.12 **CAS Registry No.** 814-78-8

Synonyms Isopropenyl methyl ketone; methyl isopropenyl ketone

EINECS No. 212-405-1 **RTECS No.** EN 0175000

Physical properties

B. Pt. 98°C **Flash point** 21°C **Volatility** v.den. 2.9

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 180 mg kg^{-1} (1).
LD_{Lo} oral guinea pig 60 mg kg^{-1} (2).
LC_{Lo} (4 hr) inhalation rat 125 ppm (1).
LD_{50} dermal rabbit 230 mg kg^{-1} (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119.
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M180 *N*-methylbutylamine

$$CH_3CH_2CH_2CH_2NHCH_3$$

$C_5H_{13}N$ **Mol. Wt.** 87.16 **CAS Registry No.** 110-68-9

Synonyms butylamine, *N*-methyl-; butylmethylamine; methylbutylamine; 1-butanamine, *N*-methyl-; *N*-methylbutamine

EINECS No. 203-791-2 **RTECS No.** EO 5250000

Uses Used in the preparation of pharmaceuticals. Catalyst. Used in co-surfactants. Chemical intermediate.

Physical properties

M. Pt. –75°C **B. Pt.** 90.5-91.5°C **Flash point** 1°C **Specific gravity** 0.736 **Partition coefficient** log P_{ow} 1.33 **Volatility** v.den. 3.0

Occupational exposure

UN No. 2945 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 420 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (1).
LD_{50} dermal rabbit 1260 mg kg^{-1} (2).
LD_{50} intravenous mouse 120 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 470 mg kg^{-1} (3).

Irritancy

74 mg instilled into rabbit eye caused severe irritation (unspecified duration) (1).

Other effects

Other adverse effects (human)

Very damaging to the tissue of the upper respiratory tract and mucous membranes. Inhalation can cause spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema. These effects may be severe enough to cause death (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Processes) Statutory Instrument No. 472, 1991 (5).

References

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M181 methyl *tert*-butyl ether

$CH_3OC(CH_3)_3$

$C_5H_{12}O$ **Mol. Wt.** 88.15 **CAS Registry No.** 1634-04-4

Synonyms *tert*-butyl methyl ether; 2-methoxy-2-methylpropane; methyl 1,1-dimethylethyl ether; MTBE; 2-oxa-3,3-dimethylbutane

EINECS No. 216-653-1 **RTECS No.** KN 5250000

Uses Fuel additive, especially as an alternative for lead in gasoline. Catalyst. Solvent for cholesterol gallstones. Chromatographic eluent. Cholelitholytic agent.

Physical properties

M. Pt. –109°C **B. Pt.** 55.2°C **Flash point** –10°C **Specific gravity** 0.7404 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.94 **Volatility** v.p. 249 mmHg at 25°C
Solubility Water: 51 g l^{-1} at 25°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

SE-LEVL 50 ppm (180 mg m^{-3}) **SE-STEL** 75 ppm (250 mg m^{-3})
UK-LTEL 25 ppm (92 mg m^{-3}) **UK-STEL** 75 ppm (275 mg m^{-3})
US-TWA 40 ppm (144 mg m^{-3})

UN No. 2398 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 110 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 11.4 ppm, Microtox test (2).
The growth of three species of microorganisms was differentially sensitive to methyl *tert*-butyl ether injected into sealed vessels containing defined liquid growth media. *Navicula pelliculosa* and *Synechococcus leopoliensis* were negatively affected at a nominal 2400 mg l^{-1} methyl *tert*-butyl ether. *Selanastrum capricornutum* was negatively affected at a nominal 4800 mg l^{-1} and positively affected at a nominal 600 mg l^{-1} (3).

Toxicity to other species
LC_{50} *Rana temporaria* tadpole 2500 mg l^{-1} (exposure not specified). Exposure to 100 mg l^{-1} caused a marked increase in body weight and accelerated tadpole development, metamorphosis occurring 2 days earlier than in controls (4).

Bioaccumulation
Bioconcentration factor for Japanese carp 1-5 (5).

Environmental fate

Degradation studies
Degradation by activated sludge 1% of ThOD in 21 days (6).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 5-6 days (7,8).
Volatilisation $t_{1/2}$ 4.1 hr from model river water at 25°C, and 2.0 days from model pond water (9,10).

Adsorption and retention
Estimated K_{oc} of 11.2 indicates that adsorption to soil and sediments would not be significant (9).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 4000 mg kg^{-1} (10,11).
LC_{50} (4 hr) inhalation rat 24,000 ppm (11).
LC_{50} (15 min) inhalation mouse 140 mg m^{-3} (12).
LD_{50} dermal rat >7.5 mg g^{-1} (13).
LD_{50} intraperitoneal mouse 1500 mg kg^{-1} (10).
LD_{50} intravenous mouse 230 mg kg^{-1} (10).
Rats exposed once for 6 hr to 8000 ppm, and to a lesser extent, to 4000 ppm vapour showed signs of acute reversible CNS depression. The no-observed-adverse-effect level for these effects was 800 ppm (14).

Sub-acute and sub-chronic data

No persistent or cumulative neurotoxic effects were observed in rats following exposure to methyl *tert*-butyl ether vapour at concentrations up to 8000 ppm for 6 hr day^{-1}, 5 days wk^{-1} for 13 wk (14).
Inhalation ♂ and ♀ Fischer 344 rats (13 wk) 0, 800, 4000, and 8000 ppm for 6 hr day^{-1}, 5 days wk^{-1}. At 8000 ppm, ♂ and ♀ rats showed a decrease in body weights compared with controls. The only notable effect on clinical observation was ataxia at 8000 ppm, apparent during the first 4 wk of treatment. At 8000 ppm, animals showed increased serum levels of corticosteroids. At necropsy, there were no treatment-related gross lesions. Absolute and relative organ weights (liver, adrenals, kidneys) were increased in both sexes at 4000 and 8000 ppm. Male rats showed mild increased size of hyaline droplets within the kidney, mild increase in haemosiderosis in the spleen and higher incidence of hyperplasia in the lymph nodes at 8000 ppm. The highest no-observed-adverse-effect level was judged to be 800 ppm (15).

Carcinogenicity and chronic effects

♀ but not ♂ CD-1 mice exposed to 8000 ppm methyl *tert*-butyl ether developed hepatocellular adenomas; liver cancer was not induced in ♀ or ♂ mice exposed to 400 ppm (16).
Chronic inhalation of toxic concentrations caused renal tubular cell neoplasms in ♂ rats and hepatocellular adenomas in ♀ mice. Oral administration produced no evidence of meaningful neoplastic changes in rats. Neoplasms were produced by a non-genetic mechanism requiring exposure above the toxic dose (17).

Teratogenicity and reproductive effects

Inhalation, Sprague-Dawley rats 0, 400, 3000, or 8000 ppm, 6 hr day^{-1}. F0 adults exposed for 10 wk prior to mating and through gestation and lactation (♀), or to the delivery of their last litter sired (♂). F1 adults exposed beginning postnatal day-28 for at least 8 wk to produce F2 litters. Exposure to methyl *tert*-butyl ether vapour produced no reproductive toxicity to two generations of rats, even in the presence of parental toxicity at 3000 and 8000 ppm. Postnatal toxicity was observed in the offspring of both generations, but only in the presence of maternal toxicity. The no-observed-effect level for both parental and postnatal toxicity is 400 ppm, and for reproductive toxicity is at least 8000 ppm (18).

Metabolism and toxicokinetics

Metabolised by rat hepatic microsomes, yielding equimolar amounts of *tert*-butanol and formaldehyde (19).
Ten volunteers were exposed to 5, 25 or 50 ppm methyl *tert*-butyl ether (MTBE) on three occasions during a 2-hr period of light physical activity. The respiratory uptake of MTBE, 42-49%, was rather low and exhalation, 32-47%, rather high. Metabolic blood clearance, 0.34-0.52 l hr^{-1} kg^{-1}, was low compared with many other solvents. The kinetic profile of MTBE in blood could be described in four phases, with half-lives of 1, 10 and 90 min and 19 hr and the decay curve of MTBE in urine in two phases with half-lives of 20 and 180 min. The average post-exposure half-lives of butyl alcohol (TBA), a metabolite, in blood and urine were 10 and 8.2 hr, respectively. Urinary excretion of MTBE and TBA was <1% of the absorbed dose, which pointed to futher metabolic steps. TBA in blood and urine appeared to be a more appropriate marker for MTBE than the parent compound (20).

Irritancy

Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (dose, species unspecified) (21).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA104, TA1535 with and without metabolic activation negative. A high degree of toxicity was seen with the highest dose levels 7400 μg MTBE $tube^{-1}$ (22).
Mouse bone marrow micronucleus test negative (22).

Other effects

Other adverse effects (human)

Presence in the lungs may cause chemical pneumonia which can be fatal (21).
Skin irritant and may cause central nervous system depression (23).
A case of renal failure was reported in 1/8 patients infused with methyl *tert*-butyl ether for the removal of gallstones. Haemolysis due to extravasation after leakage alongside the catheter was suspected to be the cause of renal failure. Renal function recovered after 18 days dialysis (24).

Any other adverse effects

Toxic effects in dogs, rabbits and mice include haemolysis, nerve paralysis, acute cholecystitis, hepatocyte cloudy swelling and focal necrosis, and acute duodenitis (10).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (25).

Other comments

Residues have been detected in groundwaters (26).
Autoignition temperature 224°C.
Environmental fate reviewed (26).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (27).
Toxicology and carcinogenesis studies of methyl *tert*-butyl ether administered by inhalation or gavage to laboratory animals reviewed (17).
Environmental behaviour and fate of methyl *tert*-butyl ether reviewed (28).

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M182 2-methyl-3-butyn-2-ol

$$(CH_3)_2C(OH)C{\equiv}CH$$

C_5H_8O **Mol. Wt.** 84.12 **CAS Registry No.** 115-19-5

Synonyms 1,1-dimethyl-2-propyn-1-ol; dimethylacetylenecarbinol; dimethylacetylenylcarbinol; α,α-dimethylpropargyl alcohol; 1,1-dimethylpropynol; ethynyldimethylcarbinol

EINECS No. 204-070-5 **RTECS No.** ES 0810000

Physical properties

M. Pt. 2.6°C **B. Pt.** 104-105°C **Flash point** 25°C **Specific gravity** 0.8672 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 0.33 **Volatility** v.den. 2.49

Solubility Water: miscible. Organic solvents: miscible with acetone, benzene, carbon tetrachloride, mineral spirits, petroleum ether

Ecotoxicity

Fish toxicity

LC_{50} fathead minnow 3290 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1800, 1950 mg kg^{-1}, respectively (2,3).

LD_{50} intraperitoneal mouse 3600 mg kg^{-1} (4).

LD_{50} subcutaneous mouse 2340 mg kg^{-1} (5).

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M183 2-methylbutyraldehyde

$$CH_3CH_2CH(CH_3)CHO$$

$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 96-17-3

Synonyms 2-methylbutanal; 2-ethylpropanal; 2-formylbutane; methylbutyraldehyde; α-methylbutanal; 2-methylbutyric aldehyde

EINECS No. 202-485-6 **RTECS No.** ES 3400000

Uses Organic synthesis.

Occurrence Aroma component of fruits, vegetables and cooked meat.

Physical properties

B. Pt. 90-92°C **Flash point** 4°C **Specific gravity** 0.804 at 20°C

Solubility Organic solvents: diethyl ether, ethanol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 740 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 6400, 3200 mg kg^{-1}, respectively (2,3).

LC_{50} (4 hr) inhalation rat 14,000 ppm (4).

LD_{50} dermal rabbit 5700 mg kg^{-1} (4).

LD_{50} dermal guinea pig >20,000 mg kg^{-1} (2).

Metabolism and toxicokinetics

In vitro rabbit liver undergoes oxidative cleavage, with olefin formation catalysed by cytochrome P_{450} (5).

Irritancy

500 mg instilled into rabbit eye for 24 hr caused severe irritation (2).

Dermal rabbit, 500 mg caused mild irritation (exposure not specified) (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA102 with metabolic activation positive (6).

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M184 methyl carbamate

$NH_2CO_2CH_3$

$C_2H_5NO_2$ **Mol. Wt.** 75.07 **CAS Registry No.** 598-55-0

Synonyms methylurethane; NCI-C55594; urethylane

EINECS No. 209-939-2 **RTECS No.** FC 2450000

Uses Manufacture of resins and pharmaceuticals.

Occurrence Isolated from *Salsola* species (1).

Physical properties

M. Pt. 56-58°C **B. Pt.** 176-177°C **Specific gravity** 1.1361 at 56°C with respect to water at 4°C

Solubility Water: 2170 g l^{-1} at 11°C. Organic solvents: acetone, diethyl ether, ethanol

Environmental fate

Adsorption and retention

Adsorbs strongly to Na-, Mg-, Al- and Cu- montmorillonites by interaction between the C=O group and the exchangeable cations (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 6200 mg kg^{-1} (3).

LD_{50} subcutaneous mouse 4500 mg kg^{-1} (4).

LD_{Lo} intraperitoneal mouse 200 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Gavage rat, mouse (13 wk) 50-1000 mg kg^{-1} day^{-1} 5 days wk^{-1} in rats, 100-2000 mg kg^{-1} day^{-1} 5 days wk^{-1} in mice. Treatment in rats resulted in dose-related lesions in the liver, weight loss, testicular hypoplasia, bone marrow hyperplasia and pigmentation of the spleen. The highest dose reduced the mean survival time. Only weight loss and inflammatory changes of the liver were observed in mice. The proliferative nature of hepatic lesions in rats suggests that methyl carbamate is potentially hepatocarcinogenic (6).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (7).

Subcutaneous mouse (6 month) 3 × 0.1 mg kg^{-1} at 2-day intervals. After 3 months, 3/29 killed mice had lung adenomas compared with 3/22 controls and with 23/27 mice given 1 mg kg^{-1} urethane plus 1 mg kg^{-1} methyl carbamate. At 6 months 2/26 killed mice had lung adenomas compared with 0/26 controls and 6/28 mice administered urethane plus methyl carbamate (8).

Intraperitoneal mouse (4 month) 0, 1000, 2000 or 3000 mg kg^{-1} once wk^{-1} for 13 wk. Lung adenomas occurred in 17% of untreated controls, 16% of the lower-dose group, 9% of the 1000 mg kg^{-1} treated group and 22% of the 2000 mg kg^{-1} treated group. The high dose caused early deaths (9).

Intraperitoneal mouse (24 wk) 12 × 5 mg $animal^{-1}$ over 4 wk, lung adenomas occurred in 1/16 treated animals, in 6/31 vehicle controls and in 2/31 mice which received no treatment (10).

Dermal mouse (18 wk) 75 mg $animal^{-1}$ wk^{-1} for 15 wk. Three days after the start of methyl carbamate treatment, 18 wkly applications of croton oil (0.3 ml of a 0.5% solution in acetone) were given. 1/18 treated mice developed a skin tumour compared with 1/20 controls given croton oil only, and 7/18 treated mice had a total of 12 lung adenomas (incidence of lung adenomas in controls was not reported) (11).

National Toxicology Program tested rats and mice via gavage. No evidence of carcinogenicity in ♂ and ♀ mice, clear evidence for carcinogenicity in ♂ and ♀ rats (12).

Metabolism and toxicokinetics

Rats injected intraperitoneally with methyl carbamate or the corresponding *N*-hydroxycarbamate excreted methyl carbamate and *N*-hydroxycarbamate in the urine (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (14).

Bacillus subtilis reverse mutation without metabolic activation positive (15).

In vitro Chinese hamster ovary cells, chromosomal aberrations and sister chromatid exchanges negative (16).

In vitro mouse lymphoma L5178Y cells, tk^+/tk^- with and without metabolic activation negative (16).

Did not bind significantly to rat liver or kidney DNA *in vivo*, while ethyl carbamate was found to bind to rat liver DNA to a significant extent (17).

Other comments

Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity and mutagenicity reviewed (1,18).

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M185 methylcellulose

$(C_7H_{12}O_5)n$ **CAS Registry No. 9004-67-5**

Synonyms methyl cellulose ether; cellulose methyl ether; cellulose methylate; cellumeth; methoxycellulose; methulose; *O*-methyl cellulose; visosal; Adulsin; Bulkaloid; Celacol M; Culminal MC; Morpolose M400; Methocel A; Methocel MC; Tylose SL400; Benecel; Cologel

RTECS No. FJ 5959000

Uses Binding agent used in ceramics, mortar and cosmetics. Laxative. Bulk producer in the preparation of diabetic foods.

Physical properties

Solubility Water: miscible. Organic solvents: glacial acetic acid

Environmental fate

Degradation studies

LC_{100} *Ruminococcus flavefaciens* 0.1% (wt/vol) in a culture metabolising cellulose. However, methylcellulose did not inhibit growth on cellobiose or cellulooligosaccharides (1). Degraded by UV irradiation (2).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 280 mg kg^{-1} (3).
LD_{Lo} intravenous mouse 1000 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Oral rat (6 month) 6200 mg kg^{-1} day^{-1} caused no observable adverse effects (5).

Teratogenicity and reproductive effects

Oral rat (3 generations) 5% diet did not produce any adverse effects, including reproductive function (5).
Gavage rat 10 mg kg^{-1} day^{-1} on days 6-15 of gestation induced the formation of a thin central tendon in the diaphragm of all foetuses. In some weaned pups the liver protruded within this tendon (6).

Metabolism and toxicokinetics

Oral doses of 5000 or 10,000 mg to humans were almost entirely eliminated in the faeces (5).

Irritancy

Reported to be non-irritating to the eye (species unspecified) (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (8).
Escherichia coli WP2, with and without metabolic activation negative (8).
Paramecium tetraurelia, formation of macronuclear anlagen negative (9).

Other effects

Any other adverse effects

Intravenous administration of low viscosity solution (15 CP) to dogs caused a progressive decrease in the volume of urine. Necrotising vascular disease and death were due to renal failure (5).
Injection of 2% solution (volume not specified) into the anterior chamber of rabbit eye caused an increase in intraocular pressure which peaked in 3 hr, returning to normal in 9 hr. Corneal thickness was increased (peak at 12 hr), returning to normal after 6 days. Endothelial cell diameter decreased by 6% after 2 wk. The endothelial cells also showed decreased microvilli and enlargement of intercellular spaces (10).

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M186 methyl chloroacetate

$$ClCH_2CO_2CH_3$$

$C_3H_5ClO_2$ **Mol. Wt.** 108.52 **CAS Registry No.** 96-34-4

Synonyms methyl monochloroacetate; monochloroacetic acid, methyl ester; chloroacetic acid, methyl ester

EINECS No. 202-501-1 **RTECS No.** AF 9500000

Uses Solvent.

Physical properties

M. Pt. –33°C **B. Pt.** 130-132°C at 740 mmHg **Flash point** 51°C **Specific gravity** 1.238 at 20°C with respect to water at 20°C

Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

DE-MAK 1 ppm (4.5 mg m^{-3})

UN No. 2295 **HAZCHEM Code** 2W **Conveyance classification** toxic substance

Supply classification toxic

Risk phrases Flammable – Toxic by inhalation and if swallowed – Irritating to respiratory system and skin – Risk of serious damage to eyes (R10, R23/25, R37/38, R41)

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)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 240 mg kg^{-1} (1).

LC_{50} (2 hr) inhalation mouse 1 g m^{-3} (1).

LC_{Lo} (7 hr) inhalation rat 250 ppm (2).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation negative (3).

Other effects

Any other adverse effects

In inhalation studies with rats, nutritional and gross metabolic weight loss or decreased weight gain was observed (2).

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M187 methyl 2-chloroacrylate

$$CH_2=C(Cl)CO_2CH_3$$

$C_4H_5ClO_2$ **Mol. Wt.** 120.54 **CAS Registry No.** 80-63-7

Synonyms methyl 2-chloro-2-propenoate

EINECS No. 201-298-7 **RTECS No.** AS 6380000

Uses Manufacture of polymers.

Physical properties

B. Pt. 52°C at 51 mmHg **Specific gravity** 1.189 at 20°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether

Mammalian & avian toxicity

Acute data

LC_{50} (2 hr) inhalation rat, mouse, rabbit, guinea pig, cat 500 mg m^{-3} (1).

Irritancy

Dermal rabbit, 500 mg caused severe irritation (exposure not specified) (2).
Vapours are irritating to the eyes (humans) at 5-10 ppm (3).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (4).

Other effects

Other adverse effects (human)

Inhalation exposure has been reported to cause pulmonary oedema (3).
Skin contact causes painful keratitis and dermatitis with vesiculation (5).

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3. Lefaux, R. *Practical Toxicology of Plastics* 1968, 90, CRC Press, Cleveland, OH, USA.
4. Rosen, J. D. et al *Mutat. Res.* 1980, **78**, 113-119.
5. Grant, W. M. *Toxicology of the Eye* 3rd ed., 1986, 615, Charles C. Thomas, Springfield, IL, USA

M188 methyl chloroformate

$$ClCO_2CH_3$$

$C_2H_3ClO_2$ **Mol. Wt.** 94.50 **CAS Registry No.** 79-22-1

Synonyms MCF; methoxycarbonyl chloride; methyl carbonochloridate; methyl chlorocarbonate

EINECS No. 201-187-3 **RTECS No.** FG 3675000

Uses Acylating agent. Organic synthesis. Insecticide.

Physical properties

M. Pt. < –81°C **B. Pt.** 70-72°C **Flash point** 17°C **Specific gravity** 1.223 at 20°C with respect to water at 4°C
Volatility v.p. 127 mmHg at 20°C ; v.den. 3.26
Solubility Water: miscible. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 1238 **HAZCHEM Code** 3WE **Conveyance classification** toxic substance, danger of fire (flammable liquid), corrosive
Supply classification highly flammable, toxic
Risk phrases Highly flammable – Toxic by inhalation – Irritating to eyes, respiratory system and skin (R11, R23, R36/37/38)
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 – Take precautionary measures against static discharges – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S16, S33, S45)

Environmental fate

Abiotic removal
Hydrolysis $t_{1/2}$ 35 min at 19.6°C (1).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 74 days (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, guinea pig 60, 67, 140 mg kg^{-1}, respectively (3).
LC_{50} (1 hr) inhalation rat 88 ppm (4).
LD_{50} dermal mouse, rabbit 1750, 7100 mg kg^{-1}, respectively (3,4).
LD_{50} intraperitoneal mouse 40 mg kg^{-1} (5).

Irritancy
Vapour is strongly irritating to the eyes (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
Chronic inhalation exposure causes changes in neuromuscular excitability, body temperature, respiration rate and organ weights (species not specified) (3).

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).

Other comments

Physical properties, use, toxicity and safety precautions reviewed (10,11).
Autoignition temperature 505°C.

References

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9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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M189 methyl 2-chloropropionate

$$CH_3CHClCO_2CH_3$$

$C_4H_7ClO_2$ **Mol. Wt.** 122.55 **CAS Registry No.** 17639-93-9

Synonyms 2-chloropropanoic acid, methyl ester; methyl α-chloropropionate

EINECS No. 241-624-5 **RTECS No.** UE 9100000

Physical properties

B. Pt. 132-133°C **Flash point** 38°C **Specific gravity** 1.075 at 20°C

Occupational exposure

UN No. 2933 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 250 mg kg^{-1} (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Lachrymator.

References

1. *Summary Tables of Biological Tests* 1954, **6**, 228, National Research Council Chemical-Biological Coordination Centre.
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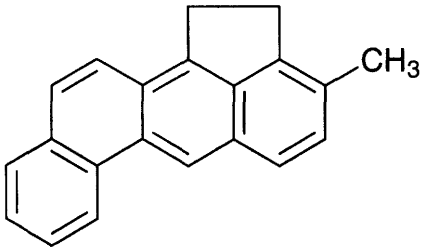
M190 3-methylcholanthrene



$C_{21}H_{16}$ **Mol. Wt.** 268.36 **CAS Registry No.** 56-49-5

Synonyms 1,2-dihydro-3-methylbenz[*j*]aceanthrylene; 3-MC; 20-MC; 20-methylcholanthrene

EINECS No. 200-276-4 **RTECS No.** FZ 3675000

Uses Experimentally in cancer research.

Physical properties

M. Pt. 180°C **B. Pt.** 280°C at 80 mmHg **Specific gravity** 1.28 **Partition coefficient** log P_{ow} 6.75
Solubility Organic solvents: benzene, toluene, xylene

Ecotoxicity

Fish toxicity
Carp, tench (48 hr) 10 mg kg^{-1} induced changes in the RNA and DNA of the cells (1).

Environmental fate

Degradation studies
A Gram-positive, rod-shaped bacterium mineralised 3-methylcholanthrene, 1.6% of the original amount, to CO_2 when grown for 2 wk in pure culture with organic nutrients (2).

Adsorption and retention
Soil sorption coefficient log K_{OM} 6.25 (3).

Mammalian & avian toxicity

Acute data
LD_{Lo} intraperitoneal mouse 100 mg kg^{-1} (4).

Carcinogenicity and chronic effects
Pregnant rats exposed to 7, 21 or 63 mg kg^{-1} on days 15-17 of gestation via gavage. Adult offspring developed neoplastic changes in the lungs 6 months after *in utero* exposure (5).
Displayed potent carcinogenic activity in mouse skin and rat mammary gland (6).
In vitro slices of mouse lung 0.5 or 1 mg, dose-dependent carcinogenesis (proliferation) and toxic (dystrophy and necrosis) effects were observed (7).
Incidence of liver and lung tumours in mice exposed transplacentally was significantly influenced by the sensitivity of both mothers and foetuses to induction of cytochrome P_{450} by polycyclic aromatic hydrocarbons (8).
Oral (3 month) 6 ♂ rats 0.03%, report of study in preparation (9).
In pregnant mice caused lung and liver tumours in the offspring, the incidences of which were greatly influenced by the *Ah* locus-regulated induction phenotype for arylhydrocarbon hydroxylase activity in the mother and foetuses (10).

Metabolism and toxicokinetics
Metabolic products vary with the type of enzyme induction (10).

In foetal rat liver, 1- or 2-hydroxy-, *cis*- and *trans*-1,2-dihydroxy-, 11,12-dihydroxy-, 11,12-dihydro-, and 1- and 2-keto-3-cholanthrene were produced (11).
When incubated with human bone marrow preparations in air for 60 min at 37°C, major metabolites were: 1-hydroxy-3-methylcholanthrene, 1-keto-3-methylcholanthrene and cholanthrene. It can undergo biochemical reactions in preparations of human bone marrow, giving rise to the formation of metabolites which are known to be carcinogenic in rats and mice (12).
Peyer's patches have an importance in the absorption from the gut and subsequent retention and hence may be a likely target organ for lymphoid carcinogenesis following oral exposure to carcinogenic polycyclic aromatic hydrocarbons (13).

Genotoxicity

In vitro Chinese hamster cells chromosomal aberrations and sister chromatid exchanges marginally positive (metabolic activation unspecified) (14).
In vitro human cells with or without metabolic activation negative (details unspecified) (15).
In vitro Syrian hamster embryo cells morphological transformation positive (metabolic activation unspecified) (16).
Rat primary lung cells *in vitro* without metabolic activation and *in vivo* caused high frequencies of sister chromatid exchanges (17).
Human peripheral blood lymphocytes from non-smoking, non-drug-taking individuals were cultured in 10% foetal or calf serum. The level of *ss*-DNA increased, but not that of *ds*-DNA, on exposure to 3-methylcholanthrene. The time-dependent changes increased for ≥4 days of exposure, indicating that the repair enzymes were not able to compensate for the DNA damage (18).
In vitro carp kidney cells, chromosomal aberrations and micronucleated erythrocytes positive(19).
BALBc 3T3 cells simultaneous cell transformation and mutation assay positive (20).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (21).

Other comments

Promotes the induction or activation of cytochrome P_{450} of the aryl hydrocarbon hydroxylase system (22).
Known to induce the metabolism of PAHs in some species of polychaete worms (23).

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22. *Patty's Industrial Hygiene and Toxicology* 3rd rev. ed., 1981, **2B**, John Wiley & Sons, New York, USA.
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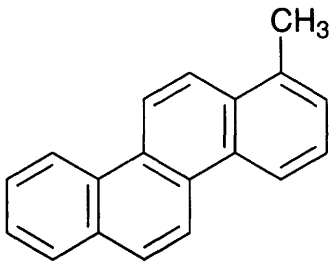
M191 1-methylchrysene



$C_{19}H_{14}$ **Mol. Wt.** 242.32 **CAS Registry No.** 3351-28-8

Synonyms

EINECS No. 222-112-0 **RTECS No.** GC 1320000

Occurrence In fossil fuels. Has been identified in tobacco and marijuana smoke (1).

Physical properties

M. Pt. 253-257°C **B. Pt.** sublimes at 130-140°C (in vacuum)
Solubility Organic solvents: acetone, benzene, ethanol, hexane, toluene

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (2).

Dermal mouse (72 wk) 100 μg animal^{-1} 3 × wk^{-1} for 72 wk, at which time 7/20 treated animals were still alive. No skin tumours were observed in treated animals or vehicle controls (3,4).

Dermal mouse (24 wk) 100 μg animal^{-1} on alternate days for 20 days, followed 10 days later by applications of 2.5 μg animal^{-1} 12-*O*-tetradecanoylphorbol 13-acetate 3 × wk^{-1} for 20 wk, at which time 19/20 mice were still alive. In this group 6 animals each had a skin tumour, as compared with none in vehicle controls and 10 skin tumours in 6/20 surviving positive controls treated with benzo[*a*]pyrene (4).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (5).

Other comments

Physical properties, occurrence, carcinogenicity and metabolism of methylchrysenes reviewed (1,6).

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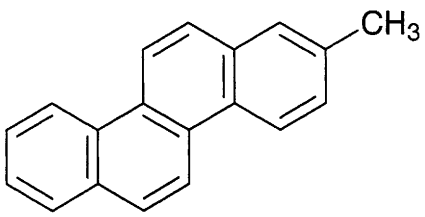
4. Hecht, S. S. et al *J. Natl. Cancer Inst.* 1974, **53**, 1121-1133.
5. Coombs, M. M. et al *Cancer Res.* 1976, **36**, 4525-4529.
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M192 2-methylchrysene



$C_{19}H_{14}$ **Mol. Wt.** 242.32 **CAS Registry No.** 3351-32-4

RTECS No. GC 1350000

Occurrence In fossil fuels. Has been identified in tobacco smoke, marijuana smoke, engine exhausts and in vegetables (1).

Physical properties

M. Pt. 225-230°C

Solubility Organic solvents: acetic acid, acetone, benzene, cyclohexane, ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (2).

Dermal mouse (72 wk) 100 μg animal^{-1} 3 × wk^{-1} for 72 wk. The first skin tumour was reported at 40 wk at which time 18/20 animals were still alive. At 72 wk 10/20 treated mice were still alive; 21 skin tumours were observed in 11 tumour-bearing animals. Seven of these tumours were carcinomas. No skin tumours were reported in vehicle controls (3).

Dermal mouse (24 wk) 100 μg animal^{-1} on alternate days for 20 days, followed 10 days later by applications of 5 μg animal^{-1} of 12-*O*-tetradecanoylphorbol 13-acetate 3 × wk^{-1} for 20 wk. At this time 19/20 mice were still alive. In this group 13 skin tumours were present in 8 mice, as compared with none in vehicle controls and 10 skin tumours in 6/20 surviving positive controls treated with benzo[*a*]pyrene (3).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (4).

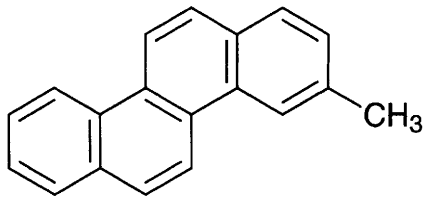
Other comments

Physical properties, occurrence, carcinogenicity and metabolism of methylchrysenes reviewed (1).

References

1. *IARC Monograph* 1983, **32**, 379-397.
2. *IARC Monograph* 1987, **Suppl. 7**, 66.
3. Hecht, S. S. et al *J. Natl. Cancer Inst.* 1974, **53**, 1121-1133.
4. Coombs, M. M. et al *Cancer Res.* 1976, **36**, 4525-4529

M193 3-methylchrysene



$C_{19}H_{14}$ **Mol. Wt.** 242.32 **CAS Registry No.** 3351-31-3

RTECS No. GC 1380000

Occurrence In fossil fuels. Has been identified in tobacco smoke, marijuana smoke, engine exhausts and in vegetables (1).

Physical properties

M. Pt. 170-174°C

Solubility Organic solvents: acetone, benzene, cyclohexane, ethanol, petroleum ether

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (2).

Dermal mouse (72 wk) 100 μg animal^{-1} 3 × wk^{-1}. The first skin tumour was observed at 15 wk at which time all 20 treated mice were still alive. At 72 wk 8/20 treated mice were still alive, 5 of which were bearing a total of 6 skin tumours. Four of these were carcinomas. No skin tumours occurred in vehicle controls (3,4).

Dermal mouse (24 wk) 10, 30 or 100 μg animal^{-1} on alternate days for 20 days, followed 10 days later by application of 2.5 μg animal^{-1} of 12-*O*-tetradecanoylphorbol 13-acetate 3 × wk^{-1} for 20 wk. At this time survival rates were 17/20, 16/20 and 20/20, respectively. Skin tumour incidences were 3 in 3 tumour bearing mice, 8 in 4 tumour-bearing mice, and 26 in 14 tumour-bearing mice for each treated group, respectively. No skin tumours occurred in vehicle controls, while 6/20 surviving positive controls treated with benzo[*a*]pyrene had a total of 10 skin tumours (3).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (5).

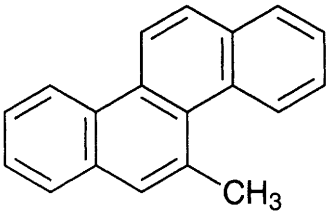
Other comments

Physical properties, occurrence, carcinogenicity and metabolism of methylchrysenes reviewed (1).

References

1. *IARC Monograph* 1983, **32**, 379-397.
2. *IARC Monograph* 1987, **Suppl. 7**, 66.
3. Hecht, S. S. et al *J. Natl. Cancer Inst.* 1974, **53**, 1121-1133.
4. Hoffmann, D. et al *Science* 1974, **183**, 215-216.
5. Coombs, M. M. et al *Cancer Res.* 1976, **36**, 4525-4529

M194 5-methylchrysene



$C_{19}H_{14}$ **Mol. Wt.** 242.32 **CAS Registry No.** 3697-24-3

RTECS No. GC 1575000

Uses No commercial production or known use.

Physical properties

M. Pt. 117-119°C

Solubility Organic solvents: acetone

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (1).

Dermal 20 Swiss ♀ albino Ha/ICR/Mil mice (72 wk) 100 μg 0.1 ml^{-1} acetone. All the mice developed skin tumours by 25 wk, by 35 wk all mice had died, 99 tumours had developed in 20/20 animals (2,3).

Dermal 20 Swiss ♀ Ha/ICR mice (62 wk) treated with concentrations of 0.01 or 0.005% (solvent unspecified). At 55 wk all 20 mice in 0.01% group had died, with a total of 38 skin tumours. At the low dose 7/20 animals survived, 22 tumours (site unspecified) were found in 9 tumour-bearing mice (2).

Subcutaneous ♂ Swiss mice 2 mg $animal^{-1}$. No injection-site tumour was observed, but only 4/20 animals were alive 6 months after injection. First tumour developed at 114 days, and average latency was 125 days (site unspecified) (4).

Subcutaneous ♂ C57B1 mice 0.05 mg $animal^{-1}$ fortnightly for 20 wk, 22/25 mice had 24 fibrosarcomas with an average latent period of 25 wk (site unspecified) (5).

Metabolism and toxicokinetics

In vitro rat liver cytosol and *in vivo* rat dorsal subcutaneous tissue. Undergoes dealkylation in *in vitro* rat liver cells to yield chrysene, and a bioxygenation to yield the corresponding hydroxyalkyl substituted chrysene. Substitution of a methyl group may be a necessary step in the metabolic activation and carcinogenicity of this compound (6).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (7).

Produced a DNA repair response in humans but not in rat hepatocytes (8).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

Reviews on experimental toxicology and human health effects listed (10).

References

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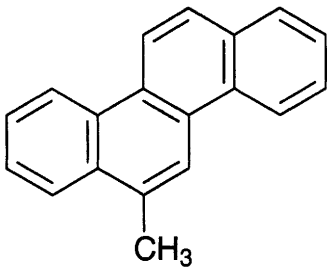
M195 6-methylchrysene



$C_{19}H_{14}$ **Mol. Wt.** 242.32 **CAS Registry No.** 1705-85-7

EINECS No. 216-942-2 **RTECS No.** GC 1750000

Occurrence In fossil fuels. Has been identified in tobacco smoke, marijuana smoke, engine exhausts and in vegetables (1).

Physical properties

M. Pt. 161°C

Solubility Organic solvents: acetone, ethanol, ethyl acetate

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (2).

Dermal mouse (72 wk) 100 μg animal^{-1} 3 × wk^{-1}. The first skin tumour was reported after 20 wk, at which time 19/20 animals were still alive. At 72 wk 12 mice were still alive, 3 of which had a total of 3 skin tumours, including 1 adenoma. No such tumours occurred in vehicle controls (3,4).

Dermal mouse (24 wk) 100 μg animal^{-1} on alternate days for 20 days followed 10 days later by application of 2.5 μg animal^{-1} of 12-*O*-tetradecanoylphorbol 13-acetate 3 × wk^{-1} for 20 wk. At this time 19/20 mice were still alive, of which 7 animals were bearing 11 skin tumours. No skin tumours occurred in vehicle controls while 6/20 surviving positive controls treated with benzo[*a*]pyrene had a total of 10 skin tumours (3).

Metabolism and toxicokinetics

Metabolised in rat liver by demethylation to give chrysene, by alkylation to give dimethylchrysene, and by oxidation to give hydroxyalkyl substituted chrysene (5).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (6).

Other comments

Physical properties, occurrence, carcinogenicity and metabolism reviewed (1,7).

References

1. *IARC Monograph* 1983, **32**, 379-397.
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3. Hecht, S. S. et al *J. Natl. Cancer Inst.* 1974, **53**, 1121-1133.
4. Hoffmann, D. et al *Science (Washington, D. C. 1883-)* 1974, **183**, 215-216.
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M196 methyl 2-cyanoacrylate

$$CH_2=C(CN)CO_2CH_3$$

$C_5H_5NO_2$ **Mol. Wt.** 111.10 **CAS Registry No.** 137-05-3

Synonyms Adhere; Coapt; cyanolyt; mecrylate; methyl 2-cyano-2-propenoate

EINECS No. 205-275-2 **RTECS No.** AS 7000000

Uses Manufacture of adhesives and polymers. Surgical tissue adhesive.

Physical properties

B. Pt. 47-49°C at 1.8 mmHg **Specific gravity** 1.1044 at 27°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.030 (1) **Volatility** v.p. 0.18 mmHg at 25°C
Solubility Water: <1 g l^{-1} at 22°C

Occupational exposure

DE-MAK 2 ppm (9.2 mg m^{-3})
FR-VME 2 ppm (8 mg m^{-3})
FR-VLE 4 ppm (18 mg m^{-3})
SE-LEVL 2 ppm (9 mg m^{-3})
SE-STEL 4 ppm (18 mg m^{-3})
UK-LTEL 2 ppm (9.2 mg m^{-3})
UK-STEL 4 ppm (18 mg m^{-3})
US-TWA 0.2 ppm

Supply classification irritant
Risk phrases Irritating to eyes, respiratory system and skin (R36/37/38)
Safety phrases Keep out of reach of children (if sold to general public) – 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 (S2, S23, S24/25, S26)

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor 0.62 indicates that environmental accumulation is unlikely (2).

Environmental fate

Degradation studies

Biodegradation in screening tests using sewage seed, 28% ThOD after 5 days, and 66% ThOD after 5 days with acclimated sewage seed (3).

Abiotic removal

Reaction with photochemically produced hydroxyl radicals and ozone in the atmosphere, $t_{1/2}$ 2.18 days (4). 95% removal from atmosphere containing 10 ppm by activated carbon up to 200 mg kg^{-1} carbon (5).

Adsorption and retention

Calculated K_{oc} 25 indicates that adsorption to soil and sediments would not be significant (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral starling >100 mg kg^{-1} (6).
LC_{50} (6 hr) inhalation rat 100 ppm (7).
LD_{50} dermal guinea pig >10 ml kg^{-1} (7).

Teratogenicity and reproductive effects

Intratesticular monkey, lowest toxic dose 100 mg kg^{-1} (effects on spermatogenesis, details unspecified) (8).

Metabolism and toxicokinetics

Rapidly absorbed through the skin of guinea pigs and eliminated in the urine. Initial metabolites possessed the carbon skeleton of the monomer, whereas metabolites excreted from day-2 onward represented absorbed and degraded polymeric material (9).

Irritancy

Human volunteers exposed to 40-60 ppm suffered irritation of the eyes and blurred vision. After 2 hr exposure 5 and 20 ppm caused lachrymation and rhinorrhoea (10).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive, TA97, TA98, TA1535, TA1537 with and without metabolic activation negative (11,12).

Other effects

Other adverse effects (human)

Instillation into the eyes may cause double vision and lachrymation. There is usually no residual damage (13).

Any other adverse effects

In vitro rat polymorphonuclear leukocytes. Cell degranulation increased and migration decreased in a concentration-dependent manner. Cytotoxicity decreased in the presence of inhibitors of prostaglandin synthase (14).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (15).

References

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2. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds* 1982, McGraw-Hill, New York, USA.
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5. Benson, L. A. *Am. Hyg. Ind. Assoc. J.* 1975, **36**(10), 741-744.

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11. Rietveld, E. C. et al *Mutat. Res.* 1987, **188**(2), 97-104.
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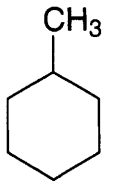
M197 methylcyclohexane



C_7H_{14} **Mol. Wt.** 98.19 **CAS Registry No.** 108-87-2

Synonyms cyclohexylmethane; hexahydrotoluene; Sextone B; toluene hexahydride

EINECS No. 203-624-3 **RTECS No.** GV 6125000

Uses Solvent for cellulose ethers. Organic synthesis.

Physical properties

M. Pt. -126°C **B. Pt.** 101°C **Flash point** -3.8°C **Specific gravity** 0.770 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.88 (1) **Volatility** v.p. 144 mmHg at 20°C ; v.den. 3.38
Solubility Water: 14 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 500 ppm (2000 mg m^{-3})
FR-VME 400 ppm (1600 mg m^{-3})
JP-OEL 400 ppm (1600 mg m^{-3})
US-TWA 400 ppm (1610 mg m^{-3})

UN No. 2296 **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)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) golden shiner 72 mg l^{-1} (emulsion) (2).

Invertebrate toxicity

LC_{50} (96 hr) *Cyclops viridis* 865 mg l^{-1} (3).

LC_{50} (96 hr) *Thiara tuberculata* 1160 mg l^{-1} (3).

LC_{50} (96 hr) *Chironomus* larvae 1000 mg l^{-1} (3).

Bioaccumulation

Confirmed to be non-accumulative or low accumulative in fish despite its high log P_{ow} (4).

Environmental fate

Degradation studies

m-Xylene-adapted microorganisms in an aquifer column were unable to metabolise the compound (5).

Biodegradation 75% after 192 hr at 13°C, initial concentration 0.05 µg l^{-1} (method unspecified) (6).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rabbit 4000 mg kg^{-1} (7).

LD_{50} oral mouse 2250 mg kg^{-1} (7).

LC_{50} (2 hr) inhalation mouse 41,500 mg m^{-3} (8).

Sub-acute and sub-chronic data

Inhalation (10 wk) rabbit 4600 mg m^{-3}, 6 hr day^{-1}, 5 day wk^{-1}, appeared to be non-toxic (9).

Metabolism and toxicokinetics

In rats it is primarily excreted in the urine with ~15% eliminated in exhaled air. The primary urinary metabolites are *cis*- and *trans*-isomers of methylcyclohexanols, which are further conjugated with glucuronic acid (10,11).

Oral ♂ rats, urinary metabolites included: cyclohexylmethanol, 3-methylcyclohexanol; *trans*-4-methylcyclohexanol; 2-*cis*-hydroxy-4-*cis*-methylcyclohexanol; 2-*cis*-hydroxy-4-*trans*-methylcyclohexanol; and 2-*trans*-hydroxy-4-*cis*-methylcyclohexanol. Metabolism of the ring is favoured (11).

Other effects

Any other adverse effects

Lethal concentrations cause mucous secretions, lachrymation, salivation, laboured breathing and diarrhoea (species unspecified) (9).

Histopathological examination revealed only very slight renal tissue damage following oral administration to rats (11).

Subtle liver and kidney damage and convulsions have been noted in inhalation tests on rabbits (12).

Legislation

Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).

The log P_{ow} value exceeds the European Community recommended level (6th and 7th amendments) (14).

Other comments

Experimental toxicology, human health effects, epidemiology and workplace experience reviewed (15,16).

Narcosis in aquatic species including fathead minnows, guppies, *Daphnia magna* and *Artemia* discussed (17).

Autoignition temperature 285°C.

References

1. Sangster, J. *J. Phys. Ref. Data.* 1989, **18** (3), 1111-1129.
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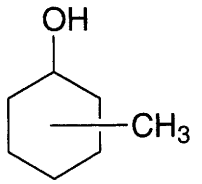
M198 methylcyclohexanol



$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 25639-42-3

Synonyms hexahydrocresol; hexahydromethylphenol; methylhexalin; Sextol

EINECS No. 247-152-6 **RTECS No.** GW 0175000

Uses Solvent. Antioxidant in lubricants.

Physical properties

M. Pt. -50°C **B. Pt.** 155-180°C **Flash point** 63°C (closed cup) **Specific gravity** 0.924 at 15.5°C with respect to water at 15.5°C **Volatility** v.p. 1.5 mmHg at 30°C ; v.den. 3.93

Solubility Water: 35 g l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 50 ppm (235 mg m^{-3})
JP-OEL 50 ppm (230 mg m^{-3})
UK-LTEL 50 ppm (237 mg m^{-3}) **UK-STEL** 75 ppm (356 mg m^{-3})
US-TWA 50 ppm (234 mg m^{-3})

UN No. 2617 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Harmful by inhalation (R20)
Safety phrases Avoid contact with skin and eyes (S24/25)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit 1660, 2000 mg kg^{-1}, respectively (1,2).

Oral rabbit, single dose of 1750 mg kg^{-1} caused rapidly developing anaesthesia with spasmodic jerking of the head and rhythmic movement of the forelegs. The only histopathological evidence observed was degenerative changes in the liver. No significant abnormalities of the blood were observed (2).

LD_{Lo} dermal rabbit 6800 mg kg^{-1} (3).

LD_{50} subcutaneous rat 2900 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Inhalation rabbit (10 wk) 500 ppm 6 hr day^{-1} 5 days wk^{-1} induced salivation, conjunctival congestion and irritation, and lethargy (1).

Inhalation dog (6 days) exposure to saturated air (0.2%) 10 min day^{-1} caused no signs of intoxication (4).

Dermal rabbit (6 days) 10 ml applied to intact skin 1 hr day^{-1} was fatal (2).

Metabolism and toxicokinetics

Following inhalation exposure and dermal application, methylcyclohexanol is excreted in the urine as the glucuronide (species unspecified) (5).

Irritancy

Rabbits exposed to 2300 mg m^{-3} showed symptoms of eye irritation (exposure not specified) (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

25639-42-3 is the general Registry Number for methylcyclohexanols.

Autoignition temperature 296°C.

References

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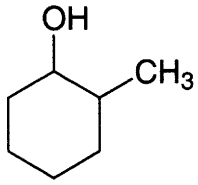
M199 2-methylcyclohexanol



$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 583-59-5

Synonyms 2-methylcyclohexyl alcohol

EINECS No. 209-512-0 **RTECS No.** GW 0220000

Uses Solvent.

Physical properties

M. Pt. -21°C **B. Pt.** 163-166°C **Flash point** 58°C **Specific gravity** 0.930 **Volatility** v.den. 3.39
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2617 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Harmful by inhalation (R20)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Invertebrate toxicity
LC_{50} (96 hr) algae 395.0 mg l^{-1} (1).
LC_{50} (48 hr) *Daphnia magna* 267 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} intramuscular mouse 1000 mg kg^{-1} (2).

Other effects

Other adverse effects (human)
Vapour irritating to eyes and respiratory system. Inhalation of high concentrations of vapour leads to signs of narcosis (3).

Legislation

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

Other comments

Mixture of *cis*- and *trans*-isomers.

References

1. Haley, M. V. *Gov. Rep. Announce. Index (US)* 1989, **89**(18), Abstr. No. 949,416.
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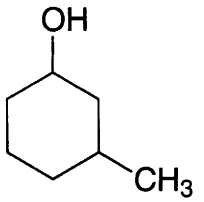
M200 3-methylcyclohexanol



$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 591-23-1

Synonyms 3-methyl-1-cyclohexanol; *m*-methylcyclohexanol

EINECS No. 209-709-1 **RTECS No.** GW 0200000

Occurrence Isolated from *Mentha pulegium*.

Physical properties

B. Pt. 163°C **Flash point** 62°C **Specific gravity** 0.914 at 20°C

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2617 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} intramuscular mouse 1000 mg kg^{-1} (1).

Other comments

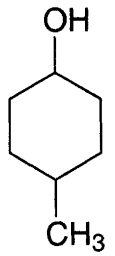
Mixture of *cis*- and *trans*-isomers.

Autoignition temperature 295°C

References

1. *J. Sci. Ind. Res. Sect. C: Biol. Sci.* 1962, **21**, 342

M201 4-methylcyclohexanol



$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 589-91-3

Synonyms hexahydro-*p*-cresol; methyladronal; methylanol; 4-methyl-1-cyclohexanol; 4-methylcyclohexyl alcohol; *p*-methylcyclohexanol; Sextol

EINECS No. 209-664-8

Physical properties

M. Pt. -50°C **B. Pt.** 171-173°C **Flash point** 70°C **Specific gravity** 0.914 at 20°C
Partition coefficient log P_{ow} 1.79 **Volatility** v.p. 1.5 mmHg at 30°C ; v.den. 3.94
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2617 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Environmental fate

Degradation studies
Adapted activated sludge, 94% COD at 40 mg l^{-1} COD g^{-1} dry inoculum hr^{-1} at 20°C, when utilised as sole carbon source (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 1750-2000 mg kg^{-1} (2).

Sub-acute and sub-chronic data
Inhalation rabbit (50 day) lowest lethal concentration 500 ppm for 6 hr day^{-1}; no-adverse-effect level 230 ppm for 6 hr day^{-1} (2).

Other comments

Mixture of *cis*- and *trans*-isomers.
Autoignition temperature 295°C.

References

1. Pitter, P. *Water Res.* 1976, **10**, 231-235.
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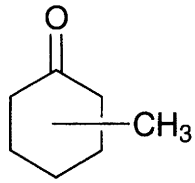
M202 methylcyclohexanone



$C_7H_{12}O$ **Mol. Wt.** 112.17 **CAS Registry No.** 1331-22-2

Synonyms methylcyclohexan-1-one

EINECS No. 215-556-1 **RTECS No.** GW 1575000

Uses Solvent. Manufacture of lacquers, varnishes and plastics. In the leather industry. Rust remover.

Physical properties

M. Pt. –14°C **B. Pt.** 160-170°C **Flash point** 48°C (closed cup) **Specific gravity** 0.925 at 15°C with respect to water at 5°C **Volatility** v. den. 3.86

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 50 ppm (230 mg m^{-3})

UK-LTEL 50 ppm (230 mg m^{-3}) **UK-STEL** 75 ppm (345 mg m^{-3})

US-TWA 50 ppm (229 mg m^{-3}) **US-STEL** 75 ppm (344 mg m^{-3})

UN No. 2297 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Risk phrases Flammable – Harmful by inhalation (R10, R20)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the eyes (S2, S25)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2140 mg kg^{-1} (1).

LD_{Lo} oral rabbit 1000 mg kg^{-1} (2).

LD_{Lo} dermal rabbit 4900 mg kg^{-1} (2).

Metabolism and toxicokinetics

Metabolised via methylcyclohexanol and conjugated with glucuronic acid (species unspecified) (3).

Other effects

Other adverse effects (human)

Narcotic and causes eye and respiratory tract irritation at high concentrations (3).

Legislation

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

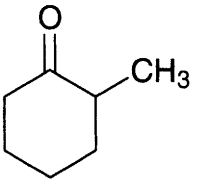
Other comments

Physical properties, toxicity and safety precautions reviewed (1).

References

1. *Chemical Safety Data Sheets: Solvents* 1989, **1**, 228, The Royal Society of Chemistry, London, UK.
2. *J. Ind. Hyg. Toxicol.* 1943, **25**, 199.
3. Tao, C. C. *Biochem. J.* 1962, **84**, 38P.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M203 2-methylcyclohexanone



$C_7H_{12}O$ **Mol. Wt.** 112.17 **CAS Registry No.** 583-60-8

Synonyms 1-methylcyclohexan-2-one; methylanone; methanon; Sexton B

EINECS No. 209-513-6 **RTECS No.** GW 1750000

Uses Organic synthesis. Solvent.

Physical properties

M. Pt. –14°C **B. Pt.** 162-162.5°C **Flash point** 46°C (closed cup) **Specific gravity** 0.924 at 20°C with respect to water at 4°C **Volatility** v.den. 3.86

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 50 ppm (230 mg m^{-3})
FR-VME 50 ppm (230 mg m^{-3})
JP-OEL 50 ppm (230 mg m^{-3})
UK-LTEL 50 ppm (233 mg m^{-3}) **UK-STEL** 75 ppm (350 mg m^{-3})
US-TWA 50 ppm (229 mg m^{-3}) **US-STEL** 75 ppm (344 mg m^{-3})

UN No. 2297 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation (R10, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the eyes (S2, S25)

Ecotoxicity

Invertebrate toxicity

Toxicity threshold, cell multiplication test *Pseudomonas putida, Microcystis aeruginosa, Scenedesmus quadricauda* and *Entosiphon sulcatum* 26-160 mg l^{-1} (exposure not specified) (1,2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, rat 1000, 2140 mg kg^{-1}, respectively (3,4).
LC_{50} (4 hr) inhalation rat 2500 ppm (3).
LD_{50} dermal rabbit 1640 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Inhalation rabbit (50 day) no-adverse-effect level 180 ppm 6 hr day^{-1}. Higher concentrations caused lethargy, salivation, lachrymation and eye irritation (6).

Metabolism and toxicokinetics

In vivo undergoes reduction to the *cis*- and *trans*-methylcyclohexanols which are excreted in the urine as sulfuric and glucuronic acid conjugates (species unspecified) (7,8).

Other effects

Other adverse effects (human)

Reported to be narcotic at concentrations >100 ppm, and an eye and respiratory irritant at >50 ppm (4).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

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

References

1. Bringmann, G. et al Z. *Wasser/Abwasser Forsch.* 1980, (1), 26-31.
2. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
3. *Documentation of Threshold Limit Values for Substances in Workroom Air* 1980, **4**, 272, American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH, USA.
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6. Gerarde, H. W. *Arch. Environ. Health* 1963, **6**, 329.
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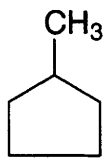
M204 methylcyclopentane



C_6H_{12} **Mol. Wt.** 84.16 **CAS Registry No.** 96-37-7

EINECS No. 202-503-2 **RTECS No.** GY 4640000

Uses Solvent.

Occurrence In fossil fuels. Has been detected in human respired air in smokers and traces in non-smokers (1).

Physical properties

M. Pt. –142°C **B. Pt.** 72°C **Flash point** –23°C **Specific gravity** 0.750 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.37 **Volatility** v.p. 100 mmHg at 17.9°C
Solubility Organic solvents: acetone, benzene, carbon tetrachloride, diethyl ether, ethanol, petroleum ether

Occupational exposure

UN No. 2298 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Environmental fate

Degradation studies
Degraded by *Pseudomonas* spp., *Nocardia* spp. and *Micrococcus* spp. isolated from gasoline-contaminated soil (2). Biodegradation by natural flora in groundwater, in the presence of other components of high octane gasoline, 10% after 192 hr at 0.4 μg l^{-1} at 13°C (3).

Mammalian & avian toxicity

Acute data
LC_{Lo} inhalation (duration unspecified) mouse 95 g m^{-3} (4).

Sub-acute and sub-chronic data
Gavage rat (4 wk) 500 or 2000 mg kg^{-1} day^{-1} 5 days wk^{-1} induced nephropathy. The low dose caused 10% mortality and the high dose 40% mortality (5).

Irritancy
Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (dose, duration unspecified) (6).

Other effects

Other adverse effects (human)
Polyneuropathy of the motor type was reported among exposed workers (7).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).
The log P_{ow} value exceeds the European Community recommended level of 3.0 (6th and 7th amendments) (9).

References

1. Conkle, J. P. *Arch. Environ. Health* 1975, **30**(6), 290.
2. Ridgeway, H. F. et al *Appl. Environ. Microbiol.* 1990, **56**(11), 3565-3575.
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4. *Naunyn-Schmiedeberg's Arch. Exp. Pathol. Pharmakol.* 1930, **149**, 116.
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6. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2330, Sigma-Aldrich, Milwaukee, WI, USA.
7. Brugnone, F. et al *Int. Arch. Occup. Environ. Health* 1979, **42**(3-4), 355-363.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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

M205 methyl dichloroacetate

$Cl_2CHC(O)OCH_3$

$C_3H_4Cl_2O_2$ **Mol. Wt.** 142.97 **CAS Registry No.** 116-54-1

EINECS No. 204-146-8 **RTECS No.** AG 6625000

Uses Chemical intermediate. Used in the synthesis of pharmaceuticals.

Physical properties

M. Pt. –52°C **B. Pt.** 143°C **Flash point** 80°C **Specific gravity** 1.38 at 19°C **Volatility** v.den. 4.93

Occupational exposure

UN No. 2299 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

Helminthicidal effects on *Meloidogyne* and *Ditylenchus* larvae (1).

Mammalian & avian toxicity

Acute data

LC_{Lo} (30 min) inhalation cat 2000 ppm (2).

Inhalation rat single exposure ≥30 min at ≥ 2000 ppm caused some deaths. Irritation caused to eyes and lungs, fatty degenerative and congestive changes to kidney. No deaths occurred when exposed to 1000 ppm for 7 hr (2).

Sub-acute and sub-chronic data

Inhalation rat 7 exposures of 2 or 4 hr at 1000 ppm caused discomfort and weight loss, followed by recovery (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorines: guide level 1 $\mu g\ l^{-1}$ (3).

Other comments

Trace impurity in the anaesthetic methoxyfluorane (2).

Contaminant in water samples as a result of chlorination. Found in water containing fulvic and humic acids.

Hydrolyses on contact with moisture.

References

1. Smolina, A. I. et al *Khim Sel'sk. Khoz. (1963)* 1972, **10**, 122.
2. Torkelson, T. R. et al *Toxicol. Appl. Pharmacol.* 1971, **19**, 1.
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

M206 methyldiethanolamine

$$CH_3N(CH_2CH_2OH)_2$$

$C_5H_{13}NO_2$ **Mol. Wt.** 119.16 **CAS Registry No.** 105-59-9

Synonyms 2,2'-(methylimino)bisethanol; diethanol methylamine; MDEA; methylenediethanolamine; methyliminodiethanol; bis(2-hydroxyethyl)methylamine; 2,2'-(methylimino)diethanol

EINECS No. 203-312-7 **RTECS No.** KL 7525000

Physical properties

B. Pt. 246-248°C at 747 mmHg **Flash point** 126°C **Specific gravity** 1.0377 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) – Avoid contact with the skin (S2, S24)

Environmental fate

Degradation studies

Analysis of partially degraded aqueous methyldiethanolamine solutions, most important degradation products were: methanol; ethylene oxide; trimethylamine; ethylene glycol; 2-(dimethylamino)ethanol; 1,4-dimethylpiperazine; triethanolamine; *N*-(hydroxyethyl)methylpiperazine; and *N,N*-bis(hydroxyethyl) piperazine (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 500, 4780 mg kg^{-1}, respectively (2,3).

Irritancy

Dermal rabbit (24 hr) 10 and 502 mg caused mild irritation (2,4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (5).

References

1. Chakma, A. et al *J. Chromatogr.* 1988, **457**, 287-297.
2. *Arch. Ind. Health* 1954, **10**, 61.
3. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
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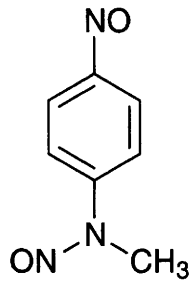
5. Zeiger, E. et al *Environ. Mol. Mutagen.* 1987, **9** (Suppl. 9), 1-109

M207 *N*-methyl-*N*,4-dinitrosoaniline



$C_7H_7N_3O_2$ **Mol. Wt.** 165.15 **CAS Registry No.** 99-80-9

Synonyms *N*-methyl-*N*,4-dinitrosobenzenamine; Nitrosan K

EINECS No. 202-788-3 **RTECS No.** BX 9350000

Physical properties

M. Pt. 101°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

Gavage weanling rat 0.1, 0.3, 1, 3, 10 or 30 mg rat^{-1}, 5 × wk^{-1} for 52 wk (commercial preparation containing 33% of the compounds). The highest concentrations showed carcinogenic activity. Tumours affected breast, pituitary gland, testicles, thyroid gland and lung (2,3).

Intraperitoneal rat 5 mg rat^{-1} wk^{-1} for 6 months (total dose, 600 mg kg^{-1} body weight). The 24 rats showed 1 hepatoma, 1 thymoma, 2 local sarcomas, 1 pancreatic adenoma and 1 pituitary tumour. 1 hepatoma was observed in the controls (4).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 66.
2. Weistburger, J. H. et al *Naturwissenschaften* 1966, **53**, 508.
3. Hadidian, Z. et al *J. Natl. Cancer Inst.* 1968, **41**, 985.
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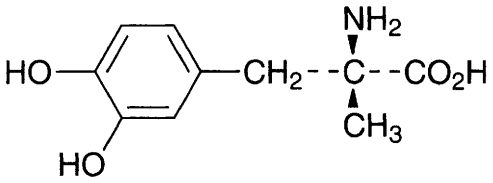
M208 methyldopa



$C_{10}H_{13}NO_4$ **Mol. Wt.** 211.22 **CAS Registry No.** 555-30-6

Synonyms 3-hydroxy-α-methyl-L-tyrosine; 3-(3,4-dihydroxyphenyl)-2-methylaniline,L-alanine; Aldomet; Dopegyt; Medomet; Presinol

EINECS No. 209-089-2 **RTECS No.** AY 5950000

Uses Antihypertensive.

Physical properties

M. Pt. >300°C **Partition coefficient** log P_{ow} –2.09 (1)
Solubility Water: 10 g l^{-1} at 25°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5000 mg kg^{-1} (2).
LD_{50} intravenous rabbit 713 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 300 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 150 mg kg^{-1} (3).

Sub-acute and sub-chronic data

TD_{Lo} (17 wk) oral woman 1830 mg kg^{-1}, peripheral nervous system effects (4).
TD_{Lo} (3 yr) oral woman 44 g kg^{-1}, gastro-intestinal tract effects (diarrhoea, constipation, ulceration) (5).
TD_{Lo} (22 wk) oral man 1070 mg kg^{-1}, skin effects (erythema, rash, sensitisation of skin, petechial haemorrhage) (6).

Teratogenicity and reproductive effects

Maternal mouse (route, duration, dose unspecified), there were no adverse effects on live litter size, survival and growth of live pups to post-natal day-4 or pup survival and growth to post-natal day-21. *In utero* exposure to ≥ 250 mg kg^{-1} day^{-1} may result in depressed brain growth relative to body growth (7).

Metabolism and toxicokinetics

Variably and incompletely absorbed by an amino-acid active transport system. Bioavailability is 50%. Extensively metabolised and excreted in urine, mainly as unchanged drug and the *O*-sulfate conjugate. Crosses the blood-brain barrier and is decarboxylated in the central nervous system to α-methylnoradrenaline. Crosses the placenta and small amounts are excreted in breast milk (8).
Analysis of solution on both sides of the monolayer, used as a model of the blood-brain barrier, failed to show any metabolites of methyldopa. May traverse the blood-brain barrier by means of a carrier transport system, notably the large neutral amino acid transport (9).
Three volunteers were perfused with 21, 211 or 2112 mg kg^{-1} at pH 6. At higher concentrations of drug in the perfusion solution, the free fraction in plasma samples was increased significantly. Although absorption is more efficient at lower concentrations, bioavailability may not be substantially enhanced due to increased sulfation in the gut wall (10).

Sensitisation

Reported to cause skin sensitisation in humans (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, with and without metabolic activation negative (11,12). *In vitro* rat bone marrow cells, no clastogenic effect. *In vitro* human lymphocyte cultures, increased frequency of sister chromatid exchanges, without any effect on the frequency of chromosomal aberrations (metabolic activation unspecified in all cell types) (13).

Other effects

Other adverse effects (human)

Drowsiness, dizziness, light-headedness, nausea, headache, weakness and fatigue, decreased libido and impotence have been reported frequently. Can impair concentration and memory; cause mild psychoses, depression, disturbed sleep and nightmares, paraesthesia, Bell's palsy, involuntary choreoathetotic movements and Parkinsonism (8).

Ischaemic heart disease was prevalent in treated group irrespective of blood pressure levels. Risk factors such as body mass index, skinfold thickness, serum cholesterol, albumin, creatinine, blood urea nitrogen, and uric acid at entry were elavated in the treated group (14).

Any other adverse effects

Potency for protection was related to affinity for α-adrenergic binding sites labelled with [^{3}H]clonidine (15). Intravenous dog 5 and 10 mg kg^{-1} min^{-1} for 30 min decreased the arterial blood pressure and renal vascular resistance by 27, 48, 63 and 79%, respectively (16).

Other comments

Human health effects reviewed (17).

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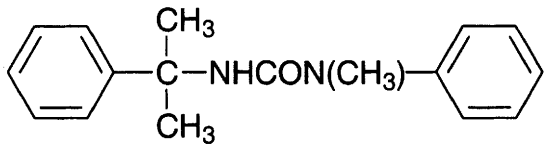
M209 methyldymron



$C_{17}H_{20}N_2O$ **Mol. Wt.** 268.36 **CAS Registry No.** 42609-73-4

Synonyms urea, *N*-methyl-*N'*-(1-methyl-1-phenylethyl)-*N*-phenyl-; methyldimuron; Dimelon-methyl; K1441

RTECS No. YT 7790000

Uses Herbicide. Cell division inhibitor.

Physical properties

M. Pt. 72°C **Specific gravity** 1.1-1.2 **Partition coefficient** log P_{ow} 3.01 (1)
Solubility Water: 120 mg l^{-1} at 20°C. Organic solvents: acetone, hexane, methanol

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 14 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♀ rat 3950 mg kg^{-1}; ♂ rat 5850 mg kg^{-1} (1,2).
LD_{50} oral ♀ mouse 5270 mg kg^{-1}; oral ♂ mouse 5000 mg kg^{-1} (2).
LD_{50} dermal rat 11.4 g kg^{-1} (2).
LD_{50} subcutaneous mouse 7600-7800 mg kg^{-1} (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (5).
WHO Toxicity Class Table 5 (6).

Other comments

Rapidly metabolised in plants. Inhibits cell division (2).

References

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3. *Shokubutsu Boeki* 1978, **32**, 488.
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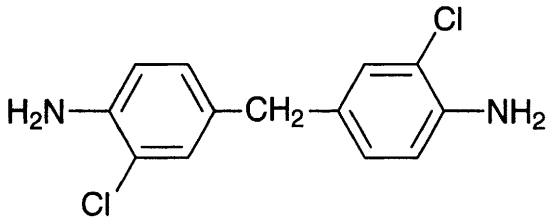
5. *1967 Directive on Classification, Packaging, and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

M210 4,4′-methylenebis(2-chloroaniline)



$C_{13}H_{12}Cl_2N_2$ **Mol. Wt.** 267.16 **CAS Registry No.** 101-14-4

Synonyms methylenebis(3-chloro-4-aminobenzene); 4,4′-methylenebis(2-chlorobenzenamine); 3,3′-dichloro-4,4′-diaminodiphenylmethane; 4,4′-methylenebis(*o*-chloroaniline); bis(4-amino-3-chlorophenyl)methane; 2,2′-dichloro-4,4′-methylenedianiline; Bisamine S; MOCA; DACPM; Quodrole

EINECS No. 202-918-9 **RTECS No.** CY 1050000

Uses Curing agent for polyurethanes and epoxy resins.

Physical properties

M. Pt. 110°C **Specific gravity** 1.44 at 4°C

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

Occupational exposure

FR-VME 0.02 ppm (0.22 mg m^{-3})

UK-LTEL MEL 0.005 mg m^{-3}

US-TWA 0.01 ppm (0.11 mg m^{-3})

Supply classification toxic, 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 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) – 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)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 880 mg kg^{-1} (1).

LD_{50} oral rat 2100 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 64 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (3).

Subcutaneous rat (89 wk) 25-27 g kg^{-1} total dose induced liver and lung tumours in rats. Hepatocarcinogenicity was increased in rats fed a protein-deficient diet (4).

Oral rat and mouse (2 yr) 100 or 200 mg kg^{-1} diet. A statistically significant incidence of hepatoma in ♀ mice but not in ♂ mice reported (5).

Oral rat (2 yr) 200 ppm in diet induced lung tumours in animals of both sexes. When combined with a protein-deficient diet, animals of both sexes developed lung tumours and in addition ♂ developed liver tumours and ♀ malignant mammary tumours (6).

No evidence of liver tumours was found in 31 workers exposed to 4,4'-methylenebis(2-chloroaniline) from between 6 months and 31 yr. Only 2 of these workers were exposed for more than 16 yr. Under industrial hygiene controls used in the production area, no cyanosis anaemia syndrome was observed. Skin absorption from direct contact was the major route of exposure (7).

Metabolism and toxicokinetics

Intraperitoneal, subcutaneous rats 0.5-50 mg kg^{-1} and 5-500 mg kg^{-1}, respectively, and 4-100 mg kg^{-1} to guinea pigs (single doses) resulted in the dose-related formation of haemoglobin adducts which remained in the blood for 10 wk (guinea pigs) (8).

Covalent binding to rat liver DNA was demonstrated following intraperitoneal administration (9).

In rats <0.2% of oral dose was recovered unchanged in the urine; glucuronide and sulfate conjugates in the urine were indicated. The predominant metabolite in the bile was the *N*-glucuronyl derivative. *In vitro*, *N*-hydroxylation metabolite was identified in rat and human liver microsomes (10).

The major metabolite identified in the urine of exposed workers was a *N*-glucuronide (11).

4,4'-Methylenebis(2-chloroaniline) can be absorbed through the skin. A worker splashed in the face with molten substance complained of stomach pain and urinary levels of 3.6 mg l^{-1} were detected (12).

Irritancy

Dermal guinea pig, 40% solution caused mild irritation (period of exposure unspecified) (13).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (14).

Drosophila melanogaster wing-spot test positive (14).

In vitro rat fibroblast, 6-thioguanine resistance test positive (14).

In vitro primary rat hepatocytes, DNA repair test positive (15).

In vitro mouse bone marrow cells, micronuclei induction positive (2).

In vitro Chinese hamster ovary cells, sister chromatid exchanges positive, chromosomal aberrations negative.

CASE (Computer Automated Structure Evaluation) method (16).

In vitro L5178Y mouse lymphoma cell forward mutation assay with metabolic activation positive (17).

Other effects

Other adverse effects (human)

A 30-yr-old ♂ polyurethane worker was exposed to an accidental spill of 4,4'-methylenebis(2-chloroaniline) (MBOCA) at a plant producing MBOCA-cured plastic products. The worker experienced a very high dose of MBOCA as judged by his urinary levels (peak value of 1700 ppb 4 hr after exposure). There were no acute symptoms or other abnormalities noted (18).

Any other adverse effects

In vitro rat liver cells, gap-junction communication was inhibited at 2-4 g l^{-1}, whereas cytotoxicity was not seen until 4-8 g l^{-1}. The *N*-hydroxy-, mononitroso- and *o*-hydroxy- metabolites did not inhibit gap-cell communication at noncytotoxic concentrations (19).

Legislation

There are no adequate studies documenting a carcinogenic risk for 4,4'-methylenebis(2-chloroaniline). In humans, however, it is structurally similar to aromatic amines which cause bladder cancer in workers with occupational exposure. Manufacture in the US ceased in 1979. An estimated 1400-33,000 workers were potentially exposed in the manufacture of MBOCA-cured products. There are no federal regulations limiting occupational exposure to MBOCA. NIOSH recommended in 1978 that MBOCA be treated as a potential human carcinogen and that worker exposure be controlled so that it does not exceed 3 μg m^{-3} of air detected as a time-weighted average concentration for up to a 10 hr workshift (20).

Other comments

Residues have been isolated from fish tissues, water and sediments.
Biotransformation, genotoxicity and carcinogenicity reviewed (4,21).

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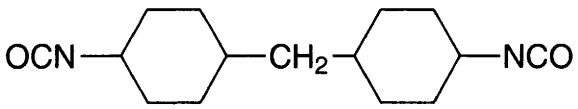
M211 4,4'-methylenebis(cyclohexyl isocyanate)



$C_{15}H_{22}N_2O_2$ **Mol. Wt.** 262.35 **CAS Registry No.** 5124-30-1

Synonyms methylenebis(4-cyclohexyl isocyanate); 1,1'-methylenebis(4-isocyanatocyclohexane); Nacconate H12; bis(4-isocyanatocyclohexyl)methane; HMDI

EINECS No. 225-863-2 **RTECS No.** NQ 9250000

Physical properties

M. Pt. 19-23°C **B. Pt.** decomposes **Flash point** >110°C **Specific gravity** 1.066

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)
US-TWA 0.005 ppm (0.054 mg m^{-3})
Supply classification toxic
Risk phrases Toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by inhalation and skin contact (R23, R36/37/38, R42/43)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S28, S38, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 9900 mg kg^{-1} (1).

LC_{50} (5 hr) inhalation rabbit 20 ppm (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

Other comments

Mixture of isomers.

References

1. *Documentation of the Threshold Limit Values and Biological Exposure Indices* 5th ed., 1986, 392, Cincinnati, OH, USA.
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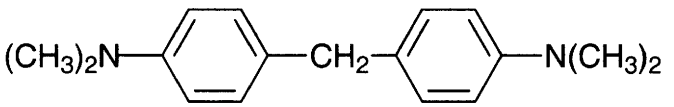
M212 4,4′-methylenebis(*N,N*-dimethylaniline)



$C_{17}H_{22}N_2$ **Mol. Wt.** 254.38 **CAS Registry No.** 101-61-1

Synonyms 4,4′-methylenebis(*N,N*-dimethylbenzenamine); Arnold's base; Michler's base; Michler's methane; tetrabase; tetramethyldiaminodiphenylmethane

EINECS No. 202-959-2 **RTECS No.** BY 5250000

Uses Manufacture of dyes. Reagent for lead determination.

Physical properties

M. Pt. 90-91°C **B. Pt.** 390°C (sublimes without decomp.)

Solubility Organic solvents: benzene, carbon disulfide, diethyl ether

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 3160 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral (4 wk) mice up to 11,380 mg kg^{-1} in diet caused no death or growth inhibition, oral (4 wk) rats 3155 mg kg^{-1} in diet did not affect survival, but caused severe reduction in weight gain (2).

Oral (30 wk) mouse, rat 1250 or 2500 mg kg^{-1} of diet (mouse), 375 or 750 mg kg^{-1} of diet (rat) caused no reduction in body-weight gain, but increased compound-dependent non-neoplastic proliferative lesions of the thyroid (2).

Carcinogenicity and chronic effects

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

Oral (59 wk) ♂, ♀ rats, 750, 375 ppm in feed, followed by 45 wk observation period. No significant association between administered dose and toxicity. Dose-dependent increase in incidences of follicular-cell carcinomas of the thyroid. Non-neoplastic proliferative lesions of the thyroid were observed in dosed animals (4).

Oral (78 wk) ♂, ♀ mice 1250, 2500 ppm in food, followed by 13 wk observation period. No significant association between administered dose and toxicity. Liver neoplasms were observed in both ♂ and ♀ mice as well as increased incidences of hepatocellular adenomas. Incidences of hepatocellular carcinomas were not significantly increased above controls. Both sexes had a significant positive association for the incidence of a combination of hepatocellular adenomas and hepatocellular carcinomas; however, for ♂ this was not statistically significant. Non-neoplastic proliferative lesions of the thyroid were observed in dosed animals of both sexes (4).

Genotoxicity

Salmonella typhimurium TA98, TA97, TA100, TA1535, TA1537 with and without metabolic activation negative (5).

Saccharomyces cerevisiae with and without metabolic activation, mitotic recombination negative (6).

In vitro mouse lymphoma tk+/tk- with and without metabolic activation positive (7).

In vitro mouse embryo cell line C3H/10T1/2 positive (8).

Other effects

Any other adverse effects

Following injection to rats of [^{3}H]-4,4′-methylenebis(*N*,*N*-dimethylaniline), radioactivity found bound to liver nucleic acids (9).

References

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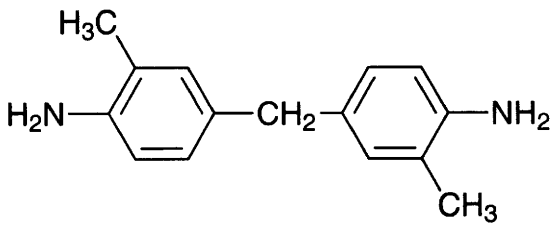
M213 4,4′-methylenebis(2-methylaniline)



$C_{15}H_{18}N_2$ **Mol. Wt.** 226.32 **CAS Registry No.** 838-88-0

Synonyms 4,4′-methylenebis(2-methylbenzenamine); 4,4′-methylenebis(*o*-toluidine)

EINECS No. 212-658-8 **RTECS No.** BY 5300000

Uses In the production of dyes.

Physical properties

M. Pt. 149°C
Solubility Water: miscible. Organic solvents: ethanol

Occupational exposure

Supply classification toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer – Harmful if swallowed – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R22, 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 – Restricted to professional users (S53, S45, S60, S61)

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (1).
Oral (55 wk) rat, 1000 ppm induced liver tumours in both sexes, and skin and mammary tumours in ♂ (2).
Oral (7 yr) ♀ dog 100 ng 3 × wk^{-1} for 6 wk; then 100 ng 5 × wk^{-1} for 5 wk; and then 50 ng 5 × wk^{-1} for ≤7 yr. Treated dogs developed renal atrophy with elevated blood urea nitrogen ~6 months prior to being killed *in extremis*. 3/6 dogs survived 5.2-7.0 yr, these developed hepatocellular carcinomas, and 2/3 developed primary lung tumours. No liver or lung tumours were seen in the controls, which were kept for 8.3-9 yr (3).
Oral (16 month) 24 ♂ rats, total dose 10.2 g kg^{-1} body weight. Over a 10-month period from the start of study, 18 malignant and 2 benign liver tumours and 12 subcutaneous tumours were detected (4).
Oral (1 yr) ♂, ♀ rats 200 ppm in diet. Tumours developed in lung, liver and skin (5).
Oral (180 day) ♂ rats 50 mg kg^{-1} body weight. Tumours developed in the liver, lung, mammary gland and skin (5).

Irritancy
100 mg instilled into rabbit eye for 24 hr caused moderate irritation (6).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

May be present in waste streams from plants which produce it as an intermediate for further processing. Reviews on experimental toxicology and human health effects listed (8).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 66.
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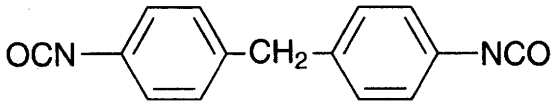
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M214 4,4′-methylenebis(phenyl isocyanate)



$C_{15}H_{10}N_2O_2$ **Mol. Wt.** 250.26 **CAS Registry No.** 101-68-8

Synonyms 1,1′-methylenebis(4-isocyanatobenzene); methylenebis(4-phenyl isocyanate); bis(4-isocyanatophenyl)methane; 4,4′-diisocyanatodiphenylmethane; isocyanic acid, methylenedi-, 4-phenylene ester; 4,4′-methylenediphenyl diisocyanate; MDI; diphenylmethane 4,4′-diisocyanate

EINECS No. 202-966-0 **RTECS No.** NQ 9350000

Uses Intermediate in manufacture of polyurethanes and surface coatings. Fungicidal coating for electric insulators, metal pipes or plastic tubes. Component in adhesives. Lubricant additive.

Physical properties

M. Pt. 42-44°C (98% pure) **B. Pt.** 200°C at 5 mmHg **Flash point** >110°C **Specific gravity** 1.19 at 50°C
Volatility v.p. 1×10^{-3} mmHg at 40°C
Solubility Organic solvents: acetone, benzene, dimethyl sulfoxide, kerosene, nitrobenzene

Occupational exposure

DE-MAK 0.05 mg m^{-3}
FR-VME 0.01 ppm (0.1 mg m^{-3}) **FR-VLE** 0.02 ppm (0.2 mg m^{-3})
JP-OEL 0.05 mg m^{-3}
SE-LEVL 0.005 ppm (0.05 mg m^{-3}) **SE-CEIL** 0.01 ppm (0.1 mg m^{-3})
UK-LTEL MEL 0.02 mg m^{-3} (as NCO) **UK-STEL** MEL 0.07 mg m^{-3} (as NCO)
US-TWA 0.005 ppm (0.051 mg m^{-3})

UN No. 2489 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
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)

Environmental fate

Abiotic removal
Forms polyureas in soil and water which are chemically inert and appear to cause no toxicological effects to the environment (1).
Undergoes rapid hydrolysis in aqueous environments, toluene diamine and methylene dianiline are produced in low concentrations (1,2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 2200 mg kg^{-1} (3).

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

Teratogenicity and reproductive effects

4,4'-Methylenebis(phenyl isocyanate) was administered to ♀ rats by whole-body inhalation at 1, 3 and 9 mg m^{-3} for 6 hr day^{-1} from days 6 to 15 post-conception. Treatment caused a dose-dependent decrease in food consumption in all treated groups. Lung weights in the high-dose group were significantly increased. No other maternal or foetal parameters were affected except for a slight but significant increase in litters with foetuses displaying asymmetric sternebra in the highest-dose group. A no-embryotoxic-effect level of 3 mg m^{-3} was determined (5).

Metabolism and toxicokinetics

♀ rats were treated topically with [^{14}C]4,4'-methylenebis(phenyl isocyanate) in acetone. Faecal excretion of radioactivity was 20% of administered dose, urinary excretion was 1%. 10% of the radioactivity was retained at the site of application, however analysis did not reveal isocyanate-DNA adducts. In the liver, lung and kidneys, nuclear protein radioactivity was much lower than in the epidermis (6).

Irritancy

Dermal rabbit (24 hr) 500 mg caused irritation (4).
100 µg instilled into rabbit eye caused mild irritation (7).

Sensitisation

Application to guinea pig skin caused immune response in a 24 hr spot test (7,8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (9).
In vitro human lymphocyte cells (24 hr) 0.54-4.30 µl ml^{-1} with and without metabolic activation induced chromosomal aberrations; (48 hr) 2.17 µl ml^{-1} with and without metabolic activation induced sister chromatid exchanges (10).

Other effects

Other adverse effects (human)

Of 44 workers exposed during polyurethane foam production (16 month), 19 had stress breathlessness but no change in lung ventilation and 30 suffered hyperaemia of the conjunctiva (11).
Of 120 workers, 19% had chronic lung disease and 21% simple bronchitis (12).
Epidemiological survey showed recurrent exposure-related asthma attacks and chronic pulmonary obstruction among exposed workers, with evidence of hypersensitivity pneumonitis (13).

Other comments

Environmental fate reviewed. Since this compound is converted into chemically and biologically inert material the ecological impact is predicted to be slight and reversible (14).
Adverse respiratory effects reviewed (15).
Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology, workplace experience and exposure are listed (16).

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M215 1,1′-methylenebis(thiosemicarbazide)

$H_2NC(S)NHNHCH_2NHNHC(S)NH_2$

$C_3H_{10}N_6S_2$ **Mol. Wt.** 194.28 **CAS Registry No.** 39603-48-0

Synonyms hydrazinecarbothioamide 2,2′-methylenebis-; bisthiosemi; Kayanex

RTECS No. MV 1407500

Uses Superseded rodenticide.

Physical properties

Solubility Organic solvents: dimethyl sulfoxide

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, guinea pig 30-32 mg kg^{-1} (1).
LD_{50} oral cat 150 mg kg^{-1} (1).
LD_{50} oral chicken 120 mg kg^{-1} (1).

Sub-acute and sub-chronic data

No-observed-effect level (NOEL) oral (90 day) mice 100 mg kg^{-1} diet; rats 50 mg kg^{-1} diet (1).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).
WHO Toxicity Class III (3).

Other comments

Toxicity studied (4).

References

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2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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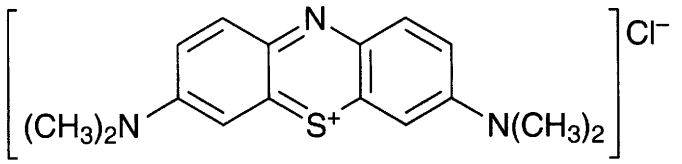
M216 Methylene Blue



$C_{16}H_{18}ClN_3S$ **Mol. Wt.** 319.86 **CAS Registry No.** 61-73-4

Synonyms 3,7-bis(dimethylamino)phenothiazin-5-ium chloride; C.I. Basic Blue 9; methylenium ceruleum; Sandocryl Blue BRL; tetramethylthionine chloride; Yamamoto Methylene Blue ZF; C.I. 52915

EINECS No. 200-515-2 **RTECS No.** SO 5600000

Uses Stain in bacteriology. Analytical reagent. Oxidation-reduction indicator. Antimethaemoglobinaemic. Antidote for cyanide. Antiseptic.

Physical properties

M. Pt. 190°C (decomp.) **Specific gravity** 0.908
Solubility Water: 40 g l^{-1}

Ecotoxicity

Invertebrate toxicity
LC_{50} (96 hr) *Penaeus californiensis* 100 mg l^{-1} (1).

Environmental fate

Nitrification inhibition
At the highest concentration tested, 100 mg l^{-1}, no inhibition of ammonia oxidation by activated sludge observed (2).

Abiotic removal
Methylene Blue-sensitised photolysis rates were highest at basic pH (3).

Adsorption and retention
Adsorption onto sodium-montmorillonite was as much as 120% of the cation-exchange capacity (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 3500 mg kg^{-1} (5).
LD_{Lo} oral dog 500 mg kg^{-1} (6).
LD_{50} intravenous rat 1250 mg kg^{-1} (7).
LD_{50} intravenous mouse 77 mg kg^{-1} (5).
LD_{Lo} intravenous monkey, dog 10, 50 mg kg^{-1}, respectively (6).
LD_{50} intraperitoneal mouse, rat 150, 180 mg kg^{-1}, respectively (8,9).

Teratogenicity and reproductive effects
TD_{Lo} (1-22 day pregnancy) oral rat 2500 mg kg^{-1}, unspecified reproductive effects (10).
There have been several reports of haemolytic anaemia and hyperbilirubinaemia in neonates exposed to Methylene Blue in the amniotic cavity (11-14).

Metabolism and toxicokinetics
Absorbed from the gastro-intestinal tract, and believed to be reduced in the tissue to the leucoform which is slowly excreted, mainly in the urine, together with some unchanged dye (15).
74% of a 10 mg dose was recovered in the urine as unchanged dye or Leucomethylene Blue (16).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 (metabolic activation unspecified) negative (17).

Other effects

Other adverse effects (human)

High doses may cause nausea, vomiting, abdominal and chest pain, headache, dizziness, mental confusion, profuse sweating, dyspnoea and hypertension. May cause necrotic abscesses if injected subcutaneously (15).

Any other adverse effects

Mice bearing Ehrlich ascites tumour, intraperitoneal (1-2 day) (dose unspecified) after tumour transplants, high toxicity was induced but no specific cytotactic effects (18).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (19).

Other comments

Adsorbs completely on DNA-sepharose and DNA-polyacrylamide gels, but not on DNA-cellulose gels (20).

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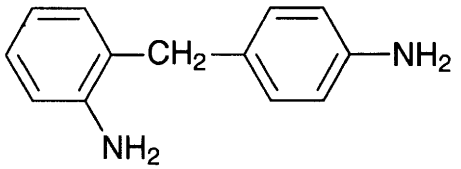
M217 2,4′-methylenedianiline



$C_{13}H_{14}N_2$ **Mol. Wt.** 198.27 **CAS Registry No.** 1208-52-2

Synonyms 2,4′-diaminodiphenylmethane; *o,p′*-diaminodiphenylmethane; 2′,4-bis(aminophenyl)methane; 2,4′-methylenebis(aniline); 2-[(4-aminophenyl)methyl]benzenamine

EINECS No. 214-900-8 **RTECS No.** BY 5400000

Uses Cross-linking agent for epoxy resins.

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rat 3300 mg kg^{-1} (1).

Carcinogenicity and chronic effects

A study in rats showed that the substance was not carcinogenic (1).

References

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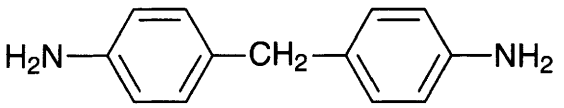
M218 4,4′-methylenedianiline



$C_{13}H_{14}N_2$ **Mol. Wt.** 198.27 **CAS Registry No.** 101-77-9

Synonyms 4,4′-diaminodiphenylmethane; *p,p′*-diaminodiphenylmethane; 4,4′-methylenebisbenzenamine; bis(4-aminophenyl)methane; DDM; MDA

EINECS No. 202-974-4

Uses Cross-linking agent for epoxy resins. Preparation of azo-dyestuffs. Corrosion inhibitor. Used in the production of 4,4′-methylenediphenyl diisocyanate. In the determination of tungsten and sulfates.

Physical properties

M. Pt. 89-91°C **B. Pt.** 398-399°C **Flash point** 221°C **Specific gravity** 1.056 at 100°C with respect to water at 4°C **Volatility** v.p. 1 mmHg at 197°C

Solubility Water: <1 mg l^{-1} at 19°C. Organic solvents: acetone, benzene, diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

JP-OEL 0.4 mg m^{-3}

UK-LTEL MEL 0.01 ppm (0.08 mg m^{-3})

US-TWA 0.1 ppm (0.81 mg m^{-3})

UN No. 2651 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic, dangerous for the environment
Risk phrases May cause cancer – Harmful by inhalation, in contact with skin and if swallowed – May cause sensitisation by skin contact – Harmful: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R20/21/22, R43, R48/20/21, R51/53)
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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S53, S45, S61)

Ecotoxicity

Fish toxicity
Steelhead trout, bridgelip sucker, sockeye salmon exposed to 10 mg l^{-1} died within 6-8 hr (1).

Invertebrate toxicity
Toxic to *Scenedesmus* sp. 30 mg l^{-1}; *Colpoda* sp. 124 mg l^{-1}; *Daphnia* sp. 0.25 mg l^{-1}; *Pseudomonas* sp. 15 mg l^{-1} (2).

Environmental fate

Degradation studies
ThOD 2.9 mg l^{-1} O_2; permanganate value 12.6 mg l^{-1} O_2 (2).
Biodegradation of ^{14}C-labelled 4,4'-methylenedianiline began immediately after mixing with aerobic soil, with the recovery of 2-3% $^{14}CO_2$ after only 3 days and 11-14% $^{14}CO_2$ after 28 days. After 1 yr an apparent 34-40% biodegradation had occurred (3).

Adsorption and retention
K_{oc} sorption constant under aerobic and anaerobic conditions on loam soil after 8 hr contact 3800-5700. Sorption was slightly stronger under aerobic than anaerobic conditions (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 148 mg kg^{-1} (4).
LD_{50} oral rat, mouse 347, 745 mg kg^{-1}, respectively (5,6).
LD_{50} intraperitoneal rat 193 mg kg^{-1} (6).
LD_{50} subcutaneous rat 200 mg kg^{-1} (7).

Sub-acute and sub-chronic data
Gavage ♀ rats 150 mg kg^{-1} (dihydrochloride) 14 daily doses caused increased weight of adrenal gland, uterus and thyroid gland in ovariectomised ♀ (8).
Atrophy of liver parenchyma and increased spleen weight associated with hyperplasia of the lymphatic system were observed in rats given 83 mg kg^{-1} day^{-1} for 12 wk (9).
Oral administration to rats of 1000 mg kg^{-1} over 12 wk caused severe bile-duct proliferation with concurrent oval-cell and inflammatory cell infiltration, fibrosis and dilation of smooth endoplasmic reticulum (10).
Gavage rats (16 wk) 20 mg kg^{-1} induced liver haemangiomas (11).
Oral ♂, ♀ rats (13 wk) 100 mg l^{-1} (dihydrochloride) in drinking water caused bile-duct hyperplasia in all animals (12).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (13).
Gavage rat (8 month) 4-5 doses of 20 mg. After 18 months 1/16 rat developed an adenoma of the kidney. After 2 yr, 1/16 rats developed an adenocarcinoma of the uterus (7).

Intragastric rats unspecified dose administered 5 × wk. 48/48 developed liver cirrhosis, 4/48 developed hepatomas (2 benign) and others (unspecified) developed miscellaneous tumours (14).
Treatment-related increases in the incidence of thyroid follicular-cell adenomas and hepatocellular neoplasms were observed in both ♂ and ♀ mice following oral administration (dose and duration unspecified). Oral rats treatment-related increases in the incidence of thyroid follicular-cell carcinomas and hepatic nodules were observed in ♂ and thyroid follicular-cell adenomas occurred in ♀ (15).
Oral rats administered 4,4'-methylenedianiline (dose unspecified) in conjunction with the known carcinogen *N*-bis(2-hydroxypropyl)nitrosamine, the incidence of thyroid tumours was greater than that produced by the carcinogen alone (16).
Oral rats, mice (2 yr) unspecified dose in drinking water caused mineralisation of the kidney (12).

Metabolism and toxicokinetics
♂ rats, guinea pigs and monkeys were treated dermally with 2 or 20 mg kg^{-1} of radiolabelled 4,4'-methylenedianiline. In rats, 43 and 10% of the low dose was recovered in urine and faeces, respectively, during a 96 hr period; 2% remained in tissues and skin washing removed 25% of the dose. The remainder was recovered by skin extraction and solubilisation. In guinea pigs, 10 and 18% of the low dose was excreted in urine and faeces, respectively; 1% was recovered in tissue, 41% in the skin wash and 29% from the application area (17).

Irritancy
100 mg instilled into rabbit eye for 24 hr caused moderate irritation. Irritating to skin, mucous membranes and upper respiratory tract (5).

Sensitisation
Can cause dermatitis in humans (18).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (19).
In vitro Chinese hamster V79 with metabolic activation induced DNA damage (20).
In vitro human lymphocytes failed to induce chromosomal aberrations and sister chromatid exchanges with and without metabolic activation (21).
Failed to induce sex-linked recessive lethal mutations in *Drosophila melanogaster* (21).
Induced DNA damage in rat liver after intraperitoneal injection (22).
Induced sister chromatid exchange in femoral bone marrow cells in mice after intraperitoneal injection (23) and in recovered bone marrow cells (24).

Other effects

Other adverse effects (human)
Absorption into the body leads to formation of methaemoglobin, which in sufficient concentration can cause cyanosis (25).
Accidental contamination of flour and subsequent ingestion led to an outbreak of jaundice in humans, "Epping Jaundice" (26).
Biopses showed portal inflammation, eosinophil infiltration, cholangitis, cholestasis and different degrees of hepatocellular damage. All patients recovered (27).
Review of working conditions at the Navy Aviation Depot, North Island, CA found workers at risk of contact dermatitis from epoxy resins (and potentially from contact with other substances used to repair composite aircraft). Concern is also expressed about hepatitis from increasing use of methylenedianiline, and lung disease from dust generated by grinding graphite epoxy laminate. Reactive airway dysfunction syndrome at the Depot could be due to significant inhalation exposure to a resin exotherm, and mass psychogenic illness syndrome was also reported (28).

Any other adverse effects
Necrosis of the proximal convoluted tubes reported (species unspecified) (29).
8-600 mg kg^{-1} administered to rats (route unspecified) caused necrotising cholangitis and 200 mg kg^{-1} (or more)

caused periportal necrosis and glycogen loss. Marked mitotic activity was observed in hepatocytes and bile duct epithelium (30).

The toxicity to rats of 4,4'-methylenedianiline (hepatic damage and bile duct necrosis) was increased when the animals were depleted of taurine using β-alanine pretreatment. Thus, taurine may play a role in the toxicity of 4,4'-methylenedianiline (31).

Other comments

Physical properties, use, analysis, carcinogenicity, mammalian toxicity and mutagenicity of 4,4'-methylenedianiline reviewed (25).

Biotransformation, genotoxicity and carcinogenicity reviewed (32).

Industrial processes involving 4,4'-methylenedianiline-containing materials, especially composites, are discussed, including likely exposure, controls and protective equipment (33).

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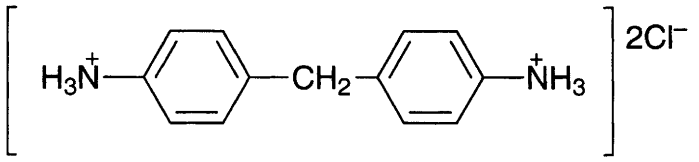
M219 4,4′-methylenedianiline dihydrochloride



$C_{13}H_{16}Cl_2N_2$ **Mol. Wt.** 271.19 **CAS Registry No.** 13552-44-8

Synonyms 4,4′-methylenedibenzenamine dihydrochloride

EINECS No. 236-934-2 **RTECS No.** BY 5426000

Physical properties

M. Pt. 288°C

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Oral (14 day) ♂ rat 1600, 3200 mg kg^{-1} in drinking water, dose-related body-weight reductions observed (1).

Gavage (14 day) ovariectomised ♀ rats 150 mg kg^{-1} body weight, increased weight of uterus, thyroid gland and adrenal gland (2).

Oral (13 wk) ♂, ♀ rats 400, 800 mg l^{-1} in drinking water, a third of low-dose and all of high-dose animals developed bile-duct hyperplasia (1).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (3).

Oral (103 wk) ♂, ♀ mice 150, 300 mg l^{-1} in drinking water, an increased incidence of follicular-cell adenomas of the thyroid was observed in the high-dose animals and a dose-related incidence of thyroid-gland follicular-cell hyperplasia in both ♂ and ♀, with 2/50 ♀ developing thyroid follicular-cell carcinomas. ♀ also had an increased incidence of hepatocellular adenomas, whilst both sexes had increased incidences of hepatocellular carcinomas. Also ♂ had significant increase in liver neoplastic nodules (1,4).

Gavage (30 day) ♀ rats (40-day-old) 30 mg every 3 days in sesame oil. Observed for a further 9 months, no increased incidence in mammary lesions were observed (5).

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M220 methyl ethyl ketone

$$CH_3CH_2COCH_3$$

C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 78-93-3

Synonyms 2-butanone; butan-2-one; ethyl methyl ketone; MEK; methylacetone

EINECS No. 201-159-0 **RTECS No.** EL 6475000

Uses Solvent. Paint stripper and cleaning fluid. Manufacture of cements and adhesives. Intermediate in inorganic synthesis. Extraction solvent in food processing.

Occurrence Natural component of some foods (1).

Physical properties

M. Pt. –87°C **B. Pt.** 80°C **Flash point** –3°C **Specific gravity** 0.8054 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 0.26 **Volatility** v.p. 71.2 mmHg at 20°C ; v.den. 2.42

Solubility Water: 27.5%. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 200 ppm (600 mg m^{-3})

FR-VME 200 ppm (600 mg m^{-3})

JP-OEL 200 ppm (590 mg m^{-3})

SE-LEVL 50 ppm (150 mg m^{-3}) **SE-STEL** 100 ppm (300 mg m^{-3})

UK-LTEL 200 ppm (600 mg m^{-3}) **UK-STEL** 300 ppm (899 mg m^{-3})

US-TWA 200 ppm (590 mg m^{-3}) **US-STEL** 300 ppm (885 mg m^{-3})

UN No. 1193 **HAZCHEM Code** 2[redacted]E **Conveyance classification** flammable liquid

Supply classification highly flammable, harmful

Risk phrases Highly flammable – Irritating to eyes and respiratory system (R11, R36/37)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Avoid contact with the eyes – Take precautionary measures against static discharges (S2, S9, S16, S25, S33)

Ecotoxicity

Fish toxicity

LC_{50} (24-96 hr) mosquito fish, goldfish, fathead minnow 5600-3220 mg l^{-1} (2-4).

Invertebrate toxicity

Cell multiplication inhibition test, *Pseudomonas putida* 1150 mg l^{-1}, *Entosiphon sulcatum* 190 mg l^{-1}, *Microcystis aeruginosa* 10 mg l^{-1}, *Scenedesmus quadricauda* 4300 mg l^{-1} (5,6).

EC_{50} (5, 15, 25 min) *Photobacterium phosphoreum* 49.4, 53.9, 51.9 mM, respectively (7).

EC_{50} (30 min) *Photobacterium phosphoreum* 3373 mg l^{-1} Microtox test (8).

EC_{50} (48 hr) *Daphnia magna* >520 mg l^{-1} (9).

Environmental fate

Degradation studies

Degraded in anaerobic systems, but time required for acclimating degrading organisms was 1 wk (10).

Readily degraded within 5-10 days in aerobic systems using activated sludge, sewage seed or inoculum from polluted surface water (11-15).

BOD_5 1.52-1.92 at 20°C, standard dilution technique and normal sewage seed (16).

Readily oxidised by microorganisms in activated sludge following selection and adaption, 80% removed within 24 hr. Metabolism in unacclimated sludges is slow (17).
IC_{50} (concentration of chemical that inhibits microorganisms by 50%, measured as percentage reductions in oxygen uptake rates compared with controls) with polytox cultures 1.900 g l^{-1}, with activated sludge 1.873 g l^{-1} (18).

Abiotic removal
Removed from soil by evaporation (19).
Reacts photochemically in the atmosphere to give acetaldehyde, $t_{1/2}$ 2 days (20).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2740 mg kg^{-1} (21).
LC_{50} (2 hr) inhalation mouse 40 g m^{-3} (22).
LD_{50} dermal rabbit 13 g kg^{-1} (23).
LD_{Lo} intraperitoneal guinea pig 2000 mg kg^{-1} (24).

Teratogenicity and reproductive effects
Inhalation rat (6-15 day gestation) 0, 400, 1000 or 3000 ppm 7 hr day^{-1}, maternal toxicity (decreased weight gain and increased water consumption). Animals exposed to 3000 ppm suffered slight foetal toxicity and skeletal aberrations. The authors conclude results do not indicate embryotoxic or teratogenic response in rats (25).
Inhalation rat (6-15 day gestation) 1000 or 3000 ppm 7 hr day^{-1} was embryotoxic, foetotoxic and potentially teratogenic. Effects reported include retardation of foetal development and low incidence of acaudia, imperforate anus and brachygnathia (26).
Inhalation pregnant rat 500-1500 ppm 23 hr day^{-1} induced a concentration-dependent increase of intra-uterine mortality, reduced body growth and a delay in the maturation of cerebellar cortex. Concentration-dependent embryotoxic and foetotoxic effects, but no teratogenic effects reported (27).
Inhalation Swiss CD-1 mice (6-15 day gestation) 0-3000 ppm, the 3000 ppm concentration group had reduced mean foetal body weight, malformations observed included cleft palate, fused ribs, missing vertebrae, syndactyly and misaligned sternebrae (28).

Metabolism and toxicokinetics
Measurable quantities (2-13 μg l^{-1}) were detected in expired air of adult humans 3 min after dermal exposure to 100 ml of methyl ethyl ketone applied to 90 cm^{-2} of skin (29).
In workers exposed to 0.3 mg l^{-1} methyl ethyl ketone, lung uptake averaged 1.05 mg min^{-1}, blood concentration averaged 2.6 mg l^{-1}. Methyl ethyl ketone did not persist in tissues. Urinary excretion averaged 487 mg l^{-1} (30).
In workers exposed to TWA concentrations of methyl ethyl ketone of 1.3-223.7 ppm with a mean value of 47.6 ppm, urinary concentrations ranged from 0.20-8.08 mg l^{-1} with a mean value of 1.19 mg l^{-1}. The urinary and blood methyl ethyl ketone levels were significantly correlated with the TWA concentrations in the air samples, and Biological Exposure Indices were calculated as 5.1 mg l^{-1} and 3.8 mg l^{-1} for urine and blood, respectively (31).
Workers exposed to 200 ppm methyl ethyl ketone had a urinary concentration of 1.4 mg l^{-1} (32).

Irritancy
Minor skin contact causes some irritation in humans (23).
Sensory irritation (in the nose and eyes) of mice shows a partial fading (desensitisation) at lower exposure concentrations. Little desensitisation occurs at higher concentrations (33).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation, assays for mitotic gene conversion and chromosomal aberrations negative (34).
Salmonella typhimurium TA102 negative (35).
Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (36).
Saccharomyces cerevisiae D61.M without metabolic activation, strongly induced aneuploidy but not recombination and point mutation (37).

Other effects

Other adverse effects (human)

Prolonged or repeated skin contact can lead to defatting of the skin, leading to cracking, secondary infection and dermatitis (23).

Workers exposed to methyl ethyl ketone were found to have substantial deficits in lung function relative to controls, and to be particularly susceptible to neurological impact (38).

A group of 41 Romanian workers exposed to methyl ethyl ketone in a cable factory and 63 matched controls submitted to a clinical examination and gave samples for the identification of biological exposure markers, underwent motor nerve conduction velocity and neurobehavioural tests, and completed a questionnaire which included questions about alcohol consumption. On the basis of the results it was proposed that the 6-hr permissible exposure limit for methyl ethyl ketone be reduced to 200 mg m^{-3} (39).

Any other adverse effects

Viability of HL-60 cells after treatment with methyl ethyl ketone compared with that of control hepatocytes 48.4%. Phagocytic activity of mouse peritoneal macrophages treated with methyl ethyl ketone compared with that of control macrophages 72% (40).

Other comments

Present in vehicle exhaust, sewage water samples and in leachate from PVC pipe cements (41).

Pharmacokinetics, experimental toxicology, exposure and human health effects reviewed (42-45).

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M221 methyl ethyl ketone oxime

$$CH_3C(=NOH)CH_2CH_3$$

C_4H_9NO **Mol. Wt.** 87.12 **CAS Registry No.** 96-29-7

Synonyms methyl ethyl ketoxime; 2-butanone oxime; MEK oxime; 2-oximinobutane; ethyl methyl ketoxime

EINECS No. 202-496-6 **RTECS No.** EL 9275000

Uses Blocking agent for polymerisation. Catalyst. Oxygen scavenger in steam generators. Extraction of silver.

Physical properties

M. Pt. -29.5°C **B. Pt.** 59-60°C at 15 mmHg **Flash point** 60°C **Specific gravity** 0.9232 at 20°C with respect to water at 4°C

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) – Do not breathe vapour – Avoid contact with the skin (S2, S23, S24)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 9.8 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (5 min) *Photobacterium phosphoreum* 955 ppm Microtox test (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 930 mg kg^{-1} (3).

LD_{50} subcutaneous rat 2700 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (6).
In vitro mouse lymphoma L5178 tk^+/tk^- without metabolic activation positive (6).

Legislation

Toxicological testing required by manufacturers under US Regulations to include testing for oncogenicity, developmental toxicity, reproductive toxicity and mutagenicity (7).
Included in priority list under the US Federal Toxic Substances Control Act (8).

Other comments

Reviews on experimental toxicology and human health effects listed (9).

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M222 methyl ethyl ketone peroxide

$C_8H_{16}O_4$ **Mol. Wt.** 240.21 **CAS Registry No.** 1338-23-4

Synonyms 2-butanone peroxide; Lupersol; MEK peroxide; methyl ethyl ketone hydroperoxide; Quickset extra; Thermacure; Sprayset MEKP

EINECS No. 215-661-2 **RTECS No.** EL 9450000

Uses Cross-linking agent for thermosetting resins.

Physical properties

B. Pt. 118°C (with decomp.) **Flash point** 82°C **Specific gravity** 1.170

Occupational exposure

FR-VLE 0.2 ppm (1.5 mg m^{-3})
SE-CEIL 0.2 ppm (1.5 mg m^{-3})
UK-STEL 0.2 ppm (1.5 mg m^{-3})
US-STEL ceiling limit 0.2 ppm (1.5 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 470-484 mg kg^{-1} (1,2).
LC_{50} (4 hr) inhalation mouse, rat 170-200 ppm (2).
LD_{50} intraperitoneal rat 65 mg kg^{-1} (1).

Irritancy

Dermal rabbit (duration unspecified) 500 mg and 3 mg instilled into rabbit eye. Results for observed irritation equivocal (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (3).

Other comments

Usually supplied as a 50% solution in dimethyl phthalate (4).
Strong oxidising agent and contact with organic materials can create a fire hazard.
Contaminant in air samples collected in the vicinity of a fibreglassing plant (5).
Reviews on experimental toxicology and human health effects listed (6).

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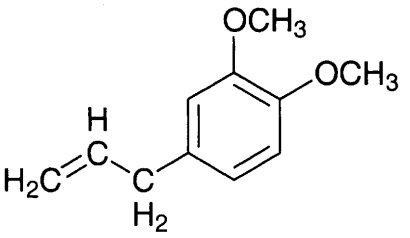
M223 methyleugenol



$C_{11}H_{14}O_2$ **Mol. Wt.** 178.23 **CAS Registry No.** 93-15-2

Synonyms 4-allyl-1,2-dimethoxybenzene; 1-allyl-3,4-dimethoxybenzene; 4-allylveratrole; 1,2-dimethoxy-4-allylbenzene; 1-(3,4-dimethoxyphenol)-2-propene; eugenol methyl ether; ENT 21040

EINECS No. 202-223-0 **RTECS No.** CY 2450000

Uses Flavouring in foods and drinks. Fragrance in perfumes, soaps, detergents. Has been used as an insect attractant in eradication programmes and as an anaesthetic in rodents.
Occurrence Found in *Clarkia breweri* flowers and in many essential oils.

Physical properties

M. Pt. –4°C **B. Pt.** 254.7°C **Flash point** >110°C **Specific gravity** 1.0396 at 20°C with respect to water at 4°C
Volatility v.p. ~0.02 mmHg at 20°C, 1 mmHg at 85°C
Solubility Water: <1 mg ml^{-1} at 19°C. Organic solvents: ≥100 mg ml^{-1} at 19°C in acetone, 95% ethanol, and DMSO

Ecotoxicity

Fish toxicity
LC_{50} *Salmo gairdneri* (96 hr) 6.0 ppm (1).
LC_{50} *Lepomis macrochiras* (96 hr) 8.1 ppm (1).

Environmental fate

Degradation studies
Dissipated rapidly from both soil and water. In soil 81% was lost within 96 hr at 22°C, $t_{1/2}$ ~6 hr. In water 77% was lost within 96 hr at 22°C, $t_{1/2}$ ~34 hr (1).

Adsorption and retention
Immobile in sand, clay and fine sandy loam soils (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral red-winged blackbird >100 mg kg^{-1} (2).
LD_{50} oral rat 1179 mg kg^{-1} (3).
LD_{50} dermal rabbit >2025 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 540 mg kg^{-1} (4).
LD_{50} intravenous mouse 112 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Gavage F344/N rats administered 0-1000 mg kg^{-1} 5 days wk^{-1} for 14 wk. All rats survived to the end of the study. Significantly lower body weights were seen in rats administered 300 or 1000 mg kg^{-1} doses compared with controls that received deionised water by gavage. Erythrocyte microcytosis was seen in ♂ rats administered 300 mg kg^{-1} and in both sexes administered 1000 mg kg^{-1}. Increased platelet counts were seen in all groups administered ≥100 mg kg^{-1} as were increased serum activities of alanine aminotransferase and sorbitol dehydrogenase (suggestive of hepatocellular injury), increased bile acid concentrations (consistent with cholestasis or altered hepatic function), hypoproteinaemia and hypoalbuminaemia, and a significant increase in the incidences of atrophy and chronic inflammation of the mucosa of the glandular stomach. Liver weights of 100-1000 mg kg^{-1} ♂s and 300-1000 mg kg^{-1} ♀s and testis weights of 1000 mg kg^{-1} ♂s were significantly increased. Increased incidences of hepatocyte cytologic alteration, cytomegaly, kupffer cell pigmentation, basophilic (♂s) or mixed foci of cellular alteration, and bile duct alteration were observed in rats dosed with 300-1000 mg kg^{-1}. One rat administered the highest dose had a hepatocellular adenoma (5).
Gavage B6C3F1 mice administered 0-1000 mg kg^{-1} 5 days wk^{-1} for 14 wk. Of the groups receiving the highest dose only one ♂ survived to the end of the study. Mean body-weight gains in mice receiving 300 mg kg^{-1} were significantly less than those of the controls receiving deionised water by gavage. A significant increase in liver weights occurred in ♂ mice dosed with 30-300 and ♀ mice with 300 mg kg^{-1}. ♂ Mice administered 10 or 30 mg kg^{-1} had significantly lower cauda epididymis, epididymis and testis weight compared with controls. Significantly lower spermatozoal concentrations were seen in mice dosed with 100 mg kg^{-1}. Increased incidences of atrophy, degeneration, necrosis, oedema, mitotic alteration and cystic glands of the fundic region of the glandular stomach were increased in one or more groups administered ≥30 mg kg^{-1} (5).

Carcinogenicity and chronic effects
The National Toxicology Program studied mice and rats via gavage. There was clear evidence of carcinogenic activity in both ♂ and ♀ mice and rats (5).

Gavage B6C3F1 mice (2 yr) received 0, 37, 75, or 150 mg kg^{-1} 5 days wk^{-1} for 104 wk. Dosed ♂ mice had survival rates similar to controls; survival rates of dosed ♀s were significantly less. Mean body weights of ♂ mice were generally less than those of controls after wk 81, 41, and 17 for 37, 75, and 150 mg kg^{-1} groups, respectively; mean body weights of ♀s were less by wk-17. Increased incidences of liver neoplasms were seen in ♂s and ♀s. Neuroendocrine tumours of the glandular stomach occurred in ♂s. Significant increases in non-neoplastic lesions of the liver and glandular stomach were seen in both sexes (5).
Gavage F344/N rats (2 yr) received 0, 37, 75, or 150 mg kg^{-1}, 5 days wk^{-1} for 105 wk or 300 mg kg^{-1} 5 days wk^{-1} for 53 wk. All 150 mg kg^{-1} ♂s died before the end of the study. Survival of 150 mg kg^{-1} ♀s was slightly lower than that for controls. Mean body weights of all dosed groups were less than controls throughout most of the study. Significantly increased incidences of liver neoplasms and neuroendocrine tumours of the glandular stomach in ♂s and ♀s and increased incidences of kidney neoplasms, malignant mesothelioma, mammary gland fibroadenoma, and subcutaneous fibrom and fibroma or fibrosarcoma (combined) in ♂s occurred. Significant increases in non-neoplastic lesions of the liver and glandular stomach were seen in both sexes (5).

Metabolism and toxicokinetics

Rapidly absorbed following oral administration to mice and rats (5).
Cytochrome P_{450} mediated metabolism of methyleugenol to the proximate carcinogen 1'-hydroxymethyleugenol was investigated in liver microsomes from untreated Fischer 344 rats. The reaction is catalysed by high affinity (Km of 74.9 ± 9.0 μM, Vmax 1.42 ± 0.17 nmol min^{-1} $nmol^{-1}$ P_{450}) and low affinity enzymic components. Administration of methyleugenol, 0-300 mg kg^{-1} day^{-1} for 5 days to rats *in vivo* caused dose-dependent auto-induction of 1'-hydroxylation *in vitro* which could be attributed to the inclusion of various cytochrome P450 isozymes. The authors suggest that high-dose rodent carcinogenicity studies are likely to over-estimate the risk to human health posed by methyleugenol. A marked variation in the rate of 1'-hydroxylation *in vitro* by 13 human liver samples (by 37-fold), with the highest activities similar to those found in rat liver microsomes from control animals, suggests that the carcinogenic risk from dietary ingestion of methyleugenol could vary widely in the human population (6).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation, gene mutations negative (5).
Sister chromatid exchanges in cultured CHO cells *in vitro* with metabolic activation positive (5).
Chromosomal aberrations in cultured CHO cells *in vitro* with and without metabolic activation negative (5).
Micronucleated eythrocytes in mouse peripheral blood *in vivo* negative (5).

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M224 methyl fluorosulfonate

FSO_3CH_3

CH_3FO_3S **Mol. Wt.** 114.10 **CAS Registry No.** 421-20-5

Synonyms fluorosulfuric acid, methyl ester; methyl fluorosulfate; Magic Methyl

EINECS No. 207-004-3 **RTECS No.** LP 0720000

Uses In organic synthesis as a methylating agent.

Physical properties

M. Pt. –95°C **B. Pt.** 92-94°C **Specific gravity** 1.412

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 112 mg kg^{-1} (1).

LC_{50} (1 hr) inhalation rat 5-6 ppm (1).

LD_{Lo} dermal rabbit 455 mg kg^{-1} (1).

Irritancy

100 mg instilled into rabbit eye for 4 sec caused severe irritation (1).

Genotoxicity

Salmonella typhimurium TA1538 without metabolic activation positive, TA98 weakly positive, TA100 and TA1535 negative. BHK 21/C13 cell transformation assay positive (2).

Other effects

Other adverse effects (human)

Can cause fatal pulmonary oedema (3).

Acute exposure resulted in the death of a research worker (4).

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M225 *N*-methylformamide

$HC(O)NHCH_3$

C_2H_5NO **Mol. Wt.** 59.07 **CAS Registry No.** 123-39-7

Synonyms monomethylformamide

EINECS No. 204-624-6 **RTECS No.** LQ 3000000

Physical properties

M. Pt. –4°C (99% pure) **B. Pt.** 198-199°C (99% pure) **Flash point** 110°C (99% pure) **Specific gravity** 1.011

Ecotoxicity

Fish toxicity

In vitro zebra fish embryo 0.01-1.5% v/v in incubation media during embryonic development, caused changes to vertebral column, neural tube, heart and blood vessels, and growth retardation (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 2.6, 4.0 g kg^{-1}, respectively (2,3).
LD_{50} subcutaneous mouse 3.1 g kg^{-1} (4).
LD_{50} intraperitoneal mouse, rat 802, 3500 mg kg^{-1}, respectively (5,3).
LD_{50} intravenous mouse 1.6 mg kg^{-1} (2).
LD_{50} intramuscular mouse 2.7 g kg^{-1} (2).

Sub-acute and sub-chronic data

Inhalation (2 wk) ♂ rat 0, 50, 130, 400 ppm 6 hr day^{-1} 5 days wk^{-1}, followed by 2 wk post-exposure recovery period. 130, 400 ppm caused liver damage, with the changes being more marked in the 400 ppm group, the effects were partially reversible. No other organs were affected. No-observed-effect level was 50 ppm (6).

Teratogenicity and reproductive effects

Logistic regression and discriminant analysis used to predict developmental toxicity in humans, negative. Designated positive for developmental toxicity in rats, mice and negative in rabbits (7).
In vitro chick embryos 0.01-1.5% v/v in incubation media during embryonic development, caused changes to vertebral column, neural tube, heart, blood vessels, and growth retardation (1).
Inhalation ♀ rats (day 7-16 of gestation) 50-150 ppm. One maternal death, embryolethality and development toxicity was observed at 150 ppm, along with significant decreases in weight gain and feed consumption. Significant foetal body-weight decreases were also observed at 50 ppm (8).

Metabolism and toxicokinetics

In vitro suspensions of mouse hepatocytes metabolised compound to *N*-alkylcarbamoylating metabolites and depleted pools of glutathione. The amount of metabolism and glutathione depletion were dose-dependent (9).
In vivo rat, mouse [^{14}C]-*N*-methylformamide metabolites detected in urine included an (unspecified) *N*-acetylcysteine conjugate, methylamine and *N*-hydroxymethylformamide. Metabolism was more extensive and faster in mice than in rats (10).
Metabolised *in vivo* (species not specified) to *N*-acetyl-*S*-(*N*-methylcarbamoyl)cysteine via oxidation at the formyl carbon. *In vitro* mice microsomes, cytosol; the metabolite was generated by microsomes but not the cytosol (11).

Irritancy

Eye (24, 48, 72 hr) rabbit 100 µl did not cause irritation (12).

Other effects

Any other adverse effects

Produced a dose-dependent zone 3 haemorrhagic necrosis in mice, the threshold dose was 100-200 mg kg^{-1}. 1000 mg kg^{-1} in rats caused hepatic damage in some animals with a slight elevation in plasma transaminases. There was a recordable difference between the hepatotoxic effects in mice and rats. Also liver nonprotein sulfhydryl was dose-dependently depleted in mice but not rats (10).
In vivo murine TL × 5 lymphoma growth was inhibited by *N*-methylformamide. *In vitro* murine TL × 5 lymphoma cells (72 hr) 0.25, 1% v/v growth rate and viability decreased dose-dependently (13).

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M226 methyl formate

$$CH(=O)OCH_3$$

$C_2H_4O_2$ **Mol. Wt.** 60.05 **CAS Registry No.** 107-31-3

Synonyms formic acid, methyl ester; methyl methanoate

EINECS No. 203-481-7 **RTECS No.** LQ 8925000

Uses Blowing agent. Organic synthesis. Resin hardener. Solvent. Fumigant and larvicide.
Occurrence Detected in cigarette smoke and gasoline engine exhaust (1,2).
Flavour component of some fruits (3).

Physical properties

M. Pt. –100°C **B. Pt.** 34°C **Flash point** –29°C (closed cup) **Specific gravity** 0.975 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.264 (3) **Volatility** v.p. 400 mmHg at 16°C ; v.den. 2.07
Solubility Water: ~ 33%. Organic solvents: ethanol, methanol

Occupational exposure

DE-MAK 50 ppm (120 mg m^{-3})
FR-VME 100 ppm (250 mg m^{-3})
SE-LEVL 100 ppm (250 mg m^{-3}) **SE-STEL** 150 ppm (350 mg m^{-3})
UK-LTEL 100 ppm (250 mg m^{-3}) **UK-STEL** 150 ppm (374 mg m^{-3})
US-TWA 100 ppm (246 mg m^{-3}) **US-STEL** 150 ppm (368 mg m^{-3})

UN No. 1243 **HAZCHEM Code** 2YE **Conveyance classification** flammable liquid
Supply classification extremely flammable
Risk phrases Extremely flammable (R12)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor 0.6 indicates that environmental pollution is unlikely (4).

Environmental fate

Abiotic removal

$t_{1/2}$ for hydrolysis at 25°C: 22 days at pH 6; 2.2 days at pH 7; 9.1 hr at pH 8; and 0.91 hr at pH 9 (5).
Estimated $t_{1/2}$ for reaction with photochemically produced hydroxyl radicals in the atmosphere 74 days (6).
$t_{1/2}$ for volatilisation from model river water 5.3 hr and from pond water 60 hr (4,7).

Adsorption and retention

Estimated K_{oc} 5 indicates that methyl formate will leach readily from soil (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit 1620 mg kg^{-1} (8).
LC_{50} (1 hr) inhalation guinea pig ~ 25,000 ppm (1).

Irritancy

Causes severe irritation. High concentrations are extremely destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin (9).

Other effects

Other adverse effects (human)

Inhalation human (1 min) 1500 ppm caused no adverse effects (2).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

Present in wastewater from urea-formaldehyde resin manufacturing plant (11).
Environmental fate reviewed (3).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).
Autoignition temperature 465°C.

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M227 *N*-methyl-*N*-formylhydrazine

$NH(CH_3)NHCHO$

$C_2H_6N_2O$ **Mol. Wt.** 74.08 **CAS Registry No.** 758-17-8

Synonyms formic acid, methylhydrazide; 1-formyl-1-methylhydrazine; MFH

RTECS No. LQ 8940000

Occurrence In the edible false morel mushroom (*Gyromitra esculenta*).

Physical properties

B. Pt. 95°C at 12 mmHg

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 118 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Swiss mice given 0.0078% in drinking water for life developed tumours: benign hepatomas, adenomas and adenocarcinomas of the lungs, adenomas of the gall bladder, cholangiomas, liver cell carcinomas and cholangiocarcinomas (2).

Administered as 40 wkly subcutaneous injections to Swiss mice at doses of 20 μg g^{-1} body weight for ♀ and 10 μg g^{-1} for ♂. Lung tumour incidence was significantly increased: 56% in ♀ and 40% in ♂. Other organs showed no detectable carcinogenic effect (3).

Metabolism and toxicokinetics

Hydrolysed non-enzymatically from acetaldehyde formylmethylhydrazone. Under physiological conditions hydrolyses to *N*-methylhydrazine and formic acid (4-6).

Detected in the peritoneal fluid of mice 3 hr after oral administration of 9 mg acetaldehyde formylmethylhydrazone (7).

Oxidation to a hydroxylamine derivative is mediated by rat liver cytochrome P_{450}, according to a spectral study (8).

Genotoxicity

In vitro rat, mouse hepatocytes DNA repair test negative (9).

Other effects

Any other adverse effects

Intragastric administration to Wistar rats had no effect on renal function (10).

Following oral administration to rats there was a transient time- and dose-dependent decrease in cytochrome P_{450} and an inhibition of cytochrome P_{450}-mediated metabolism in liver microsomes of *p*-nitroanisole and aminopyrine (11).

Lowered the cytochrome P_{450} concentration in rat liver microsomes following intragastric administration (8).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

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3. Toth, B. et al *Neoplasma* 1983, **30**(4), 437-441.
4. Nagel, D. et al *Proc. Am. Assoc. Cancer Res.* 1976, **17**, 76.
5. Nagel, D. et al *Cancer Res.* 1977, **37**, 3458-3460.
6. von Wright, A. et al *Toxicol. Lett.* 1978, **2**, 261-265.
7. von Wright, A. et al *Mutat. Res.* 1978, **54**, 167-173.
8. Braun, R. et al *Xenobiotica* 1980, **10**, 557-564.
9. Mori, H. et al *Jpn. J. Cancer Res.* 1988, **79**, 204-211.
10. Braun, R. et al *Toxicology* 1979, **13**, 187-196.
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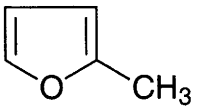
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M228 2-methylfuran



C_5H_6O **Mol. Wt.** 82.10 **CAS Registry No.** 534-22-5

Synonyms α-methylfuran; 5-methylfuran; Sylvan; Silvan

EINECS No. 208-594-5 **RTECS No.** LU 2625000

Uses Chemical intermediate.

Physical properties

M. Pt. –88.7°C **B. Pt.** 63-66°C **Flash point** –22°C **Specific gravity** 0.914 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.85 **Volatility** v.p. 139 mmHg at 20°C ; v.den. 2.8
Solubility Water: 3 g l^{-1} at 20°C

Occupational exposure

UN No. 2301 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity
LOEC reproduction (semi-chronic) *Scenedesmus quadricauda* 40 mg l^{-1} (1).
LOEC reproduction (semi-chronic) *Microcystis aeruginosa* 40 mg l^{-1} (2).
LOEC reproduction (semi-chronic) *Uronema parduczi* 26 mg l^{-1} (2).

Environmental fate

Degradation studies
Disappearance in sulfate-reducing and methanogenic aquifer slurries was measured under anaerobic conditions. Sulfate-reducing aquifer slurries 112, 29, 34% remaining after 1, 3, 8 month, respectivel; methanogenic aquifer slurries 111, 106, 102% of substrate remaining after 1, 3, 8 months, respectively (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 98 mg kg^{-1} (4).
LD_{50} oral rat 167 mg kg^{-1} (5).

LC_{Lo} (4 hr) inhalation rat 377 ppm (5).
LC_{50} (2 hr) inhalation rat 10 g m^{-3} (6).

Genotoxicity

In vitro Chinese hamster ovary cells without metabolic activation, high frequency of chromatid breaks and sister chromatid exchanges (7).

Other comments

Inhibited the mutagenicity of known mutagens Trp-P-1, B[*a*]P and 2-aminofluorene towards *Salmonella typhimurium* TA98, TA100 with metabolic activation (8).

References

1. Bringmann, G. et al *Water Res.* 1980, **14**, 231-41.
2. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9).
3. Kuhn, E. P. et al *Environ. Toxicol. Chem.* 1989, **8**, 1149-1158
4. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
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6. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
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M229 6-methyl-1-heptanol

$$(CH_3)CH(CH_2)_4CH_2OH$$

$C_8H_{18}O$ **Mol. Wt.** 130.23 **CAS Registry No.** 26952-21-6

Synonyms isooctyl alcohol; isooctanol

EINECS No. 248-133-5 **RTECS No.** NS 7700000

Physical properties

M. Pt. <100°C **B. Pt.** 186°C at 1 mmHg **Flash point** ~70-80°C **Specific gravity** 0.832 at 20°C with respect to water at 20°C
Solubility Water: 640 mg l^{-1} at 25°C

Occupational exposure

FR-VME 50 ppm (270 mg m^{-3})
UK-LTEL 50 ppm (271 mg m^{-3})
US-TWA 50 ppm (266 mg m^{-3})

Ecotoxicity

Invertebrate toxicity
EC_{50} (24 hr) *Daphnia magna* 115 mg l^{-1}; EC_0 (24 hr) *Daphnia magna* 77 mg l^{-1} (1).
NOEC (21 day) *Daphnia* reproduction test 2.3 mg l^{-1} (nominal value), 1.6 mg l^{-1} (minimum value) (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1480, 1670 mg kg^{-1}, respectively (2,3).
LD_{50} dermal rabbit 2520 mg kg^{-1} (4).

Irritancy

100 mg instilled into rabbit eyes caused severe irritation. 2600 mg kg^{-1} applied to rabbits skin for 24 hr caused moderate irritation (2).

Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (5).

References

1. Kuhn, R. et al *Water Res.* 1989, **23**(4), 501-510.
2. *Am. Ind. Hyg. Assoc. J.* 1973, **34**, 493.
3. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
4. Monick, J. A. *Alcohols and their Chemistry* 1968, Reinhold Books, New York, USA.
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

M230 5-methyl-3-heptanone

$$CH_3CH_2CH(CH_3)CH_2C(O)CH_2CH_3$$

$C_8H_{16}O$ **Mol. Wt.** 128.21 **CAS Registry No.** 541-85-5

Synonyms 5-methylheptan-3-one; ethyl *sec*-amyl ketone; ethyl isoamyl ketone

EINECS No. 208-793-7 **RTECS No.** MJ 7350000

Uses Solvent for nitrocellulose-alkyd, nitrocellulose-maleic, and vinyl resins.
Occurrence Produced by *Streptomyces cinamoneus*-like organisms and contributes to the characteristic odours of actinomycete cultures.

Physical properties

B. Pt. 157-162°C **Flash point** 59°C **Specific gravity** 0.823 at 20°C **Volatility** v.den. 4.4
Solubility Water: slightly soluble in water. Organic solvents: most organic solvents

Occupational exposure

FR-VME 25 ppm (130 mg m^{-3})
SE-LEVL 25 ppm (130 mg m^{-3}) **SE-STEL** 50 ppm (250 mg m^{-3})
UK-LTEL 25 ppm (133 mg m^{-3})
US-TWA 25 ppm (131 mg m^{-3})

UN No. 2271 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification irritant
Risk phrases Flammable – Irritating to eyes and respiratory system (R10, R36/37)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Ecotoxicity

Invertebrate toxicity

Cell multiplication inhibition test *Pseudomonas putida* 25 mg l^{-1}, *Microcystis aeruginosa* 40 mg l^{-1}, *Scenedesmus quadricauda* 53 mg l^{-1}, *Entosiphon sulcatum* 256 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3500 mg kg^{-1} (2).
LD_{50} oral mouse 3800 mg kg^{-1} (2).
LD_{50} oral guinea pig 2500 mg kg^{-1} (3).
LC_{Lo} (8 hr) inhalation rat 3484 ppm (2).
LC_{Lo} (4 hr) inhalation mouse 3484 ppm (2).

Irritancy

Dermal rabbit 500 mg caused mild irritation (2).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology, physico-chemical properties, exposure levels, epidemiology, workplace experience listed (4).

References

1. Bringmann, G. *Water Res.* 1980, **14**, 231-241.
2. *Sax's Dangerous Properties of Industrial Materials*, 8th ed., 1992, Von Nostrand Reinhold, New York, USA.
3. *Biochem. Pharmacol.* 1967, **16**, 63.
4. *ECETOC Technical Report No. 30(5)* 1994, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M231 methylheptenone

$$(CH_3)_2C{=}CHCH_2CH_2C(O)CH_3$$

$C_8H_{14}O$ **Mol. Wt.** 126.20 **CAS Registry No.** 409-02-9

EINECS No. 206-990-2

Uses In perfumery.

Occurrence Occurs as 6-methyl-5-hepten-2-one in a variety of fruits, flowers and leaves.

Physical properties

M. Pt. -67°C **B. Pt.** 173-174°C **Flash point** 50°C

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Environmental fate

Degradation studies

Epoxidation by fungi can occur (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3.5 g kg^{-1} (2).

References

1. Abraham, W. R. *J. Essent. Oil Res.* 1990, **2**(5), 251-7.
2. *Food Cosmet. Toxicol.* 1975, **13**, 859

M232 6-methyl-5-hepten-2-one

$$(CH_3)_2C{=}CHCH_2CH_2C(O)CH_3$$

$C_8H_{14}O$ **Mol. Wt.** 126.20 **CAS Registry No.** 110-93-0

Synonyms 2-methyl-2-hepten-6-one; 2-methyl-6-oxo-2-heptene; 2-oxo-6-methylhept-5-ene; 6-methyl-Δ^5-hepten-2-one; Sulcatone

EINECS No. 203-816-7 **RTECS No.** MJ 9700000

Occurrence Occurs in a variety of fruits, flowers and leaves.

Physical properties

B. Pt. 73°C at 18 mmHg **Flash point** 50°C (closed cup) **Specific gravity** 0.855 **Volatility** v.den. 4.4

Occupational exposure

UN No. 1224

Ecotoxicity

Fish toxicity

Trout, bluegill sunfish, yellow perch and goldfish (24 hr) 5 ppm non-toxic. 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; and temperature 12.8°C (1).

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 17.4 ppm Microtox test (2).

Mammalian & avian toxicity

Acute data

LD_{50} (estimated) oral redwing blackbird >111 mg kg^{-1} (3).

LD_{50} intragastric mouse, rat 2.41, 4.25 g kg^{-1}, respectively (4).

Irritancy

Skin irritation in guinea pigs, mice and rabbits (dose and duration unspecified) (4).

Sensitisation

Caused dermatitis in rabbits, mice and guinea pigs (3).

Legislation

Recommended maximum permissible concentration for occupational inhalation exposure, 6.75 mg m^{-3}.

References

1. US EPA *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, US EPA, Washington DC, USA.
2. Kaiser, K. L. E. *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
4. Migukina, N. V. et al *Gig. Tr. Prof. Zabol.* 1989, (8), 52-53 (Russ.) (*Chem. Abstr.* **112**, 50126x)

M233 5-methyl-2-hexanone

$$CH_3CH(CH_3)CH_2CH_2C(O)CH_3$$

$C_7H_{14}O$ **Mol. Wt.** 114.19 **CAS Registry No.** 110-12-3

Synonyms 5-methylhexan-2-one; isoamyl methyl ketone; isopentyl methyl ketone; methyl isoamyl ketone; methyl isopentyl ketone

EINECS No. 203-737-8 **RTECS No.** MP 3850000

Physical properties

M. Pt. -74°C **B. Pt.** 144°C **Flash point** 35.98°C **Specific gravity** 0.888 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.88
Solubility Water: 5.4 g l^{-1}. Organic solvents: miscible with most organic solvents

Occupational exposure

FR-VME 50 ppm (240 mg m^{-3})
SE-LEVL 25 ppm (120 mg m^{-3}) **SE-STEL** 50 ppm (250 mg m^{-3})
UK-LTEL 50 ppm (237 mg m^{-3}) **UK-STEL** 100 ppm (475 mg m^{-3})
US-TWA 50 ppm (234 mg m^{-3})

UN No. 2302 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification flammable
Risk phrases Flammable (R10)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 159 mg l^{-1} (1).

Invertebrate toxicity
LOEC reproduction *Microcystis aeruginosa* 90 mg l^{-1} (2).
Toxicity threshold (cell multiplication inhibition test) *Pseudomonas putida, Scenedesmus quadricauda, Entosiphon sulcatum,* and *Uronema parduczi Chatton-Lwoff* 115-980 mg l^{-1} (3,4).
EC_{50} (5 min) *Photobacterium phosphoreum* 972-1438 ppm Microtox test (5).

Environmental fate

Abiotic removal
Activated carbon adsorbability (0.169 g g^{-1} carbon), influent contained 986 mg l^{-1}, effluent contained 146 mg l^{-1}, a 85.2% reduction (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4.8 g kg^{-1} (7,8).

LC_{50} (4 hr) inhalation rat 4000 ppm (7).

LD_{50} dermal rabbit 10 g kg^{-1} (9).

References

1. Veith, G. D. et al in *Aquatic Toxicology and Hazard Assessment: 6th Symposium* 1983, ASTM STP 803, American Society for Testing and Materials, Philadelphia, PA, USA.
2. Bringman, G. et al *GWF Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9) (Ger.).
3. Bringman, G. et al *Z. Wasser/Abwasser Forsch.* 1980, (1), 26-31.
4. Bringman, G. et al *Water Res.* 1980, **14**(1), 231-241.
5. Curtis, C. A. et al *Aquatic Toxicology and Hazard Assessment: 5th Conference* 1982, 170-178, J. G. Pearson (Ed.), ASTM STP 766, American Society for Testing and Materials, Philadelphia, PA, USA.
6. Guisti, D. M. et al *J. Water Pollut. Control Fed.* 1971, **43**(8), 1716.
7. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
8. Kennedy, G. L. et al *Toxicol. Lett.* 1991, **56**(3), 317-326.
9. *Union Carbide Data Sheet* 7/8/63, Union Carbide Corp., New York, USA

M234 methylhydrazine

NH_2NHCH_3

CH_6N_2 **Mol. Wt.** 46.07 **CAS Registry No.** 60-34-4

Synonyms monomethylhydrazine; MMH

EINECS No. 200-471-4 **RTECS No.** MV 5600000

Uses Intermediate in chemical synthesis. In rocket fuel. Solvent.

Occurrence In the edible mushroom *Gyromitra esculenta*.

Physical properties

M. Pt. –52.4°C **B. Pt.** 87°C **Flash point** 21°C (closed cup) **Specific gravity** 0.874 at 25°C

Volatility v.den. 1.6

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

Occupational exposure

FR-VME 0.2 ppm (0.35 mg m^{-3})

US-TWA 0.01 ppm (0.019 mg m^{-3})

UN No. 1244 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance, corrosive, danger of fire (flammable liquid)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) guppy 2.58 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (5, 10 or 15 min) *Photobacterium phosphoreum* 15.3 ppm Microtox test (2).

Environmental fate

Nitrification inhibition

Nitrosomonas sp., denitrifying bacteria, and *Nitrobacter* sp. 50% inhibition 1.4, 4.3, 12.3 mg l^{-1}, respectively (3).

Degradation studies

Achromobacter sp., *Pseudomonas* sp. in culture media and soil samples could not utilise methylhydrazine as a sole carbon source, and did not promote degradation to its final oxidation products of carbon dioxide and water (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 33, 70 mg kg^{-1}, respectively (5,6).
LC_{50} (1-4 hr) inhalation rat, mouse, dog 34, 56, 96 ppm, respectively (7-9).
LC_{50} (1 hr) inhalation Rhesus monkey 162 ppm (10).
Intraperitoneal rat, 25-60 mg kg^{-1} caused proximal tubule damage in kidneys (11).
LD_{50} dermal rabbit, rat 95, 183 mg kg^{-1}, respectively (12,13).
LD_{50} subcutaneous rat 25 mg kg^{-1} (14).
LD_{50} intravenous rat, mouse 17, 33 mg kg^{-1}, respectively (13,15).
LD_{50} intraperitoneal rat, mouse 15, 21 mg kg^{-1}, respectively (13,16).

Carcinogenicity and chronic effects

Oral (lifetime study) Swiss mice 0.01% in drinking water. Enhanced the development of lung tumours by shortening their latent period (17).

Genotoxicity

Escherichia coli PQ37 with and without metabolic activation, SOS chromotest negative (18).
Salmonella typhimurium TA100, TA98, TA1535, TA1537, TA1538 with and without metabolic activation negative (19).
Salmonella typhimurium TA100 positive for spot test, negative for plate test with and without metabolic activation and host-mediated assay (20).

Other effects

Other adverse effects (human)

Inhalation (10 min) ♂ 90 ppm, primary effect lachrymation and bronchospasms, although these were not excessive. Clinical chemistry was normal, the only haematologic abnormality was Heinz body formation in 3-5% of erythrocytes on day-7 post-exposure, which disappeared by day-60 (10).

Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (21).
Strong reducing agent. Will ignite spontaneously in contact with strong oxidising agents. Autoignition temperature 194°C.

References

1. Slonium, A. R. *Water Res.* 1977, **11**, 889-895.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Kane, D. A. et al *Arch. Environ. Contam. Toxicol.* 1983, 447-453.
4. Ou, T. L. *Bull. Environ. Contam. Toxicol.* 1988, **41**(6), 851-857.
5. Witkin *Arch. Ind. Health* 1956, **13**, 34.
6. Gregory, et al *Clin. Toxicol.* 1971, **4**, 435.

7. *Aerospace Medical Research Laboratory Report* 1967, TR-67-137, Air Force Systems Command, Wright-Patterson Air Force Base, OH, USA.
8. *AMA Arch. Ind. Hyg. Assoc.* 1955, **12**, 609.
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10. *Patty's Industrial Hygiene and Toxicology* 3rd ed., 1981, 2A, John Wiley & Sons, New York, USA.
11. Hong, W. et al *Zhongguo Yaolixue Yu Dulixe Zazhi* 1987, **1**(5), 366-370 (Ch.) (*Chem. Abstr.* **108**, 144927d).
12. *Proc. Soc. Exp. Biol. Med.* 1969, **131**, 226.
13. *Clin. Toxicol* 1971, **435**, 4.
14. *Br. J. Cancer* 1974, **30**, 429.
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17. Toth, B. *Int. J. Cancer* 1972, **9**, 109-118.
18. Von der Hude, W. et al *Mutat. Res.* 1988, **203**(2), 81-84.
19. Mortelmans, K. et al *Environ. Mutagen.* 1986, **7**, 1-119.
20. von Wright, A. et al *Mutat. Res.* 1978, **54**, 167-173.
21. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M235 methylhydrazine sulfate

$$CH_3NHNH_2.H_2SO_4$$

$CH_8N_2O_4S$ **Mol. Wt.** 144.15 **CAS Registry No.** 302-15-8

Synonyms methylhydrazine monosulfate

EINECS No. 206-115-4 **RTECS No.** MV 7750000

Physical properties

M. Pt. 142°C

Solubility Organic solvents: slightly soluble in ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 160 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral (lifetime study) Swiss mice 0.01% in drinking water. 46% developed lung tumours, 20% of ♀ and 16% of ♂ developed malignant lymphomas and 6% of ♀ developed breast tumours (2).

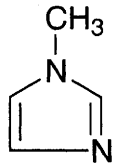
Genotoxicity

Salmonella typhimurium TA100, TA1537, TA98 with and without metabolic activation negative (3).
In vitro rat, mouse hepatocyte/DNA repair test positive (4).

References

1. *Russ. Pharmacol. Toxicol.* 1973, **36**, 27.
2. Toth, B. *Int. J. Cancer* 1972, **9**, 109-118.
3. Shimizu, H. et al *Jpn. J. Hyg.* 1978, **33**, 474-485 (Japan.).
4. Mori, H. et al *Jpn. J. Cancer Res.* 1988, **79**(2), 204-211

M236 1-methylimidazole



$C_4H_6N_2$ **Mol. Wt.** 82.11 **CAS Registry No.** 616-47-7

Synonyms 1-methyl-1*H*-imidazole

EINECS No. 210-484-7 **RTECS No.** NI 7000000

Physical properties

M. Pt. –60°C **B. Pt.** 198°C **Flash point** 92°C (closed cup) **Specific gravity** 1.030

Occupational exposure

Supply classification corrosive

Risk phrases Harmful in contact with skin and if swallowed – Causes burns (R21/22, 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 1400 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 380 mg kg^{-1} (1).

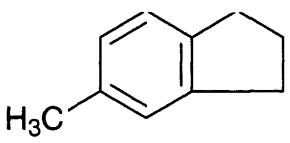
Other comments

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

References

1. *Toxicol. Appl. Pharmacol.* 1969, **14**, 301.
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

M237 5-methylindan



$C_{10}H_{12}$ **Mol. Wt.** 132.21 **CAS Registry No.** 874-35-1

Synonyms 1*H*-indene, 2,3-dihydro-5-methyl

Ecotoxicity

Invertebrate toxicity

Phaeodactylum tricornutum (24 hr) 1-2 mg l^{-1} reduced photosynthesis by 50%. 300 μg l^{-1} modified the feeding of *Trigriopus brevicornis* (1).

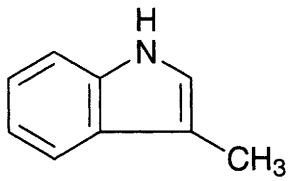
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. Lacaze, J. C. et al *Sci. Eau* 1987, **6**(4), 415-433.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M238 3-methylindole



C_9H_9N **Mol. Wt.** 131.18 **CAS Registry No.** 83-34-1

Synonyms β-methylindole

EINECS No. 201-471-7 **RTECS No.** NM 0350000

Occurrence Present in cigarette smoke. Constituent of faeces, beetroot, Nectandra woodland and coal tar.

Physical properties

M. Pt. 95°C **B. Pt.** 265-266°C at 755 mmHg **Partition coefficient** log P_{ow} 2.60

Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol

Environmental fate

Nitrification inhibition

At 7 mg l^{-1}, 75% inhibition of ammonia oxidation (activated sludge) (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3450 mg kg^{-1} (2).

LD_{Lo} oral mouse 470 mg kg^{-1} (3).

LD_{Lo} oral cattle 200 mg kg^{-1} (2).

LD_{Lo} intravenous cattle 60 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 175 mg kg^{-1} (2).

Intraperitoneal (24 hr) rat 50-300 mg kg^{-1}. A dose-dependent decrease in splenic weight 24-75% and nucleated splenic cell number 22-68% was observed (4).

Sub-acute and sub-chronic data

Intraperitoneal (28 day) mice 400 mg kg^{-1}, cellular swelling was apparent in the olfactory epithelium by 6 hr. Necrosis of the olfactory epithelium and subepithelial glands was diffuse by 48 hr. Subsequent ulceration resulted in epithelial hyperplasia, squamous metaplasia, fibroplasia and ossification (5).

Infusion (72 hr) goats 35 mg kg^{-1} body weight, prostaglandin concentrations in lungs were unaffected. Plasma and lung prostaglandin and thromboxane B_2 concentrations did not appear to be altered in 3-methylindole-induced lung disease (6).

Metabolism and toxicokinetics

Requires activation by cytochrome P_{450} to be cytotoxic in rabbit pulmonary cells (7).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation, strong mutagen activity (8).

Other effects

Any other adverse effects

A dose of 550 mg kg^{-1} specifically damaged pulmonary tissue in Swiss-Webster mice without causing any hepatic or renal necrosis. When a glutathione depleter was administered to mice 3 hr before a low dose of 3-methylindene (75 mg kg^{-1}), histopathological examination after 4 hr showed renal damage. The production of a toxic metabolite in the livers of glutathione-depleted mice that is circulated to susceptible renal cells may be the mechanism of this toxicity (9).

The electrophilic imine methide may be the intermediate which binds with and depletes glutathione. An imine methide is the primary reactive intermediate in 3-methylindole-mediated pneumotoxicity (10).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

Other comments

Toxicity reviewed (12-14).

It is a pneumotoxic metabolite of L-tryptophan that forms in the digestive tract of humans and ruminants (15).

Soluble in hot water.

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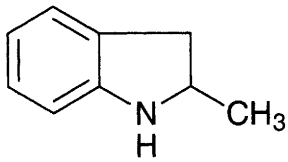
M239 2-methylindoline



$C_9H_{11}N$ **Mol. Wt.** 133.19 **CAS Registry No.** 6872-06-6

Synonyms 2,3-dihydro-2-methyl-1*H*-indole; α-methyldihydroindole

EINECS No. 229-971-0 **RTECS No.** NM 1926350

Uses Chemical intermediate.

Physical properties

B. Pt. 228-229°C (racemic mixture) **Flash point** 93°C **Specific gravity** 1.023 at 20°C

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 360 mg kg^{-1} (1).

Other comments

Occurs in coal conversion process wastewater and dyestuff manufacturing plant effluents (2).

Forms complexes with cytochrome P_{450} (3).

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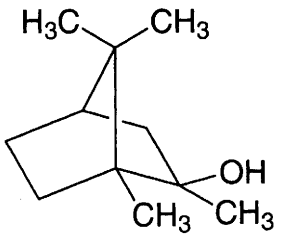
M240 2-methylisoborneol



$C_{11}H_{20}O$ **Mol. Wt.** 168.28 **CAS Registry No.** 2371-42-8

Synonyms MIB; *exo*-1,2,7,7-tetramethylbicyclo[2.2.1]-heptan-2-ol

Occurrence Product of metabolism of microorganisms such as *Streptomyces* sp. (A type) producing a musty flavour in water and some foods (1).

Ecotoxicity

Fish toxicity

Channel catfish injected with the compound showed a $t_{1/2}$ of 3.62 hr for elimination. No biotransformation was detected and significant gill excretion was judged to occur. Some concentration of the compound by peritoneal fat and subepidermal adipose tissue was noted (2).

Environmental fate

Abiotic removal

Can be removed from water by sand filtration (3).

Taste and odour can be removed from water containing the compound by ozone treatment (4) or treatment with ozone plus hydrogen peroxide (5).

Genotoxicity

Salmonella typhimurium TA1535 *umu* test with and without metabolic activation negative (6).

Other comments

Water supplies with concentrations of ≥5 ng l^{-1} are judged unpalatable (7).

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M241 methyl isobutyl ketone

$$CH_3C(O)CH_2CH(CH_3)CH_3$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 108-10-1

Synonyms hexone; 4-methyl-2-pentanone; isopropylacetone; isobutyl methyl ketone; 2-methylpropyl methyl ketone; MIBK

EINECS No. 203-550-1 **RTECS No.** SA 9275000

Uses Solvent used in industrial processes, pharmaceuticals, pesticides, adhesives and coatings (paint, varnish etc.).

Physical properties

M. Pt. –80°C **B. Pt.** 117-118°C **Flash point** 13°C (closed cup) **Specific gravity** 0.801 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.31 **Volatility** v.p. 16 mmHg at 20°C ; v.den. 3.5
Solubility Water: 20 g l^{-1}. Organic solvents: miscible with benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 20 ppm (83 mg m^{-3})
FR-VME 50 ppm (205 mg m^{-3})
JP-OEL 50 ppm (200 mg m^{-3})
SE-LEVL 25 ppm (100 mg m^{-3}) **SE-STEL** 50 ppm (200 mg m^{-3})
UK-LTEL 50 ppm (208 mg m^{-3}) **UK-STEL** 100 ppm (416 mg m^{-3})
US-TWA 50 ppm (205 mg m^{-3}) **US-STEL** 75 ppm (307 mg m^{-3})

UN No. 1245 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not breathe vapour – Take precautionary measures against static discharges (S2, S9, S16, S23, S33)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 505-537 mg l^{-1} (1,2).
LC_{50} (24 hr) goldfish 460 mg l^{-1} (3).

Invertebrate toxicity
LOEC effect on reproduction (semichronic exposure) *Microcystis aeruginosa* 136 mg l^{-1} (4).
EC_{50} (5 min) *Photobacterium phosphoreum* 79.6 ppm Microtox test (5).
Threshold concentration for growth inhibition *Pseudomonas putida*, (16 hr) 275 mg l^{-1} (6).
Threshold concentration for growth inhibition *Uronema parduczi* (20 hr) 950 mg l^{-1} (7).

Bioaccumulation
No data on bioaccumulation but its moderate water solubility and low partition coefficient suggest low bioaccumulation potential (8).

Environmental fate

Degradation studies
Microbial biodegradation can occur in soil (9,10).
When incubated with settled domestic sewage as seed was found to have a 40-day ThOD of 64.8 mg l^{-1} O_2 (11).
500 ppm incubated with three different activated sludge samples gave an average ThOD of 3% in 24 hr (12).
Standard dilution method with sludge from waste-treatment plant, BOD_5 to be 76% of ThOD (13).

Abiotic removal
In water primary removal mechanisms are volatilisation ($t_{1/2}$ 15-33 hr) and direct photolysis, chemical hydrolysis is not important (14,15).
In atmosphere degraded by hydroxyl radicals; $t_{1/2}$ 0.57 days. It is also photodegraded with the major product being acetone ($t_{1/2}$ 16 days) (16).

Adsorption and retention
Estimated soil adsorption coefficient (K_{oc}) 19-106 (17).
Highly mobile in soil and will not be adsorbed significantly (18).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird >100 mg kg^{-1} (calc.) (19).
LD_{50} oral guinea pig, rat 1.6, 2.1 g kg^{-1}, respectively (20,21).
LC_{50} inhalation mouse 23.3 g m^{-3} (22).
LD_{50} intraperitoneal mouse, rat 268, 400 mg kg^{-1}, respectively (20,23).

Sub-acute and sub-chronic data

Inhalation (90 day) rat, dog, monkey 410 mg m^{-3} continuous exposure under reduced oxygen tension and atmospheric pressure, increased liver and kidney weights. Histopathological changes in rat kidney epithelium (reversible 3-4 wk). No histopathological changes in dogs or monkeys (24).

Oral gavage (13 wk) Sprague-Dawley rats 0, 59, 250, 1000 mg kg^{-1} day^{-1} dose-related increase in liver and kidney weights, no corresponding histopathological lesions in liver. No effects were observed at 50 mg kg^{-1} (25).

Dermal rat (4 month) 300-600 mg kg^{-1} day^{-1}, dose- and time-dependent morphological changes were observed in skin, liver, brain, adrenals, spleen and testis. Body temperature decreased and oxygen consumption increased (26).

Carcinogenicity and chronic effects

No studies reported (27).

Teratogenicity and reproductive effects

Pregnant Fischer-344 rats, CD-1 mice, 1230, 4100, 12,300 mg m^{-3} (continuous) on days 6-15 (inclusive) of gestation. Animals killed on day-21 of gestation. Rats 12,300 mg m^{-3} included maternal toxicity, decreased body weight gain and decreased food consumption and also reduced foetal body weight per litter and delays in skeletal ossification. No increase in foetal malformation. 1230, 4100 mg m^{-3} showed no increase in maternal or foetal toxicity or malformations. Mice 12,300 mg m^{-3} maternal effects included increased mortality, increased liver weight and foetotoxicity (increased dead foetuses, reduced body weight delayed or reduced ossification). No increase in malformations. No significant effects seen at 1230, 4100 mg m^{-3} (28,29).

Metabolism and toxicokinetics

Two metabolites were detected in serum, after intraperitoneal injection into guinea pig of 450 mg kg^{-1} body weight. Major metabolite 4-hydroxy-4-methyl-2-pentanone formed by oxidation, and the minor metabolite 4-methyl-2-pentanol, formed by reduction. Serum $t_{1/2}$ and total clearance time are 66 min and 6 hr, respectively (30).

Inhalation (4 hr) human studies 100 ppm caused steady-state levels in blood. Completely cleared from body by 90 min after exposure (31).

Irritancy

Eye rabbit (duration unspecified) 40 mg severe irritation (21).

Dermal rabbit (24 hr) 500 mg caused mild irritation (23).

Sensitisation

No studies reported (27).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537, TA1538 with and without metabolic activation negative (32).

Escherichia coli WP_2, WP_2 *uvr*A with metabolic activation negative (33).

Saccharomyces cerevisiae JDI with and without metabolic activation mitotic gene conversion negative (33).

In vitro mouse lymphoma L51784 tk^+/tk^- with and without metabolic activation negative (32).

In vitro cultured rat liver cells chromosomal damage assay RL_4 cells negative (33).

In vitro Balb/3T3 cell transformation assay with and without metabolic activation equivocal (32).

In vivo mouse micronucleus assay negative (32).

Other effects

Other adverse effects (human)

May depress the central nervous system at high concentrations, vapour may be irritating to mucous membranes (34).

Workers exposed to 2050 mg m^{-3} for 20-30 min day^{-1} and 328 mg m^{-3} for the remainder of the day complained of weakness, loss of appetite, headache, eye irritation, stomach ache, nausea, vomiting and sore throat. After improvement in working conditions reduced levels to a maximum of 410-430 mg m^{-3}, most symptoms disappeared (35).

Legislation

Listed in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (36).

Other comments

Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicology exposure levels, workplace experience and physico-chemical properties listed (37).

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M242 methyl isobutyrate

$$CH_3CH(CH_3)CO_2CH_3$$

$C_5H_{10}O_2$ **Mol. Wt.** 102.13 **CAS Registry No.** 547-63-7

Synonyms 2-methylpropanoic acid, methyl ester; isobutyric acid, methyl ester

EINECS No. 208-929-5 **RTECS No.** NQ 5425000

Uses Chemical intermediate.

Occurrence In aromas of fruits such as blackberry and herbs such as dill. Pollutant in drinking water (1).

Physical properties

M. Pt. –84 to -85°C **B. Pt.** 90°C **Flash point** 3°C **Specific gravity** 0.891 at 20°C

Solubility Organic solvents: miscible diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 16 g kg^{-1} (2).

LD_{50} intraperitoneal rat 3.2 g kg^{-1} (2).

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M243 methyl isocyanate

$$CH_3NCO$$

C_2H_3NO **Mol. Wt.** 57.05 **CAS Registry No.** 624-83-9

Synonyms isocyanatomethane; isocyanic acid, methyl ester; MIC

EINECS No. 210-866-3 **RTECS No.** NQ 9450000

Uses Chemical intermediate in syntheses, particularly of insecticides and herbicides.

Physical properties

M. Pt. –17°C **B. Pt.** 37-39°C **Flash point** –7°C **Specific gravity** 0.967 at 20°C **Volatility** v.p. 400 mmHg at 20.6°C ; v.den. 1.97

Occupational exposure

DE-MAK 0.01 ppm (0.024 mg m^{-3})
FR-VME 0.02 ppm (0.05 mg m^{-3})
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)
US-TWA 0.02 ppm (0.047 mg m^{-3})

UN No. 2480 **Conveyance classification** toxic substance, danger of fire (flammable liquid)
Supply classification extremely flammable, toxic
Risk phrases Extremely flammable – Toxic by inhalation, in contact with skin and if swallowed – Irritating to eyes, respiratory system and skin (R12, R23/24/25, R36/37/38)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – Never add water to this product – In case of fire, use dry powder or carbon dioxide – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S30, S43, S45)

Environmental fate

Nitrification inhibition
Examination of forest nursery soils demonstrated reduced ability of bacterial and fungal populations as ammonifiers and denitrifiers after exposure during the 1984 Bhopal accident (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 51.5 mg kg^{-1} (2).
LC_{50} (6 hr) inhalation guinea pig, rat 5400, 6100 ppb, respectively (3).
LD_{50} subcutaneous rat 261 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 82-85 mg kg^{-1} (2).
Groups of 6 mice were injected intraperitoneally with 0.25 LD_{50}, 0.5 LD_{50} and LD_{50} of methyl isocyanate (LD_{50} 1117 μmol kg^{-1} body wt.) and sacrificed 45 min, 4 hr, 4 day and 7 day after administration. There was a general dose-dependent decrease in brain free amino acids (FAA) levels with the exceptions of glycine and arginine which increased above the control level with 0.25 LD_{50} and 0.5 LD_{50} doses and taurine with 0.5 LD_{50} and LD_{50} doses in 45 min. Plasma FAA increased at all dose levels with the exception of arginine with decreased with 0.25 LD_{50} in 45 min. Brain FAA levels were lower and serum FAA levels were higher than controls at 4 h, 4 days and 7 days after administration, with the exception of serine, histidine, alanine and arginine which decreased on day-7. Both in-balances were judged to be indicative of neurotoxic and systemic effects (4).
Absence of a cyanide-like action in acute toxicity has been established (2).

Carcinogenicity and chronic effects
A battery carcinogen prediction model has indicated a significant potential for carcinogenicity in rodents, but judged the potency of the compound to be low (5).

Teratogenicity and reproductive effects
Pregnant mice exposed to 9-15 ppm (3 hr) demonstrated >75% complete resorption (6).
Foetal toxicity in mice and rats is thought to be partly independent of maternal toxicity and thought to result from actions of the compound on foetal tissue (7).

Metabolism and toxicokinetics
Guinea pigs inhaling ^{14}C-methyl isocyanate at concentrations of 0.5-15 ppm (1-6 hr), retained some of the compound in the upper respiratory passage. Clearance of ^{14}C from tissues was gradual over 3 days with quantities in bile and urine being parallel with concentrations in blood. In those animals that were pregnant, the compound passed into the foetuses (8).
The compound can be absorbed through skin (9).

Irritancy
Sensory and pulmonary irritation have been established in mouse and guinea pig (10).
In humans lachrymation and irritation of the throat are produced along with skin irritation (9,11).

Sensitisation
Methyl isocyanate causes sensitisation (species unspecified) (9).

Genotoxicity

Salmonella typhimurium with and without metabolic activation negative (12).
Drosophila melanogaster sex-linked recessive lethal assay negative (12).
In vitro Chinese hamster ovary cells with and without metabolic activation, sister chromatid exchanges and chromosomal aberrations positive (12).
Mouse micronucleus test weak positive (13).
Sister chromatid exchanges *in vivo* mouse, weakly positive (14).

Other effects

Other adverse effects (human)
The major effect on Bhopal survivors was lung damage. Inhalation initially caused vomiting and coughing with damage to lungs resulting in oedema, permanent fibrosis, emphysema and bronchitis. Lingering respiratory illness has been the main long-term effect on survivors of the accident, with some evidence of neuromuscular dysfunction (15-17).
Of women who were pregnant and living near Bhopal at the time of the 1984 accident, 43% failed to give rise to live births (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (18).
Genotoxicity reviewed (19).
An industrial accident in Bhopal, India in 1984 at a chemical plant manufacturing carbaryl, resulted in over 2000 people dying and approximately 200,000 people being exposed to the vapour. The original incident has been well documented (20,21) and follow-up studies continue to be reported (1,6,15,16,17,22).

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M244 methyl isopropyl ketone

$$(CH_3)_2CHC(O)CH_3$$

$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 563-80-4

Synonyms 3-methylbutan-2-one; 2-acetylpropane; isopropyl methyl ketone; methylbutanone

EINECS No. 209-264-3 **RTECS No.** EL 9100000

Uses Perfumery.

Physical properties

M. Pt. -92°C **B. Pt.** 94-95°C **Flash point** 6°C **Specific gravity** 0.805

Occupational exposure

FR-VME 200 ppm (705 mg m^{-3})
US-TWA 200 ppm (705 mg m^{-3})

UN No. 2397 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 0.86 g l^{-1} (1).

Invertebrate toxicity
EC_{50} mixed bacterial culture 12.4 g l^{-1} (2).

Environmental fate

Degradation studies
BOD_{15} using acclimated inocula of wastewater origin 4.60 mg l^{-1} O_2, %ThOD 37.4 (3).
Using bench scale activated sludge, fill and draw operations at 6, 12 and 24 hr, respectively, 1.2, 1.3 and 2.2% ThOD (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 148 mg kg^{-1} (5).
LC_{Lo} (4 hr) inhalation rat 5700 ppm (5).
LD_{50} dermal rabbit 6350 mg kg^{-1} (6).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate to severe erythema and moderate oedemas and 100 mg instilled into rabbit eye (24 hr) caused mild irritation (6).
Dermal rabbit 500 mg, open to atmosphere caused well-defined erythema and slight oedema (7).

Genotoxicity

Salmonella typhimurium TA1535/psk1002 with and without metabolic activation, *umu* test, negative (8).
Bacillus subtilis microsome rec-assay without metabolic activation negative, with metabolic activation DNA damaging potential (9).

Saccharomyces cerevisiae D61.M point mutation and/or mitotic recombination positive, but only weakly induced mitotic aneuploidy at levels of high toxicity (10).

Other effects

Other adverse effects (human)
The threshold concentration for the eye (exposure to gas) was ~1.5 × that for the lungs (11).

Other comments

Subjective reactions by volunteers to compound as an indoor air pollutant studied (12).
Inhibits acetylcholinesterase activity (13).

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M245 methyl isothiocyanate

CH_3NCS

C_2H_3NS **Mol. Wt.** 73.12 **CAS Registry No.** 556-61-6

Synonyms isothiocyanatomethane; methyl mustard oil; Trapex

EINECS No. 209-132-5 **RTECS No.** PA 9625000

Uses Pesticide used for soil fumigation.

Physical properties

M. Pt. 35-36°C **B. Pt.** 119°C **Flash point** 32° **Specific gravity** 1.069 at 37°C
Partition coefficient log P_{ow} 1.374 **Volatility** v.p. 2.03×10^{-5} at 20°C
Solubility Water: 8.2 g l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2477 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, toxic
Supply classification toxic
Risk phrases Toxic by inhalation and if swallowed – Causes burns – May cause sensitisation by skin contact (R23/25, R34, R43)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S38, S45)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 0.13 mg l^{-1} (1).

LC_{50} (96 hr) rainbow trout, mirror carp 0.37-0.57 mg l^{-1} (1).

Invertebrate toxicity

Not toxic to bees when used as directed (1).

Toxicity to other species

Embryos of the clawed frog exposed to methyl isothiocyanate during development showed disturbances of collagen formation and of the notochordal sheath (2).

Environmental fate

Degradation studies

Disappearance from damp soil by degradation and evaporation is temperature dependent. Most disappears within 3 wk at 20°C or by 8 wk at 0°C (1).

Abiotic removal

Rapidly hydrolysed by alkalis; sensitive to oxygen and sunlight (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck 136 mg kg^{-1} (1).

LD_{50} oral ♂ rat 175-220 mg kg^{-1} (1,3).

LD_{50} oral ♂ mouse 90 mg kg^{-1} (1).

LC_{50} (1 hr) inhalation rat 1.3-1.9 mg l^{-1} (1,3).

LD_{50} dermal mouse 1.87 g kg^{-1} (1).

LD_{50} dermal rabbit 33-263 mg kg^{-1} (1,3).

LD_{Lo} oral ♀ human 1 g kg^{-1} with accompanying central nervous system effects (4).

In the rat exposure to vapour for 1 hr causes reversible damage to epithelium of proximal bronchioles and upper airways (5).

Sub-acute and sub-chronic data

LC_{50} (5 day) mallard duck 10.9 g kg^{-1} diet (1).

LC_{50} (5 day) pheasant >5 g kg^{-1} diet (1).

Carcinogenicity and chronic effects

2-yr feeding trials in the rat established a no-observed-effect concentration for rat of 10 mg l^{-1} in drinking water and for mouse of 20 mg l^{-1} in drinking water (1).

A 1-yr feeding trial with dogs established a no-observed-effect concentration of 0.4 mg kg^{-1} daily (1).

Irritancy

Strong irritant of rabbit skin and eye (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).

WHO Toxicity Class II (8).

Other comments

Pollutant of air, soil and water.
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).
Not toxic to bees when used as directed (1).

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M246 methyl isovalerate

$$(CH_3)_2CHCH_2CO_2CH_3$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 556-24-1

Synonyms 3-methylbutanoic acid, methyl ester; isovaleric acid, methyl ester; methyl isopentanoate

EINECS No. 209-117-3 **RTECS No.** NY 1510000

Occurrence In aromas of fruits and prepared meat foods. Produced by *Pseudomonas* strains on beef during cold storage (1).
Pollutant of drinking water (2).

Physical properties

B. Pt. 116-117°C **Specific gravity** 0.881 at 20°C with respect to water at 4°C
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 2400 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 5.7 g kg^{-1} (3).
LC_{50} (2 hr) inhalation mouse 2 g m^{-3} (4).

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M247 methyl lactate

$$CH_3CH(OH)CO_2CH_3$$

$C_4H_8O_3$ **Mol. Wt.** 104.11 **CAS Registry No.** 547-64-8

Synonyms methyl 2-hydroxypropanoate

EINECS No. 208-930-0 **RTECS No.** OD 5670000

Uses Solvent particularly for cellulose acetate.

Occurrence In aromas of a variety of plant leaves, in molasses from sugar mills (1). In pickles (2).

Physical properties

B. Pt. 144-145°C **Specific gravity** 1.09 at 19°C

Solubility Water: (decomp.). Organic solvents: 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)

Mammalian & avian toxicity

Irritancy

Compound is a mild irritant (species unspecified) (3).

Other comments

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

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M248 methyl mercaptoacetate

$$HSCH_2CO_2CH_3$$

$C_3H_6O_2S$ **Mol. Wt.** 106.15 **CAS Registry No.** 2365-48-2

Synonyms mercaptoacetic acid, methyl ester; methyl thioglycolate; thiglycolic acid, methyl ester; USAF EK-7119

EINECS No. 219-121-7 **RTECS No.** AI 7350000

Uses Chemical intermediate for pharmaceuticals and agrochemicals.

Occurrence Produced by *Pseudomonas* strains growing on stored, chilled beef (1).

Physical properties

B. Pt. 42-43°C at 10 mmHg **Flash point** 30°C **Specific gravity** 1.187

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 209 mg kg^{-1} (2).

LD_{50} intraperitoneal rat 252 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 100 mg kg^{-1} (3).

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1. Edwards, R. A. et al *J. Appl. Bacteriol.* 1987, **62**(5), 403-412.
2. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
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M249 methylmercury

CH_3Hg^+

CH_3Hg **Mol. Wt.** 215.62 **CAS Registry No.** 22967-92-6

Synonyms methylmercury ion(1+); methylmercury(1+)

RTECS No. OW 6320000

Occupational exposure

DE-MAK 0.01 mg m^{-3} (inhalable dust fraction)

FR-VME 0.01 mg m^{-3} (as Hg)

SE-LEVL 0.01 mg m^{-3} (as Hg)

UK-LTEL 0.01 mg m^{-3} (as Hg) **UK-STEL** 0.03 mg m^{-3} (as Hg)

US-TWA 0.01 mg m^{-3} (as Hg) **US-STEL** 0.03 mg m^{-3} (as Hg)

UN No. 2024 (liquid); 2025 (solid) **Conveyance classification** toxic substance

Supply classification very toxic

Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R26/27/28, R33)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S13, S28, S36, S45)

Ecotoxicity

Fish toxicity

Guppy and medaka exposed to 1.8 μg l^{-1} in water for 3 months suffered impaired spermatogenesis (1).

Brook trout (embryo) exposed to 0.88 μg l^{-1} in water for 17 days suffered enzyme disruption, while rainbow trout (adult) exposed to 0.04 μg l^{-1} for 64 days showed reduced growth (2).

Toxicity to other species

Rana pipiens exposed to 1.0 μg l^{-1} in water for 4 months showed arrested metamorphosis (2).

Bioaccumulation

95% of the mercury in fish is methylmercury (3,4).

Methylmercury content was significantly higher in water and sediment in anaerobic model laboratory experiments with eutrophic sediments than similar systems maintained aerobically, whereas sediment accumulation of total mercury was faster in aerobic systems (5-7).

Calculated bioaccumulation factor $\log_{10}$ 6.5 in freshwater lake, using ratios of total fish to mercury and aqueous methylmercury measurements. Calculated methylmercury accumulation factor 3 million in fish (8-10).

Environmental fate

Degradation studies

Sulfate-reducing bacteria and methanogens appear to be involved in anaerobic demethylation of freshwater sediments. Aerobic demethylation occurs in estuarine sediments but appears to be relatively unimportant in fresh water (11).

Abiotic removal

Abiotic methylation of Hg^{2+} readily occurs in aquatic systems. It requires the presence of metals which act as catalysts and organic matter for the transformation process (12).

The net of methylation and demethylation processes produces the mercury available for bioaccumulation. Environmental factors affect these processes to increase or decrease net methylation (13).

Adsorption and retention

In a freshwater lake, the concentration of methylmercury in the sediment was ~1% of total mercury, indicating substantial sediment flux (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 53 mg kg^{-1} (14).

LD_{50} intraperitoneal mouse 22 mg kg^{-1} (14).

Toxicity is manifest by initial excitation followed by depression and finally convulsions, paralysis and death (15).

Sub-acute and sub-chronic data

Gavage Sprague-Dawley rats 5 mg kg^{-1} for 7 days. One day after treatment significant inhibition of monoamine oxidase activity was observed in the synaptosomes of the cortex, cerebellum, hypothalamus, hippocampus and in blood platelets. Animals treated by gavage with 7.5 mg kg^{-1} day^{-1} for 10 days showed signs of ataxia (16).

Oral rats (8 wk) 5 or 500 μg l^{-1} $MeHgS^-$, $(MeHg)_2S$, $(MeHg)_3S^+$, or MeHgCl in drinking water. Exposure to methylmercury significantly enhanced lymphocytes responsiveness in most of the exposed groups at the low concentration. At 500 μg l^{-1} a significant decrease in the lymphocyte proliferative response was observed in the $(MeHg)_3S^+$ and MeHgCl groups, conversely the response in the $MeHgS^-$ and $(MeHg)_2S$-treated animals was modestly increased. The largest concentrations of all four mercury compounds were found in the kidney and spleen. The levels of mercury found in kidney, spleen, liver, brain, and testes were lower in the MeHgCl group than in those exposed to $(MeHg)_2S$ and $(MeHg)_3S^+$ (17).

Oral rat (12 days) 5 mg kg^{-1} day^{-1}. Loss of body weight and muscle wasting were observed. A decrease in mitochondrial enzyme activity was observed in skeletal muscle tissue (18).

Teratogenicity and reproductive effects

Effects on reproduction have been observed in mice receiving 6.5 g kg^{-1} on day-9 subcutaneously (19).

Metabolism and toxicokinetics

Detected in brain, liver, kidney, fatty tissue and hair of majority of humans examined. Also present in human breast milk (20).

Being lipophilic it is selectively accumulated in lipid-rich tissues. More than 50% is frequently found as metallothioneins (21).

Metabolism can occur by dealkylation in hepatic microsomal tissue (22).

Methylmercury can be absorbed from the gastro-intestinal tract or inhaled (23,14).

Biotic methylation, the transformation of Hg^{2+} to CH_3Hg^+, is not well understood, but appears to be a co-metabolic reaction with no known specific gene control. Demethylation, CH_3Hg^+ transformed to Hg^{2+} and then Hg^0, is primarily enzyme mediated, taking place within a single cell. The demethylation process is controlled by two genes (24).

Non-exposed neonatal hamsters nursed by foster mothers exposed to MeHg and neonates whose mothers had been administered MeHg *in utero* on day-12 of gestation and who were subsequently nursed by non-exposed foster mothers were unable to demethylate MeHg and excrete Hg into the urine and faeces. Up to 80% of the total body burden of Hg was found in the pelt (25).

Genotoxicity

Mouse glioma cells *in vitro* (chloride salt) inhibited DNA synthesis and transport systems for DNA precursors (9).

HeLa cells *in vitro* have shown inhibition of DNA, RNA and protein synthesis by the hydroxide (10).

Other effects

Other adverse effects (human)

Prenatal life is more sensitive to the toxic effects of methylmercury than is adult life. The inhibition of protein synthesis is one of the earliest detectable biochemical effects in the adult brain. Severe derangement of the developing central nervous system can be caused by prenatal exposure to methylmercury. The lowest level (maximum maternal hair mercury concentration during pregnancy) at which severe effects were observed was 404 $\mu g\ g^{-1}$ in the Iraqi outbreak. The highest no-observed-effect level for severe effect was 399 $\mu g\ g^{-1}$. Pregnant women may exhibit paraesthesia at lower methylmercury exposure levels than non-pregnant women, suggesting a greater risk for pregnant women (26).

Studies of sections of human brain, liver, kidneys, fatty tissue and hair, have indicated that methylmercury is detectable in the majority of human organs and tissues, the percentage of positive results being as high as 87-97% (27).

Human monocytes exposed *in vitro* to MeHgCl at concentrations up to 5 μM exhibited reduced phagocytic activity and an increase in cell death due to apoptosis (28).

Any other adverse effects

Methylmercury passes the blood brain barrier and nuclear membranes to react directly with both cellular and nuclear components. Accumulation of mercury in the brain, compared with blood and muscle, is much less in fish than in mammals (29).

Significant toxic effects in waterbirds are associated with liver-Hg levels of 11 ppm or above, however lower toxicity thresholds have been reported (30).

Methylmercury significantly inhibited *N*-methyl D-aspartate specific glutamate receptor binding, in neonate and adult rat brain, in a dose-dependent manner (31).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Mercury: maximum admissible concentration 1 $\mu g\ l^{-1}$ (32).

Included in Schedule 4 (Release into Air: Prescribed Substances) and Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (33).

US EPA ADI 0.1 μg methylmercury kg^{-1} body weight day^{-1} (34).

Quality objectives under EC Directives 82/176/EEC and 84/156/EEC 0.3 mg kg^- (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 (35).

Other comments

A pollutant, particularly in sea and lake water and in aquatic and land animals (36-38).
Widely detected in trace amounts, in human tissue (20,23).
Formed from inorganic and organic mercury by many microorganisms (39-42).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (43).
Environmental health reviewed (26).
Toxic effects of organomercuric compounds reviewed (27).
Pseudomonas putidas FB1, *Candida albicans* and *Saccharomyces cerevisiae* strains can all produce methylmercury from elemental mercury or inorganic salts (39,42).
Methylmercury formed in lake and sea water accumulates in aquatic animals and enters the food chain (37,23).
Low pH of lake water favours the transformation of inorganic mercury to the methylated form (36-38,44).
Methylation and demethylation transformations in aquatic systems reviewed (13,45,46).

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M250 methylmercury(II) acetate

$$CH_3HgOC(O)CH_3$$

$C_3H_6HgO_2$ **Mol. Wt.** 274.67 **CAS Registry No.** 108-07-6

Synonyms (acetato-*O*)methylmercury; acetoxymethylmercury; methylmercuric acetate

EINECS No. 203-547-5 **RTECS No.** OV 6380000

Physical properties

M. Pt. 128-129°C

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Hg) (total dust)
FR-VME 0.01 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 0.01 mg m^{-3} (as Hg) **UK-STEL** 0.03 mg m^{-3} (as Hg)
US-TWA 0.01 mg m^{-3} (as Hg) **US-STEL** 0.03 mg m^{-3} (as Hg)

UN No. 2024 (liquid)

UN No. 2025 (solid) **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R26/27/28, R33)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S13, S28, S36, S45)

Other effects

Any other adverse effects

In vitro rat forebrain, 34 mg kg^{-1} significantly reduced synaptosomal $^{45}Ca^{2+}$ uptake measured during 1 (fast uptake) or 10 (total uptake) sec of incubation. 14 mg kg^{-1} reduced total uptake of $^{45}Ca^{2+}$ by ≥70% and reduced fast uptake by 20-60%. It affects Ca^{2+} uptake in the absence of depolarisation (1).

Acute bath application of micromolar concentrations blocks the nerve evoked release of acetylcholine at the neuromuscular junction by presynaptic effects (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC, maximum admissible concentration 1 μg Hg l^{-1} (3).

Included in Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).

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

M251 methylmercury(II) dicyandiamide

$$NCNHC(=NH)NHHgCH_3$$

$C_3H_6HgN_4$ **Mol. Wt.** 298.70 **CAS Registry No.** 502-39-6

Synonyms 1-cyano-3-(methylmercurio)guanidine; (cyanoguanidinato-*N'*)methylmercury; methylmercuric cyanoguanidine; Agrosol; Morsodren; Morton Soil Drench; Pandrinox; Panogen PX

EINECS No. 207-935-5 **RTECS No.** OW 1750000

Physical properties

M. Pt. 156°C **Volatility** v.p. 6.5×10^{-5} mmHg at 35°C

Solubility Water: 21.7 g l^{-1}. Organic solvents: acetone, ethanol, ethylene glycol

Occupational exposure

DE-MAK 0.01 mg m^{-3} (as Hg) (total dust)
FR-VME 0.01 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 0.01 mg m^{-3} (as Hg) **UK-STEL** 0.03 mg m^{-3} (as Hg)
US-TWA 0.01 mg m^{-3} (as Hg) **US-STEL** 0.03 mg m^{-3} (as Hg)

UN No. 2024 (liquid)

UN No. 2025 (solid) **Conveyance classification** toxic substance

Supply classification very toxic

Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R26/27/28, R33)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S13, S28, S36, S45)

Ecotoxicity

Bioaccumulation

Readily absorbed by plants from soil; concentrations of 1 and 10 mg kg^{-1} were added to three soil types: silty loam; coarse sandstone; and humic. Mercury content accumulated in potato tubers was: 83 and 53 μg kg^{-1}, respectively (silt); 100 and 327 μg kg^{-1}, respectively (sandstone); and 67 and 196 μg kg^{-1}, respectively (humic) (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 68 mg kg^{-1} (2).
LD_{50} oral mouse 20 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 13 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 20 mg kg^{-1} (5).

Teratogenicity and reproductive effects

TD_{Lo} intraperitoneal (pregnancy day 9-13) mouse 8 mg kg^{-1}, reproductive effects (6).
TD_{Lo} intraperitoneal (day-10 pregnancy) mouse 4 mg kg^{-1}, teratogenic – nontransmissible changes produced in the offspring (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC, maximum admissible concentration 1 μg Hg l^{-1} (8).
Included in Schedule 5 (Release into Water: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

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M252 methyl methacrylate

$$CH_2=C(CH_3)CO_2CH_3$$

$C_5H_8O_2$ **Mol. Wt.** 100.12 **CAS Registry No.** 80-62-6

Synonyms methacrylic acid, methyl ester; methyl 2-methylpropenoate; MME

EINECS No. 201-297-1 **RTECS No.** OZ 5075000

Uses In production of acrylic polymers.

Physical properties

M. Pt. –48°C **B. Pt.** 100-101°C **Flash point** 10°C **Specific gravity** 0.936 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.38 **Volatility** v.p. 40 mmHg at 25.5°C ; v.den. 3.45
Solubility Organic solvents: miscible with acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 50 ppm (210 mg m^{-3})
FR-VME 100 ppm (410 mg m^{-3})
FR-VLE 200 ppm (820 mg m^{-3})
SE-LEVL 50 ppm (200 mg m^{-3})
SE-STEL 150 ppm (600 mg m^{-3})
UK-LTEL 50 ppm (208 mg m^{-3})
UK-STEL 100 ppm (416 mg m^{-3})
US-TWA 100 ppm (410 mg m^{-3})

UN No. 1247 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification highly flammable, irritant
Risk phrases Highly flammable – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact (R11, R36/37/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not empty into drains – Take precautionary measures against static discharges (S2, S9, S16, S29, S33)

Environmental fate

Abiotic removal
Use of ozone to treat gaseous discharge turns the compound into low-toxicity non-aromatic compounds (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 8.4 ml kg^{-1} (2).
LD_{Lo} oral rabbit 7 ml kg^{-1} (2).
LC_{Lo} (5 hr) inhalation rabbit, guinea pig, rat <15 mg l^{-1} (2).
Inhalation (duration unspecified) occupationally exposed workers >63.3 mg m^{-3} is toxic. Effects include damage to nervous and cardiovascular systems (3). LD_{50} dermal rabbit >40 ml kg^{-1} (4).
LD_{50} intraperitoneal mouse 1.2 ml kg^{-1} (5).
Intravenous doses of 1.25 g l^{-1} infused into dogs caused rapid fall in blood pressure and respiratory arrest (6).

Sub-acute and sub-chronic data
Guinea pigs exposed for 3 hr daily for 15 days to 39 mg l^{-1} methyl methacrylate vapour developed degenerative changes in liver (4).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (7).
National Toxicology Program tested mice and rats by inhalation and food. No evidence of carcinogenicity in either sex of either species, but non-neoplastic lesions in nasal cavity were seen in both species (8,9).
Rats receiving 6 to 2000 mg l^{-1} in drinking water for 2 yr developed no treatment-related tumours (10).
Rats painted on the back of the neck 3 × wk^{-1} for 4 months developed no local tumours during their lifespan (11).
Inhalation ♂ and ♀ Fischer 344 rats (2 yr) and ♂ and ♀ golden hamsters (18 months) 0, 25, 100 and 400 ppm, 6 h day^{-1}, 5 days wk^{-1}. All surviving rats were killed during wk 104-106, and surviving hamsters at wk-78. Body weights of ♂ rats were not affected by exposure to methyl methacrylate (MMA) but body weights of ♀ rats were lower than controls after wk-52. Hamsters (♂ and ♀) exposed to 400 ppm had body weight decreases of 9-12% after wk-48. The target organ for chronic toxicity in rats exposed to 100-400 ppm was the nasal cavity. Hamsters did not have demonstrable nasal cavity microscopic changes. Chronic exposure to MMA vapour did not cause tumours in either rats or hamsters (12).

Teratogenicity and reproductive effects

Rats receiving 0.13-0.44 mg kg^{-1} on days 5, 10 and 15 of gestation showed no teratogenic effects but reduced foetal weight was seen at all doses (5,13,14).

Pregnant rats inhaling 100 mg l^{-1} on days 6-15 of gestation for 54 or 18 min day^{-1} showed poor maternal weight gain and food consumption. Foetal weight and size were reduced and some skeletal malformations were seen (15).

Metabolism and toxicokinetics

In rats up to 88% of a single dose of 5.7 mg kg^{-1} methyl ^{14}C-methacrylate has been found to be excreted as $^{14}CO_2$ in 10 days, irrespective of route of administration. Excreted metabolites included: ^{14}C-methyl malonate, ^{14}C-succinate and possibly ^{14}C-β-hydroxyisobutyrate and 2-formylpropionate (10).

Sensitisation

Allergic responses in man are reported (16,17).

Allergic stomatitis has been reported in a patient wearing a denture containing methyl methacrylate monomer (18).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (19).

L5178Y tk^+/tk^- mouse lymphoma assay without metabolic activation negative, with metabolic activation positive (20).

Workers exposed to high doses of methyl methacrylate showed an increased frequency of sister chromatid exchanges in lymphocytes (21).

No exposure-related changes in chromosomal aberration rate were observed in 38 workers exposed to 0.9-71.9 ppm methyl methacrylate (22).

Other effects

Other adverse effects (human)

Some evidence that workers occupationally exposed to methyl methacrylate develop chronic cough and mild airways obstruction has been reported (23).

Workers exposed to various acrylic monomers were studied for cancer mortality. Workers exposed to methyl methacrylate had increased cancer risk with increasing exposure to methyl methacrylate (24).

Any other adverse effects

Exposure of mice to 164 mg l^{-1} in air for 14 min increased sleeping time induced by sodium pentobarbital (25).

Other comments

The carcinogenicity and toxicology of the compound has been assessed (26).

Environmental pollutant.

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M253 methyl methanesulfonate

$CH_3SO_3CH_3$

$C_2H_6O_3S$ **Mol. Wt.** 110.13 **CAS Registry No.** 66-27-3

Synonyms methanesulfonic acid, methyl ester; methyl mesylate; MMS

EINECS No. 200-625-0 **RTECS No.** PB 2625000

Uses Potential use as male chemosterilant for insects and mammalian pests.

Physical properties

B. Pt. 203°C at 753 mmHg **Flash point** 104°C **Specific gravity** 1.2943 at 20°C with respect to water at 4°C
Solubility Water: 200 g l^{-1}. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
Embryotoxicity and teratogenicity were observed in Japanese medaka fish embryos exposed for 2 hr to 0.08-13.2 g l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral blackbird 56.2 mg kg^{-1} (2).
LD_{50} oral quail 75 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 receiving the equivalent of about 30 mg kg^{-1} via drinking water for up to 20 months developed an increased incidence of lung tumours compared with controls (4).
♂ rats receiving the compound subcutaneously for 48 wk at doses upwards of 4 mg kg^{-1} wkly developed an increased incidence of tumours, particularly at the injection site (5).
♂ and ♀ rats receiving a single intraperitoneal injection of upwards of 72 mg kg^{-1} developed tumours of tissues within the nervous system, including malignant neurofibromas and astrocytomas (6).

♀ mice receiving 2.2 mg l^{-1} subcutaneously once wkly for 64 wk developed some sarcomas at the injection site (7).
♀ mice receiving a dermal application of 4.4 mg l^{-1} once wkly for 64 wk did not develop any tumours (7).

Teratogenicity and reproductive effects

Single intravenous injections of 20-68 mg kg^{-1} to pregnant rats on day 15 or 21 of gestation resulted in the development of neurogenic tumours in ~ 20% of offspring. No neurogenic tumours were found in offspring of pregnant ♀ treated on day-9 of gestation (8).
Single intraperitoneal doses of 50 mg kg^{-1} to ♂ rats resulted in infertility during the second or third wk, which lasted for 28 days (9).

Metabolism and toxicokinetics

In mice the compound is rapidly distributed throughout the body, including the nervous system (10).
In rats the compound has been shown able to cross the placental barrier (11).
Rats receiving 100 mg kg^{-1} intravenously yielded metabolites including, methylmercapturic acid sulfoxide, 2-hydroxy-(3-methylsulphinyl)propionic acid, (methylsulphinyl)acetic acid, methylmercapturic acid and *N*-(methylthioacetyl)glycine (12).
Conjugation with glutathione in rat liver has been demonstrated (13).

Genotoxicity

Salmonella typhimurium TA100, TA1535 without metabolic activation positive (14).
Salmonella typhimurium TA100 with metabolic activation positive (15).
Escherichia coli PQ37 SOS chromotest positive (16).
Salmonella typhimurium SV50 Ara^r assay positive (17).
Unscheduled DNA synthesis in cultured hepatocytes positive (18).
DNA repair synthesis induced in HeLa cells (19).
Caused DNA damage but not strand-break repair in human diploid fibroblasts *in vitro* (20).

Other effects

Other adverse effects (human)

Therapeutic doses of 2.8 to 800 mg kg^{-1} for up to 350 days led to significant gastro-intestinal and hepatotoxic effects in cancer patients (21).

Any other adverse effects

Methylation of nucleic acid in liver, brain and foetal tissue of rats has been observed, and *in vitro* alkylation of Chinese hamster ovary cells has been reported (22-24).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (25).
The toxicology and carcinogenicity of the compound has been reviewed (26).

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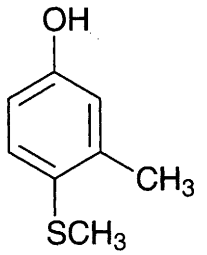
M254 3-methyl-4-(methylthio)phenol



$C_8H_{10}OS$ **Mol. Wt.** 154.23 **CAS Registry No.** 3120-74-9

Synonyms 4-(methylthio)-*m*-cresol; MMTP

EINECS No. 221-496-7 **RTECS No.** GP 2225000

Physical properties

M. Pt. 52-54°C **B. Pt.** 224-228°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat, guinea pig 1000, 3400, 3500 mg kg^{-1}, respectively (1).

LD_{Lo} intraperitoneal mouse 100 mg kg^{-1} (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Maximum admissible concentration 0.5 μg phenol l^{-1} (3).

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

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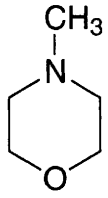
M255 *N*-methylmorpholine



$C_5H_{11}NO$ **Mol. Wt.** 101.15 **CAS Registry No.** 109-02-4

Synonyms 4-methylmorpholine

EINECS No. 203-640-0 **RTECS No.** QE 5775000

Physical properties

M. Pt. –65°C **B. Pt.** 115-116°C at 750 mmHg **Flash point** 24°C **Specific gravity** 0.920 **Volatility** v.den. 3.5

Occupational exposure

SE-LEVL 5 ppm (20 mg m^{-3}) **SE-STEL** 10 ppm (40 mg m^{-3})

UN No. 2535 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2720 mg kg^{-1} (1).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (2).
LC_{50} (2 hr) inhalation mouse 25,200 mg m^{-3} (3).
LD_{50} dermal rabbit 1242 mg kg^{-1} (1).

Irritancy

Dermal rabbit 460 mg, open to atmosphere, caused mild irritation (4).
Eye rabbit 920 µg caused severe irritation (exposure unspecified) (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

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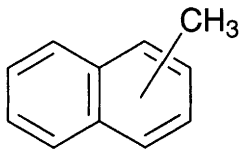
M256 methylnaphthalene



$C_{11}H_{10}$ **Mol. Wt.** 142.20 **CAS Registry No.** 1321-94-4

Synonyms methylnaftalen

EINECS No. 215-329-7 **RTECS No.** QJ 9625000

Occurrence In the aroma of a variety of foods including fruits and cheeses. Also in coal tar, exhaust fumes, in seawater and in fish (1).

Ecotoxicity

Invertebrate toxicity

Toxicity and detrimental actions to *Selenastrum capricornutum* have been demonstrated (2).

Bioaccumulation

Compound has been detected in white croaker in sea water close to Los Angeles, probably as a result of the compound entering the food chain (1).

Accumulation and retention have been demonstrated in blue crab, with the hepatopancreas and gill tissue accumulating the highest concentrations (3).

Environmental fate

Degradation studies

Following a diesel spillage, contaminated soil containing methylnaphthalene was restored to near normality in 13 wk by liming, fertilising and tilling of the soil (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4.36 g kg^{-1} (5).

Irritancy

Moderate irritant of rabbit skin at 500 mg for 24 hr (5).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

The compound occurs as a mixture of isomers.

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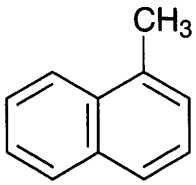
M257 1-methylnaphthalene



$C_{11}H_{10}$ **Mol. Wt.** 142.20 **CAS Registry No.** 90-12-0

Synonyms α-methylnaphthalene

EINECS No. 201-966-8 **RTECS No.** QJ 9630000

Uses Insecticide manufacture. Solvent.

Occurrence Asphalt, naphtha, coal and petroleum. Trace contaminant in some water samples (1-3).

Physical properties

M. Pt. -22°C **B. Pt.** 240-243°C **Flash point** 82°C **Specific gravity** 1.001 **Partition coefficient** log P_{ow} 3.87

Volatility v.den. 4.91

Solubility Water: 26 mg l^{-1} at 25°C. Organic solvents: benzene, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) (static bioassay) brown trout yearlings 8.4 mg l^{-1} (4).

Exposure to a low concentration decreased feeding. At a higher level all fish stopped feeding for 3 days and one stopped for 10 days (5).

LD_{50} intraperitoneal rainbow trout 2.92 g kg^{-1} (6).

LC_{50} (96 hr) fathead minnow (18-22°C) 9 mg l^{-1} (7).

Bioaccumulation

Uptake and depuration by oysters from oil-treated enclosures; concentration in oysters was 36 μg g^{-1}. The concentration in the water was 3 μg l^{-1}, the accumulation factor was 12,000 (8).

Environmental fate

Degradation studies

Degradation by free living bacteria at four sites ranged from 37-106 hr to a concentration of 1 μg l^{-1} (9).

The $t_{1/2}$ in two different sandy loam soils ranged from 1.4-2.1 days and 1.6-3.2 days, respectively (10).

Alcaligenes denitrificans WW1 can utilise it as a sole carbon source (11).

Pollution with 100-240 μg l^{-1} showed that the bacterial communities in the heavily polluted water have a higher degree of adaptation to hydrocarbon degradation than communities from slightly polluted water. Bacteria from the unpolluted water were considered as being unadapted (12).

When it was added to a fluoranthene bacteria community it was not detected (<10 ng l^{-1}) after 3 days. Recovery in killed cells was 85.2%. Recovery from *Pseudomonas putida* Pp67 cells was 64.5% (13).

Biodegradation at 0.1 mg l^{-1} after 135 hr; 0% in normal sewage and 95% in adapted sewage (14).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1840 mg l^{-1} (15).

Intraperitoneal (24 hr) rats 71 mg kg^{-1}, microscopy of lungs showed no lesions (16).

Metabolism and toxicokinetics

In vitro mammalian microsomes principal metabolite 1-methylnaphthoic acid (17).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (18).
Salmonella typhimurium TM677 with metabolic activation, positive (19).

Other effects

Any other adverse effects

Oral rats 1.5-2 g kg^{-1}, liver function was impaired but restored to normal after 3-5 days (20).
In vitro ascites sarcoma BP8 cells growth inhibited at 142 mg l^{-1} (21).

Legislation

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

Other comments

Dermal mouse bioassay at 100 µl 3 × wk^{-1}, inhibition of benzo[*a*]pyrene carcinogenesis in mouse skin was observed (23).
Reviews on ecotoxicology, environmental effects, experimental toxicity, exposure levels and human health effects listed (24).

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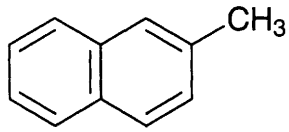
M258 2-methylnaphthalene



$C_{11}H_{10}$ **Mol. Wt.** 142.20 **CAS Registry No.** 91-57-6

Synonyms β-methylnaphthalene

EINECS No. 202-078-3 **RTECS No.** QJ 9635000

Occurrence Trace contaminant in some water samples (1-3).
Coal tar pitch fumes.

Physical properties

M. Pt. 34-36°C **B. Pt.** 241-242°C **Flash point** 97°C **Specific gravity** 1.00 at 20°C
Partition coefficient log P_{ow} 4.00

Ecotoxicity

Fish toxicity
Intra-arterial rainbow trout 10 mg kg^{-1}, terminal $t_{1/2}$ was 9.9 hr. It was metabolised mainly to water-soluble metabolites which were excreted into the urine and bile. The apparent bioavailability was 20% (4).

Invertebrate toxicity
Meretrix casta var *ovum* (96 hr) 10 mg l^{-1} specific activities of Na-K-Mg-ATPase and Na-K-ATPase were elevated and decreased in the hepatopancreas and gill, respectively (5).

Bioaccumulation
Rainbow trout (4 wk) bioaccumulation factor 23,500 (6).
The bioconcentration factor in coho salmon was 28 (7).
Bioconcentration factor flow-through method (species unspecified) 407 (8).

Environmental fate

Degradation studies
Microbial degradation to carbon dioxide, in seawater at 12°C in the dark after 24 hr incubation at 50 μg l^{-1}: 0.10 μg l^{-1} day^{-1} turnover time was 500 days (9).
In seawater with oil-oxidising microorganisms there was 17.1% breakdown after 21 days at 22°C in stoppered bottles (10).
Undergoes microbial oxidation by *Pseudomonas putida* 39D and *Pseudomonas putida* NCIB 9816 (11).
Microcosms inoculated with *Mycobacterium* sp. showed enhanced mineralisation of this compound (12).
Alcaligenes denitrificans WW1 can utilise 2-methylnaphthalene as sole carbon source (13).
Biodegradation by indigenous microorganisms, undetected after 8 days, initial concentration 9.5 μg m^{-1} (14).
Biodegraded to carbon dioxide in 30-670 days (15).
In sea water at 12°C biodegraded within 500 days (16).

Abiotic removal
Reaction with hydroxyl radicals is the dominant loss process (17).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1630 mg kg^{-1} (18).

LD_{Lo} intraperitoneal mouse 1000 mg kg^{-1} (19).
Intraperitoneal (24 hr) mice 400 mg kg^{-1}, pulmonary damage was detected, depletion of pulmonary reduced glutathione was observed. Lipid peroxidation and phospholipid content in the lung were unaffected (20).

Sub-acute and sub-chronic data
Inhalation (6.5 month) (species unspecified) 100 mg m^{-3} produced an increase in both the respiration rate and oxygen consumption (21).

Carcinogenicity and chronic effects
Dermal mouse bioassay 100 µl 3 × wk^{-1} inhibition of benzo[*a*]pyrene carcinogenesis in mouse skin was observed (22).

Metabolism and toxicokinetics
Oral rats, rabbits urinary metabolites included 2-naphthoic acid, glycine conjugate of 2-naphthoic acid, 7-methyl-1- and 2-naphthols, and 1,2-dihydro-1,2-dihydroxy-7-methylnaphthalene (23).
Metabolised to 2-naphthoic acid and a methylnaphthalene dihydrodiol *in vitro* by hepatic microsomes (24).
Metabolites produced by pulmonary and hepatic microsomes from DBA/2J mice included three dihydrodiols, 2-naphthyl alcohol, and other unidentified metabolites (25).
Metabolites from rat liver microsomes were 2-(hydroxymethyl)naphthalene, 3,4-dihydrodiol, 5,6-dihydrodiol, and 7,8-dihydrodiol (26).
Metabolites found in rat urine were 2-naphthoic acid and 2-naphthoylglycine (27).

Genotoxicity

Salmonella typhimurium TM677 (metabolic activation unspecified) weakly mutagenic (28).
In vitro human lymphocytes with or without metabolic activation, weakly positive or negative, respectively. Sister chromatid exchange frequencies were significantly increased with metabolic activation (29).

Other effects

Any other adverse effects
In vitro ascites sarcoma BP8 cells, growth inhibited at 142 mg l^{-1} (30).
Oral rat 1.5-2 g kg^{-1}, liver function was impaired but restored to normal after 3-5 days (31).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (32).

Other comments

Reviews on ecotoxicology, environmental effects, experimental toxicology, exposure levels and human health effects listed (33).
Metabolism reviewed (34).

References

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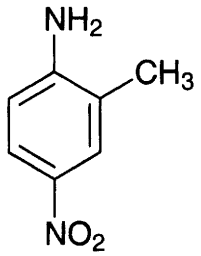
M259 2-methyl-4-nitroaniline



$C_7H_8N_2O_2$ **Mol. Wt.** 152.15 **CAS Registry No.** 99-52-5

Synonyms 2-methyl-4-nitrobenzenamine; 4-nitro-2-toluidine; C.I. 37100; Fast Red Base RL; Red RL Base

EINECS No. 202-762-1 **RTECS No.** XU 8210000

Physical properties

M. Pt. 131-133°C

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 3.57 ppm Microtox test (1).

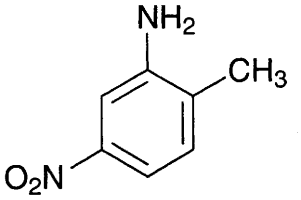
Other comments

Reviews on experimental toxicology, human health effects and workplace experience listed (2).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
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

M260 2-methyl-5-nitroaniline



$C_7H_8N_2O_2$ **Mol. Wt.** 152.15 **CAS Registry No.** 99-55-8

Synonyms 2-methyl-5-nitrobenzenamine; 5-nitro-*o*-toluidine; C.I. 37105; C.I. azoic diazo component 12; Fast Scarlet G; Scarlet G Base

EINECS No. 202-765-8 **RTECS No.** XU 8225000

Uses Dye.

Physical properties

M. Pt. 104-107°C

Occupational exposure

UN No. 2660 **HAZCHEM Code** 2Z **Conveyance classification** harmful substance
Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R33, R51/53)
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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 15.2 ppm Microtox test (1).

Mammalian & avian toxicity

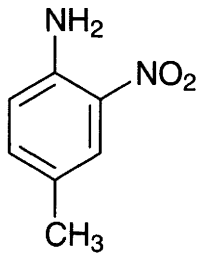
Acute data
LD_{50} oral rat 574 mg kg^{-1} (2).

Carcinogenicity and chronic effects
National Toxicology Program tested Fischer 344 rats and B6C3F1 mice via the feed. Carcinogenic in mice causing hepatocellular carcinomas in both sexes, an increase in the combined incidence of haemangiomas and haemangiosarcomas in ♂ mice and an increased incidence of haemangiosarcomas in ♀ mice. Not carcinogenic in the rats (3).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Progress Report *NIH-71-E-2144* Submitted to the National Cancer Institute 1973, Mason Research Institute, Worcester, MA, USA.
3. *National Toxicology Program Research and Testing Division* 1992, Report No. TR-107, NIEHS, Research Triangle Park, NC, USA

M261 4-methyl-2-nitroaniline



$C_7H_8N_2O_2$ **Mol. Wt.** 152.15 **CAS Registry No.** 89-62-3

Synonyms 4-methyl-2-nitrobenzeneamine; 2-nitro-*p*-toluidine; Amarthol Fast Red GL Base; Fast Red Base GL; Lithosol Scarlet Base M; C.I. 37110

EINECS No. 201-924-9

Physical properties

M. Pt. 115-116°C

Occupational exposure

Supply classification toxic, dangerous for the environment

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R33, R51/53)

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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 26.1 mg l^{-1} (1).
LC_{50} (30 min) rainbow trout 5 mg l^{-1} (2).
LC_{50} (3 hr) bluegill sunfish 5 mg l^{-1} (2).
LC_{50} (3 hr) goldfish 5 mg l^{-1} (2).
LC_{50} (4-7 hr) chinook salmon 10 mg l^{-1} (2).
LC_{50} (1-2 hr) coho salmon 10 mg l^{-1} (2).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 14.2 mg l^{-1} (1).
EC_{50} (30 min) *Photobacterium phosphoreum* 5.92 mg l^{-1} Microtox test (3).

Genotoxicity

Hepatocyte/DNA repair test with primary cultured rat hepatocytes 0.152 g l^{-1} negative (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

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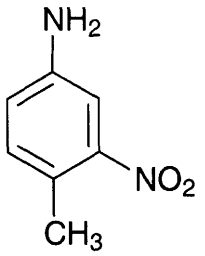
M262 4-methyl-3-nitroaniline



$C_7H_8N_2O_2$ **Mol. Wt.** 152.15 **CAS Registry No.** 119-32-4

Synonyms 4-methyl-3-nitrobenzenamine; 3-nitro-*p*-toluidine; 1-amino-3-nitro-4-methylbenzene; 5-nitro-4-toluidine; *m*-nitro-*p*-toluidine

EINECS No. 204-314-0 **RTECS No.** XU 8227000

Physical properties

M. Pt. 74-77°C **Flash point** 175°C (closed cup) **Specific gravity** 1.312 **Volatility** v.den. 5.80
Solubility Organic solvents: ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 34.0-71.3 mg l^{-1} (1,2).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 5.40 ppm Microtox test (3).
EC_{50} (48 hr) *Daphnia magna* 22.5 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 3.16 mg kg^{-1} (4).
LD_{50} oral starling 31.6 mg kg^{-1} (4).

LD_{50} oral rat 6860 mg kg^{-1} (5).
LD_{50} intravenous mouse 180 mg kg^{-1} (6).

References

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2. Pearson, J. G. et al *Aquat. Toxicol.* 1979, ASTM STP 667, Marking, L. L. et al (Ed.).
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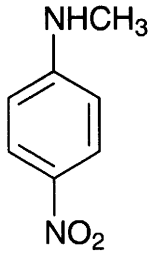
M263 *N*-methyl-4-nitroaniline



$C_7H_8N_2O_2$ **Mol. Wt.** 152.15 **CAS Registry No.** 100-15-2

Synonyms *N*-methyl-4-nitrobenzenamine; *p*-(methylamino)nitrobenzene

EINECS No. 202-823-2

Physical properties

M. Pt. 152-154°C

Ecotoxicity

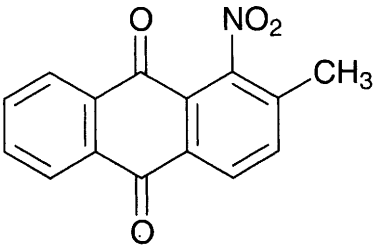
Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 1.21 ppm Microtox test (1).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431

M264 2-methyl-1-nitroanthraquinone



$C_{15}H_9NO_4$ **Mol. Wt.** 267.24 **CAS Registry No.** 129-15-7

Synonyms 2-methyl-1-nitro-9,10-anthracenedione; NCI-C01923; 1-nitro-2-methylanthraquinone; 1-N-2-MA

EINECS No. 204-932-0 **RTECS No.** CB 7920000

Uses Organic synthesis. Manufacture of dyes.

Physical properties

M. Pt. 270-271°C **Partition coefficient** log P_{ow} 2.4894 (1)

Solubility Organic solvents: benzene, chloroform, diethyl ether, nitrobenzene

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >113 mg kg^{-1} (2).

LD_{50} oral rat >500 mg kg^{-1} (3).

LD_{50} intraperitoneal rat 1100 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Oral rat (6 wk) 0.15% diet caused a reduction in body weight gain. 0.06 and 0.12% diet caused hyperplasia of the lymphoid tissue and of the stomach, as well as inflammatory changes of the stomach (5).

Carcinogenicity and chronic effects

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

Oral mouse 0, 300 or 600 mg kg^{-1} diet. All treated mice died within 338 days. Subcutaneous haemangiosarcomas developed in 88/90 treated ♂ mice and 79/82 treated ♀ mice. Four of these tumours metastasised to the lung. Mesenteric haemangiosarcomas were observed in 6 ♂ and 8 ♀ treated mice, compared with 1/49 ♂ and 0/48 ♀ controls (5).

Oral rat (109 wk) 0, 600 or 1200 mg kg^{-1} diet for 78 wk. Survival rates were 29/48, 35/49 and 27/49, respectively, for ♂ rats, and 22/50, 40/50 and 29/49, respectively, for ♀ rats. An increase in the incidence of hepatocellular carcinoma was observed only in ♂ animals: 1/48 controls, 5/48 low-dose and 9/49 high-dose rats. Fibromas of the subcutaneous tissue were observed in 3/48 control, 10/49 low-dose and 34/49 high-dose ♂ rats, and in 1/50 control, 0/50 low-dose and 13/49 high-dose ♀ rats. Subcutaneous haemangiosarcomas occurred in 3/49 high-dose ♂ rats (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 with metabolic activation positive (7).

In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations negative (8).

In vitro mouse lymphoma L5178Y cells, tk^+/tk^- with metabolic activation, equivocal results (9).

Other comments

Physical properties, use, carcinogenicity and toxicity reviewed (10,11).

References

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M265 1-methyl-3-nitro-1-nitrosoguanidine

$$O_2NHNC(=NH)N(NO)CH_3$$

$C_2H_5N_5O_3$ **Mol. Wt.** 147.09 **CAS Registry No.** 70-25-7

Synonyms *N*-nitroso-*N*-methyl-*N'*-nitroguanidine; *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine; MNNG

EINECS No. 200-730-1 **RTECS No.** MF 4200000

Uses Alkylating agent.

Physical properties

M. Pt. 118°C (decomp.)

Solubility Water: <0.5%. Organic solvents: acetone, ethanol, methanol

Occupational exposure

Supply classification toxic

Risk phrases May cause cancer – Harmful by inhalation – Irritating to eyes and skin – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R20, R36/38, R51/53)

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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S53, S45, S61)

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 6.6 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, hamster 90, 1100 mg kg^{-1}, respectively (2,3).

LD_{50} intraperitoneal mouse 66 mg kg^{-1} (4).
LD_{50} intravenous mouse, rat 37, 80 mg kg^{-1}, respectively (5,6).

Carcinogenicity and chronic effects
Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (7).
Dermal mouse, single dose of 75-750 μg $animal^{-1}$ induced skin papillomas at all doses (8).
Oral rat, 50 mg l^{-1} in 0.04% Tween 60 in drinking water, available *ad libitum* for 3 months, induced gastric cancers which developed in regimens with hyperplastic gastritis (9).
Gavage rat (2 yr) 50-100 mg kg^{-1} on 5 occasions over 10 month induced squamous papillomas and squamous cell carcinomas of the forestomach, liver and peritoneum (10,11).
Oral rat (12 month) 33, 83 or 170 mg l^{-1} in drinking water for 6-12 month induced malignant tumours of the glandular forestomach at incidences of ≥70%. Additionally malignant tumours, especially at high concentrations, were observed in the duodenum, jejunum and mesentary, together with papillomas in the forestomach and liver tumours (12-14).
Subcutaneous rat (1 yr) 5 × 45 or 90 mg kg^{-1} wk^{-1}. Fibrosarcomas and polymorphic sarcomas at the site of injection in 8/10 of the low-dose group, and in 6/6 of the high-dose group after 180-360 days (15).
Intraperitoneal rat (1 yr) single dose of 600 μg $animal^{-1}$ resulted in papillomas, carcinomas and sarcomas of the stomach and small intestine and a few tumours at other sites in 20/38 rats surviving >1 yr (16).

Teratogenicity and reproductive effects
Intraperitoneal mouse, lowest toxic dose 50 mg kg^{-1} on day-11 of gestation (teratogenic effects, musculoskeletal system) (17).

Metabolism and toxicokinetics
Following oral administration to dogs ~90% was excreted in the urine, mostly as *N*-methyl-*N'*-nitroguanidine, within 9 hr. There is evidence that denitrosation is effected by enzyme occurring in the stomach, liver and kidneys (18,19).

Irritancy
Classified as non-irritant to rabbit skin and eyes using modified Draize tests (20,21).

Sensitisation
Negative in the Buehler dermal sensitisation test on ♂ guinea pigs (20).
Reported to cause dermatitis (22).

Genotoxicity

CASE structure-activity methodology predicted positive mutagenicity to *Salmonella typhimurium* (23).
Drosophila melanogaster spot assay positive (24).
In vitro Chinese hamster ovary cells and human hepatoma cells HGPRT assay positive (25,26).
In vitro Chinese hamster V79 lung fibroblasts and rat intestinal IEC-17 and IEC-18 cells, induction of micronuclei positive (27).
In vitro, primary hepatocytes, unscheduled DNA synthesis positive (28).
In vivo rat hepatocytes, unscheduled DNA synthesis negative (29).
In vivo mouse sperm morphology, assay negative (30).

Other effects

Other adverse effects (human)
High concentrations are destructive to the eyes skin, mucous membranes and upper respiratory tract (22).
Three cases of brain tumours (gliomas) and 1 of colon cancer have been reported from staff in a genetics laboratory over a 13-year period. All subjects were exposed for at least 6-15 years prior to death, but other carcinogens may have also been used in the laboratory (31).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (32).
Physical properties, use, occurrence, analysis, carcinogenesis, mutagenicity and metabolism reviewed (33).

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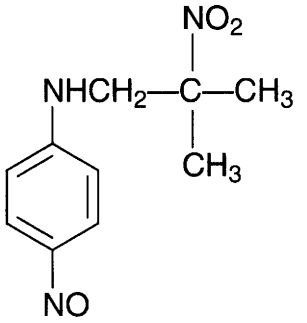
M266 *N*-(2-methyl-2-nitropropyl)-4-nitrosoaniline



$C_{10}H_{13}N_3O_3$ **Mol. Wt.** 223.23 **CAS Registry No.** 24458-48-8

Synonyms methylnitropropyl-4-nitrosoaniline; *N*-(2-methyl-2-nitropropyl)-4-nitroso-benzenamine; Nitrol; *N*-(2-methyl-2-nitropropyl)-*p*-nitroso-aniline

EINECS No. 246-267-9 **RTECS No.** BY 5760000

Physical properties

M. Pt. 131-132°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2730 mg kg^{-1} (1).

Carcinogenicity and chronic effects

TD_{Lo} (route unspecified) (2 yr) rat 81,800 mg kg^{-1} (total dose), carcinogenic effects (effects unspecified) (2).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

Other comments

Reviews on experimental toxicology, environmental effects and human health effects listed (4).

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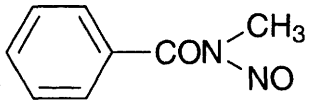
M267 *N*-methyl-*N*-nitrosobenzamide



$C_8H_8N_2O_2$ **Mol. Wt.** 164.16 **CAS Registry No.** 63412-06-6

Synonyms MNB

RTECS No. CV 5585350

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 70 mg kg^{-1} (1).

References

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M268 *N*-(*N*-methyl-*N*-nitrosocarbamoyl)-L-ornithine

$$HO_2C(NH_2)CH(CH_2)_3NHC(O)N(NO)CH_3$$

$C_7H_{14}N_4O_4$ **Mol. Wt.** 218.21 **CAS Registry No.** 63642-17-1

Synonyms *N*-(*N*-nitroso-*N*-methylcarbamoyl)-L-ornithine

RTECS No. RM 2983000

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Induces acinar cell tumours in rat (1).

Induces duct-like pancreatic carcinomas in hamster (2).

Genotoxicity

In vivo (alkaline elution analysis) and *in vitro* ♂ Syrian hamster, Lewis rat pancreatic acinar cell DNA damaged in a dose-related manner (3).

References

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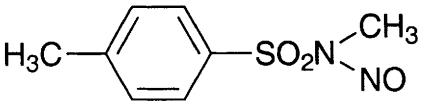
M269 *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide



$C_8H_{10}N_2O_3S$ **Mol. Wt.** 214.25 **CAS Registry No.** 80-11-5

Synonyms *N*,4-dimethyl-*N*-nitrosobenzenesulfonamide; Diazald; Diazale

EINECS No. 201-252-6 **RTECS No.** XT 5950000

Uses In preparation of diazomethane.

Physical properties

M. Pt. 62°C

Solubility Organic solvents: benzene, carbon tetrachloride, chloroform, diethyl ether, petroleum ether

Occupational exposure

***Safety* phrases** Avoid contact with skin and eyes (S24/25)

Mammalian & avian toxicity

Acute data

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

LD_{50} oral rat 2700 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 19 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Reported to be non-carcinogenic (4).

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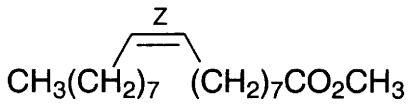
M270 *Z*-methyl oleate



$C_{19}H_{36}O_2$ **Mol. Wt.** 296.49 **CAS Registry No.** 112-62-9

Synonyms 9-octadecenoic acid, methyl ester, (Z)-; *cis*-oleic acid, methyl ester; methyl *cis*-9-octadecenoate; Emerest 2301; Emerest 2801; Emery 2310

EINECS No. 203-992-5 **RTECS No.** RK 0895000

Uses Lubricant and chemical intermediate. In liposomes for experimental and therapeutic purposes (1).

Occurrence In a variety of fruits, flowers and plant extracts, including Eucalyptus oil (2).
In cellular membranes (3).

Physical properties

M. Pt. –20°C **B. Pt.** 168-170°C at 2 mmHg **Flash point** 177°C **Specific gravity** 0.874 at 20°C with respect to water at 4°C
Solubility Organic solvents: miscible with diethyl ether, ethanol

Environmental fate

Degradation studies
Readily biodegraded by *Pseudomonas aeruginosa* strain (4).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Dermal application of 0.05 ml 20% (v/v) in acetone 3 × wk^{-1} for 1 yr had a promoting effect on skin tumours initiated by 7,12-dimethylbenz[*a*]anthracene; even without initiation it had some activity in lymphoma carcinogenesis (5).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (6).

References

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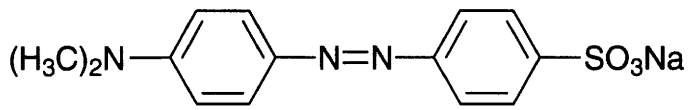
M271 Methyl Orange



$C_{14}H_{14}N_3NaO_3S$ **Mol. Wt.** 327.34 **CAS Registry No.** 547-58-0
Synonyms sodium 4-[(4-dimethylamino)phenylazo]benzenesulfonate; Diazoben; Helianthine; C.I. 13025; C.I. Acid Orange 52
EINECS No. 208-925-3 **RTECS No.** DB 6327000
Uses As an indicator in aqueous solution for titrating mineral acids, strong bases, estimating alkalinity of waters. Dyeing and printing of textiles.

Physical properties

M. Pt. >200°C (decomp.)
Solubility Water: 2-3 g ml^{-1} at 25°C

Ecotoxicity

Invertebrate toxicity
LC_{50} (96 hr) freshwater shrimp 3.7 mg l^{-1} (1).

Environmental fate

Abiotic removal
Hydrolytic and photolytic degradation occurs to yield 4-hydroxy-*N,N*-dimethyl aniline and *N,N*-dimethyl aniline (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 64-100 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 101 mg kg^{-1} (4).

Genotoxicity

Salmonella typhimurium TA98, with metabolic activation positive (5).
SOS-Chromotest *Escherichia coli* PQ37 negative (6).
In vitro mouse embryo oncogenic transformation positive (7).

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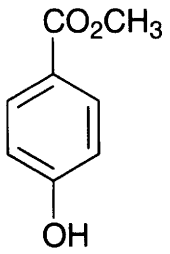
M272 methylparaben



$C_8H_8O_3$ **Mol. Wt.** 152.15 **CAS Registry No.** 99-76-3

Synonyms methyl *p*-hydroxybenzoate; 4-hydroxybenzoic acid, methyl ester; Nipagin M; Tegosept M; Methyl Chemosept; Methyl Parasept; Paridol Methyl

EINECS No. 202-785-7 **RTECS No.** DH 2450000

Uses Preservative in foods, beverages and cosmetics. Has antibacterial and antifungal properties.

Occurrence In several animal species as a volatile aromatic component of scent (1,2).

Physical properties

M. Pt. 126-128°C **B. Pt.** 270-280°C (decomp.)

Solubility Water: 2.5 g l^{-1}. Organic solvents: acetone, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 6.34 ppm Microtox test (3).

Environmental fate

Degradation studies

Pseudomonas cepacia can grow in the presence of methylparaben and can contribute to its degradation (4).

Abiotic removal

A sterile 0.1% solution of pH 6 has a half life of 6675 days (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig 3 g kg^{-1} (5).

LD_{50} oral dog 3 g kg^{-1} (6).

LD_{50} intraperitoneal mouse 960 mg kg^{-1} (7).

LD_{50} subcutaneous mouse 1200 mg kg^{-1} (8).

Metabolism and toxicokinetics

Can be absorbed from mammalian intestines and through skin and body of goldfish (9).

Present in an injectable preparation of gentamicin and was excreted in the urine of preterm infants, following intramuscular injection, mainly in the conjugated form. *p*-Hydroxybenzoic acid was detected as the urinary metabolite (10).

Irritancy

Can cause stinging of skin, particularly the face, possibly through calcium channel activation (11).

Genotoxicity

- *Salmonella typhimurium* TA100, TA1537, TA98 and TA1535 with and without metabolic activation negative (12). Induced chromosomal aberrations in Chinese hamster cells without, but not with, metabolic activation (13).

Other effects

Other adverse effects (human)

Hypersensitivity reactions occur with hydroxybenzoates, generally delayed reaction contact dermatitis. Immediate reactions with urticaria and bronchospasm have been reported. Activity can be adversely affected by the presence of other excipients or active ingredients (14-16).

Other comments

Sorption by nylon can reduce the activity of the compound (5).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (17,18).
Contact dermatitis in humans reviewed (19-22).

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M273 2-methylpentane

$$CH_3CH_2CH_2CH(CH_3)_2$$

$C_6H_{14} **Mol. Wt.** 86.18 **CAS Registry No.** 107-83-5

Synonyms isohexane

EINECS No. 203-523-4

Physical properties

M. Pt. −154°C **B. Pt.** 62°C **Flash point** −23°C (closed cup) **Specific gravity** 0.653 **Volatility** v.den. 3.00

Occupational exposure

DE-MAK 200 ppm (720 mg m^{-3})
FR-VME 500 ppm (1800 mg m^{-3})

UN No. 2288 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Environmental fate

Degradation studies

Incubation with natural flora in groundwater in the presence of other components of high octane gasoline (100 µl l^{-1}). Biodegradation 6% after 192 hr at 13°C, initial concentration 1.72 µl l^{-1} (1).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Gavage (4 wk) ♂ F-344 rats (dose unspecified) 5 days wk^{-1} nephrotoxicity was observed (2).

Metabolism and toxicokinetics

Pulmonary retention 15-18%. Absorption rate measured was 0.11 µg cm^{-2} hr^{-1} in the rat and is expected to be lower in humans (3).

In vitro rate of dermal absorption was found to be 0.11 µg cm^{-2} hr^{-1} (4).

Other effects

Any other adverse effects

An intraperitoneal 2 wk dose to ♀ rats of 1.5 g kg^{-1} resulted in a 24 hr urinary excretion of 2.64 µg β_2-microglobulin and 352 µg albumin (5).

Legislation

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

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M274 3-methylpentane

$$CH_3CH_2CH(CH_3)CH_2CH_3$$

C_6H_{14} **Mol. Wt.** 86.18 **CAS Registry No.** 96-14-0

EINECS No. 202-481-4

Physical properties

B. Pt. 63.3°C **Flash point** –7°C **Specific gravity** 0.664 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.60 **Volatility** v.p. 100 mmHg at 10.5°C ; v.den. 2.97

Occupational exposure

DE-MAK 200 ppm (720 mg m^{-3})

UN No. 1208 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid

Environmental fate

Degradation studies
Incubation with natural flora in groundwater in the presence of the other components of high-octane gasoline (100 µl l^{-1}). Biodegradation 7% after 192 hr at 13°C initial concentration 1.30 µl l^{-1} (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).
The log P_{ow} value exceeds the European Community recommended value 3.0 (6th and 7th amendments) (3).

Other comments

Physico-chemical properties, legislation and storage reviewed (4).

References

1. Jamison, V. W. et al *Proc. Third Int. Biodegrad. Symp.* 1976, Applied Science Publishers.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC, 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK.
4. Institut National de Recherche et de Securite *Cah. Notes Doc.* 1989, **135**, 381-384

M275 2-methyl-2,4-pentanediol

$$CH_3CH(OH)CH_2C(OH)(CH_3)CH_3$$

$C_6H_{14}O_2$ **Mol. Wt.** 118.18 **CAS Registry No.** 107-41-5
Synonyms 2-methylpentane-2,4-diol; diolane; hexylene glycol; Isol; 1,1,3-trimethyltrimethylenediol
EINECS No. 203-489-0 **RTECS No.** SA 0810000
Uses Cosmetics. Hydraulic brake fluid. Coupling agent for castor oil.

Physical properties

M. Pt. –40°C **B. Pt.** 197.1°C **Flash point** 93°C **Specific gravity** 0.9234 at 20°C **Volatility** v.p. 0.05 mmHg at 20°C ; v.den. 4.0
Solubility Organic solvents: diethyl ether

Occupational exposure

FR-VLE 25 ppm (125 mg m^{-3})
SE-CEIL 25 ppm (120 mg m^{-3})

UK-LTEL 25 ppm (123 mg m^{-3}) **UK-STEL** 25 ppm (123 mg m^{-3})
US-STEL ceiling limit 25 ppm (121 mg m^{-3})
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) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) Mississippi silverside 10 g l^{-1} (1).
LC_{50} (24 hr) goldfish >5 g l^{-1} (2).

Invertebrate toxicity
EC_{50} (5 min) *Photobacterium phosphoreum* 3038 ppm Microtox test (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3700 mg kg^{-1} (4).
LD_{50} oral mouse 3097 mg kg^{-1} (5).
LD_{50} oral rabbit 3200 mg kg^{-1} (6).
LD_{50} oral guinea pig 2800 mg kg^{-1} (6).
LD_{50} dermal rabbit 8560 mg kg^{-1} (7).
LD_{50} intraperitoneal rat 1500 mg kg^{-1} (8).
LD_{50} intraperitoneal mouse 1299 mg kg^{-1} (9).

Sub-acute and sub-chronic data
TC_{Lo} inhalation human (15 month) 50 ppm, eye effects: irritation, diplopia, cataracts and eyeground. Pulmonary system effects: effects on respiration and respiratory pathway (7,10).

Metabolism and toxicokinetics
Eliminated in the urine, partly in conjugated forms (species unspecified) (11).

Irritancy
Dermal rabbit (24 hr) 465 mg, caused moderate irritation (12).
Eye rabbit 93 mg caused severe irritation (exposure unspecified) (13).

Other effects

Other adverse effects (human)
Eyes irritant. Central nervous system depression produced by oral administration (14).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

Other comments

It has been defined as inert (16).

References

1. Verschueren, K. *Handbook of Environmental Data of Organic Chemicals* 1983, Van Nostrand Reinhold Co. Inc., New York, USA.
2. Bridie, A. L. et al *Water Res.* 1979, **13**, 627-630.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. *Raw Material Data Handbook, Vol. 1 Organic Solvents* 1974, 68.
5. *J. Am. Pharm. Assoc., Sci. Ed.* 1956, **45**, 669.
6. *Fed. Proc.* 1945, **4**, 142.

7. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, 731, Academic Press, New York, USA.
8. *J. Pharm. Pharmacol.* 1959, **11**, 150.
9. Lewis, R. J. (Ed.) Sax's *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, USA.
10. *J. Ind. Hyg. Toxicol.* 1946, **28**, 262.
11. Jacobsen, E. *Acta Pharmacol. Toxicol.* 1958, **14**, 207-213.
12. *J. Pharmacol. Exp. Ther.* 1944, **82**, 377.
13. *BIOFAX Industrial Bio-Test Laboratories, Inc., Data Sheets* 1970, 12-14.
14. *Chemical Safety Data Sheets: Vol. 1 Solvents* 1989, The Royal Society of Chemistry, London, UK.
15. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
16. Shell Chemical Corporation *Industrial Hygiene Bulletin* SC:57-101 and SC57-102, New York, USA

M276 3-methyl-2,4-pentanedione

$$CH_3C(O)CH(CH_3)C(O)CH_3$$

$C_6H_{10}O_2$ **Mol. Wt.** 114.14 **CAS Registry No.** 815-57-6

Synonyms 3-methylacetoacetone

EINECS No. 212-420-3

Uses Organic synthesis.

Physical properties

B. Pt. 172-174°C **Flash point** 56°C **Specific gravity** 0.981 at 20°C with respect to water at 4°C

Ecotoxicity

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 1400 ppm, Microtox test (1).

Mammalian & avian toxicity

Irritancy

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

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2402, Sigma-Aldrich, Milwaukee, WI, USA

M277 2-methyl-1-pentanol

$$CH_3CH_2CH_2CH(CH_3)CH_2OH$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 105-30-6

Synonyms amyl methyl alcohol; 1,3-dimethylbutanol; isopropyl dimethyl carbinol; methylamyl alcohol; methyl isobutyl carbinol; 2-methylpent-1-ol; 2-methyl-2-propylethanol

EINECS No. 203-285-1 **RTECS No.** SA 7175000

Uses Solvent. Organic synthesis.

Physical properties

B. Pt. 148°C **Flash point** 50°C **Specific gravity** 0.8263 at 20°C with respect to water at 4°C
Volatility v.p. 1.1 mmHg at 20°C ; v.den. 3.52
Solubility Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

UN No. 1987

Mammalian & avian toxicity

Acute data
LD_{50} dermal rat 1400 mg kg^{-1} (1).
LD_{50} dermal rabbit 3600 mg kg^{-1} (1).

Irritancy
Dermal rabbit (24 hr) 10 mg caused mild irritation (2).
750 μg instilled into rabbit eye for 24 hr caused severe irritation (3).

Other effects

Other adverse effects (human)
Inhalation human, 50 ppm caused lung irritation (exposure not specified) (4).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
2. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
3. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, Prague, Czechoslovakia.
4. *J. Ind. Hyg. Toxicol.* 1946, **28**, 262.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M278 2-methyl-3-pentanol

$$CH_3CH_2CH(OH)CH(CH_3)_2$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 565-67-3

Synonyms ethyl isopropyl carbinol; 1-isopropylpropanol

EINECS No. 209-286-3 **RTECS No.** SA 7400000

Uses Fuel.

Physical properties

B. Pt. 128°C **Flash point** 46°C **Specific gravity** 0.8243 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.65 (1)
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1987

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 320 mg kg^{-1} (2).

References

1. Leahy, D. E. *J. Pharm. Sci.* 1986, **75**(7), 629-636.
2. *Report* US Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD 21010, USA

M279 3-methyl-3-pentanol

$$CH_3CH_2C(CH_3)(OH)CH_2CH_3$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 77-74-7

Synonyms diethyl carbinol; 1-ethyl-1-methyl-1-propanol; 3-hydroxy-3-methylpentane; methyldiethyl carbinol

EINECS No. 201-053-4 **RTECS No.** SA 7450000

Physical properties

M. Pt. –38°C **B. Pt.** 123°C **Flash point** 46°C **Specific gravity** 0.824
Solubility Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies
In activated sludge, biodegradation resulted in formation of the corresponding fatty acid (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 710 mg kg^{-1} (2).
LD_{Lo} oral mouse 750 mg kg^{-1} (3).
LD_{50} subcutanous mouse 1100 mg kg^{-1} (4).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. Nitsuma, T. et al *Tohoku Gakuin Daigaku Kogakubu Kenkyu Hokoku* 1988, **23**(1), 57-60 (Japan.).
2. *J. Pharmacol. Exp. Ther.* 1955, **115**, 230.
3. Leube, F. *Narkoseversuche mit hoeheren Alkoholen und Stickstoffderivaten* 1931 (Ger.).
4. *Arzneim.-Forsch.* 1955, **5**, 161 (Ger.).
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M280 4-methyl-1-pentanol

$$CH_3CH(CH_3)CH_2CH_2CH_2OH$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 626-89-1

Synonyms isohexanol; isohexyl alcohol

EINECS No. 210-969-3 **RTECS No.** NR 3020000

Physical properties

B. Pt. 160-165°C **Flash point** 51°C **Specific gravity** 0.821 **Partition coefficient** log P_{ow} 1.25

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) zebra fish 340 mg l^{-1} (1).
LC_{50} (48 hr) ide 287-332 mg l^{-1} (1).

Invertebrate toxicity

LOEC *Microcystis aeruginosa* and *Scenedesmus quadricauda* 32-72 mg l^{-1} (2,3).
ICG_{50} (50% growth inhibitory concentration) *Tetrahymena pyriformis* 0.542 g l^{-1} (4).

Environmental fate

Degradation studies

Biodegradability of higher alcohols in the activated sludge process decreases with increasing number of carbon atoms (5).
Oxidised by a thermophilic obligate methane-oxidising bacterium H-2 (type I) (6).

Other comments

US EPA have recommended testing for environmental and health effects (7).

References

1. Wellens, H. Z. *Wasser/Abwasser Forsch.* 1982, **15**, 49.
2. Bringmann, G. et al *GWF, Gas- Wasserfach: Wasser/Abwasser* 1976, **117**(9).
3. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
4. Schultz, T. W. et al *Bull. Environ. Contam. Toxicol.* 1993, **51**, 681-688.
5. Niitsuma, T. et al *Tohoku Gakuin Daigaku Kogakubu Kenkyu Hokoku* 1988, **23**(1), 57-60 (Japan.) (*Chem. Abstr.* **110**, 140816k).
6. Imai, T. et al *Appl. Environ. Microbiol.* 1986, **52**(6), 1403-1406.
7. *Fed. Regist.* 6 Mar. 1991, **56**(44), 9534-9572

M281 4-methyl-2-pentanol

$$(CH_3)_2CHCH_2CH(OH)CH_3$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 108-11-2

Synonyms isobutyl methyl carbinol; isobutylmethylmethanol; MAOH; MIBC; 3-MIC

EINECS No. 203-551-7 **RTECS No.** SA 7350000

Uses Solvent for dyes, oils, gums, resins, waxes, nitrocellulose and ethylcellulose. Organic synthesis. Froth flotation. Brake fluids.

Physical properties

M. Pt. -90°C **B. Pt.** 131.8°C **Flash point** 41°C **Specific gravity** 0.802 at 20°C **Volatility** v.p. 2.8 mmHg at 20°C ; v.den. 3.53

Solubility Water: 17 g l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol, hydrocarbons

Occupational exposure

DE-MAK 25 ppm (110 mg m^{-3})
FR-VME 25 ppm (100 mg m^{-3})
SE-LEVL 40 ppm (170 mg m^{-3}) **SE-CEIL** 25 ppm (110 mg m^{-3})
UK-LTEL 25 ppm (106 mg m^{-3}) **UK-STEL** 40 ppm (170 mg m^{-3})
US-TWA 25 ppm (104 mg m^{-3}) **US-STEL** 40 ppm (167 mg m^{-3})

UN No. 2053 **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) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 360 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (duration and species unspecified) 2.45 g l^{-1} (2).

Environmental fate

Degradation studies
Oxidation parameters, BOD_5 2.12 mg l^{-1} O_2 NEN3235 (Nederlandse norm) 5.4 mg $l^{-1}O_2$; COD 2.60 mg $l^{-1}O_2$ NEN3235 5.3 mg $l^{-1}O_2$ (Nederlandse norm) (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2590 mg kg^{-1} (4).
LD_{Lo} oral mouse 1000 mg kg^{-1} (5).
LC_{Lo} (4 hr) inhalation rat 2000 ppm (6).
LD_{50} intraperitoneal mouse 812 mg kg^{-1} (7).
LD_{50} dermal rabbit 3560 mg kg^{-1} (4).

Metabolism and toxicokinetics

Inhalation (2 hr) humans 10, 100 and 200 mg m^{-3}. The pulmonary uptake was ~60%. The concentration in blood rose rapidly after the onset of exposure and no plateau level was reached during exposure. Apparent blood clearance rate was 1.6 l hr^{-1} kg^{-1}. Only 0.04% was eliminated unchanged via the kidneys within 3 hr post-exposure. Concentrations of the metabolites 4-hydroxy-4-methyl-2-pentanone and 4-methyl-2-pentanol were below the detection limits (8).

Irritancy

Dermal rabbit (24 hr) 10 mg caused mild irritation (4).
Eye rabbit 20 mg (uncovered) caused severe irritation (duration unspecified) (4).

Genotoxicity

Salmonella typhimurium and *Escherichia coli* with and without metabolic activation negative (8).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

Other comments

Detected in trace amounts in some water samples.
Metabolite of methyl isobutyl ketone in humans (10).

References

1. Bridie, A. L. et al *Water Res.* 1979, **13**, 623.
2. Vaishnav, D. D. *Toxic Assess.* 1986, **1**(2), 227-240.
3. Shell Chemie *Shell Industrie Chemicalien gids* 1/1/1975 Shell Nederland Chemie, Afd. Industrie-chemicalien, Wassenaarseweg 80, s-Gravenhage, Netherlands.
4. *Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119.
5. *University of California, Pub. Pharmacol.* 1949, **2**, 217.
6. Lewis, R. J. (Ed.) Sax's *Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, USA.
7. *J. Ind. Hyg. Toxicol.* 1949, **31**, 343.
8. Shimizu, H. et al *Sangyo Igaku* 1985, **27**(6), 400-419.
9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
10. Hjelm, E. W. et al *Int. Arch. Occup. Environ. Health* 1990, **62**(1), 19-26

M282 2-methyl-1-pentene

$$CH_3CH_2CH_2C(CH_3)=CH_2$$

C_6H_{12} **Mol. Wt.** 84.16 **CAS Registry No.** 763-29-1

Synonyms 2-methylpentene; 2-methylpent-1-ene; 1-methyl-1-propylethene

EINECS No. 212-108-7 **RTECS No.** SB 2230000

Uses Organic synthesis.

Occurrence Has been detected in engine exhausts (1).

Physical properties

M. Pt. -136°C **B. Pt.** 62°C **Flash point** -26°C **Specific gravity** 0.684 at 15.5°C with respect to water at 15.5°C

Volatility v.p. 326 mmHg at 37.3°C ; v.den. 2.9

Solubility Water: 78 mg l^{-1} at 20°C. Organic solvents: benzene, chloroform, ethanol, petroleum ether

Occupational exposure

UN No. 1993

Environmental fate

Degradation studies

Degradation by activated sludge 1.0% of ThOD after 6 hr; 1.1% of ThOD after 12 hr; 1.7% of ThOD after 24 hr (initial concentration not specified) (2).

Mammalian & avian toxicity

Acute data

LC_{50} (4 hr) inhalation rat 115 g m^{-3} (3).

LC_{50} (2 hr) inhalation mouse 130 g m^{-3} (3).

Irritancy

Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (3).

Other effects

Other adverse effects (human)

Symptoms of exposure include burning sensation, coughing, wheezing, laryngitis, shortness of breath, headache, nausea and vomiting (3).

Other comments

Autoignition temperature 250°C.

References

1. Lipari, F. *J. Chromatogr.* 1990, **503**(1), 51-68.
2. Gerhold, R. M. et al *J. Water Pollut. Control Fed.* 1966, **38**(4), 562.
3. *Russ. Pharmacol. Toxicol. (Engl. Transl.)* 1968, **31** 4. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2406, Sigma-Aldrich, Milwaukee, WI, USA

M283 2-methyl-2-pentene

$$CH_3CH_2CH{=}C(CH_3)CH_3$$

C_6H_{12} **Mol. Wt.** 84.16 **CAS Registry No.** 625-27-4

Synonyms 2-ethyl-1,1-dimethylethylene; 2-methylpent-2-ene

EINECS No. 210-883-6 **RTECS No.** SB 2240000

Uses Organic synthesis.

Occurrence In gasoline.

Physical properties

M. Pt. −135°C **B. Pt.** 67°C **Flash point** −23°C **Specific gravity** 0.690 at 20°C with respect to water at 4°C

Volatility v.den. 2.9

Solubility Organic solvents: benzene, carbon tetrachloride, chloroform, ethanol, petroleum ether

Occupational exposure

UN No. 1993

Mammalian & avian toxicity

Acute data

LC_{50} (4 hr) inhalation rat 114 g m^{-3} (1).

LC_{50} (2 hr) inhalation mouse 130 g m^{-3} (1).

Sub-acute and sub-chronic data

Gavage rat (4 wk) 500 or 2000 mg kg^{-1} day^{-1} 5 days wk^{-1} for 4 wk caused fatality of 1/10 animals in each group (2).

Irritancy

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

References

1. *Russ. Pharmacol. Toxicol. (Engl. Transl.)* 1968, **31**.
2. Halder, C. A. et al *Toxicol. Ind. Health* 1985, **1**(3), 67-87.
3. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2406, Sigma-Aldrich, Milwaukee, WI, USA

M284 4-methyl-1-pentene

$$CH_3CH(CH_3)CH_2CH{=}CH_2$$

C_6H_{12} **Mol. Wt.** 84.16 **CAS Registry No.** 691-37-2

Synonyms isobutylethylene; 4-methylpent-1-ene

EINECS No. 211-720-1

Uses Preparation of polymers.

Physical properties

M. Pt. –153.6°C **B. Pt.** 53-54°C **Flash point** –31°C **Specific gravity** 0.664 at 20°C **Volatility** v.p. 424 mmHg at 38°C ; v.den. 2.9
Solubility Water: 48 mg l^{-1} at 20°C. Organic solvents: benzene, chloroform, ethanol, petroleum ether

Environmental fate

Degradation studies
Degradation by activated sludge 0.9% of ThOD after 6 hr; 1.4% of ThOD after 12 hr (initial concentration not specified) (1).

Mammalian & avian toxicity

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

Other comments

Autoignition temperature 250°C.

References

1. Gerhold, R. M. et al *J. Water Pollut. Control Fed.* 1966, **38**(4), 562.
2. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2407, Sigma-Aldrich, Milwaukee, WI, USA

M285 4-methyl-2-pentene

$$CH_3CH(CH_3)CH{=}CHCH_3$$

C_6H_{12} **Mol. Wt.** 84.16 **CAS Registry No.** 4461-48-7
Synonyms 1-isopropyl-2-methylethylene; 4-methylpent-2-ene
EINECS No. 224-721-7
Uses Organic synthesis.
Occurrence In fossil fuels.

Physical properties

M. Pt. –134.4°C **B. Pt.** 58°C **Flash point** –32°C **Specific gravity** 0.670 at 20°C with respect to water at 4°C
Volatility v.den. 2.90
Solubility Organic solvents: benzene, chloroform, petroleum ether

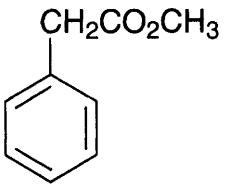
Environmental fate

Degradation studies
Degradation by activated sludge 0.6% of ThOD after 6 hr; 1.3% of ThOD after 24 hr (initial concentration not specified) (1).

References

1. Gerhold, R. M. et al *J. Water Pollut. Control Fed.* 1966, **38**(4), 562

M286 methyl phenylacetate



$C_9H_{10}O_2$ **Mol. Wt.** 150.18 **CAS Registry No.** 101-41-7

Synonyms methyl phenylethanoate; methyl benzeneacetate

EINECS No. 202-940-9 **RTECS No.** AJ 3175000

Uses Organic synthesis. In perfumes.

Occurrence Aroma component of cooked meat and many plants.

Physical properties

B. Pt. 218°C **Flash point** 89°C **Specific gravity** 1.044 at 20°C **Partition coefficient** log P_{ow} 1.83

Volatility v.den. 5.18

Solubility Organic solvents: ethanol, fixed oils

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2600 mg kg^{-1} (1).

LD_{50} dermal rabbit 2400 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused irritation (1).

References

1. *Food Cosmet. Toxicol.* 1974, **12**, 807

M287 methylphosphonic dichloride

$CH_3P(O)Cl_2$

CH_3Cl_2OP **Mol. Wt.** 132.91 **CAS Registry No.** 676-97-1

EINECS No. 211-634-4 **RTECS No.** TA 1840000

Uses Chemical intermediate and dehydrating agent.

Physical properties

M. Pt. 32°C **B. Pt.** 162°C

Mammalian & avian toxicity

Acute data

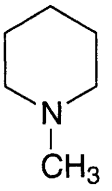
LC_{50} (4 hr) inhalation rat 26 ppm (1).

Compound is an inhibitor of cholinesterases (2).

References

1. *Am. Ind. Hyg. Assoc. J.* 1964, **25**, 470.
2. Ashani, Y. et al *Biochemistry* 1990, **29**(10), 2456-2463

M288 1-methylpiperidine



$C_6H_{13}N$ **Mol. Wt.** 99.18 **CAS Registry No.** 626-67-5

Synonyms *N*-methylpiperidine

EINECS No. 210-959-9 **RTECS No.** TN 1225000

Physical properties

B. Pt. 107°C **Flash point** 3°C **Specific gravity** 0.821 at 15°C **Partition coefficient** log P_{ow} 1.30

Occupational exposure

UN No. 2399 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive

Mammalian & avian toxicity

Acute data

LD_{Lo} subcutaneous rabbit 400 mg kg^{-1} (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. *Ber. Dtsch. Chem. Ges., Abt. B: Abhand.* 1901, **32**, 2408.
2. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M289 2-methyl-2-propen-1-ol

$$CH_2=C(CH_3)CH_2OH$$

C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 513-42-8

Synonyms methallyl alcohol; isopropenylcarbinol; 2-methylallyl alcohol; 3-hydroxy-2-methylpropene

EINECS No. 208-161-0 **RTECS No.** UD 5250000

Uses Organic synthesis.

Physical properties

B. Pt. 113-115°C **Flash point** 33°C **Specific gravity** 0.852 at 20°C with respect to water at 4°C
Volatility v.den. 2.5
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2614 **HAZCHEM Code** 2W **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{Lo} oral mouse 500 mg kg^{-1} (1).
LC_{Lo} (2 hr) inhalation mouse 2900 ppm (1).
LD_{Lo} dermal rabbit 2000 mg kg^{-1} (1).

Irritancy
Dermal rabbit, 500 mg caused moderate irritation (exposure not specified) (1).

References

1. Shell Chemical Co. *Report* 1961, 6

M290 methyl propionate

$$CH_3CH_2CO_2CH_3$$

$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 554-12-1

Synonyms methyl propanoate; methyl propylate; propionic acid, methyl ester

EINECS No. 209-060-4 **RTECS No.** UF 5970000

Uses In organic synthesis.

Physical properties

M. Pt. -88°C **B. Pt.** 79°C **Flash point** 6°C **Specific gravity** 0.915 at 20°C with respect to water at 4°C
Volatility v.p. 40 mmHg at 11°C ; v.den. 3.0
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1248 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Do not breathe vapour – Do not empty into drains – Take precautionary measures against static discharges (S2, S16, S23, S29, S33)

Ecotoxicity

Invertebrate toxicity
LOEC *Scenedesmus quadricauda* 11 mg l^{-1} (duration unspecified) (1).
LOEC *Microcystis aeruginosa* 13 mg l^{-1} (duration unspecified) (2).
EC_{50} (24 hr) *Daphnia magna* 516 mg l^{-1} (3).
NOEC (21 day) *Daphnia magna* 6.3 mg l^{-1} (3).
EC_{50} (48 hr) cell multiplication inhibition test *Scenedesmus subspicatus* >500 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 5000 mg kg^{-1} (5).
LD_{50} oral mouse 3460 mg kg^{-1} (6).
LD_{Lo} oral rabbit 2550 mg kg^{-1} (7).
LC_{50} inhalation mouse 27,000 mg m^{-3} (duration unspecified) (6).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (5).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).
Autoignition temperature 469°C.

References

1. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
2. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9).
3. Kuehn, R. et al *Water Res.* 1989, **23**(4), 501-510.
4. Kuehn, R. et al *Water Res.* 1990, **24**(1), 31-38.
5. *Food Chem. Toxicol.* 1982, **20**, 765.
6. *Gig. Tr. Prof. Zabol.* 1974, **18**(3), 48.
7. *AMA Arch. Ind. Health* 1960, **21**, 100.
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

M291 methyl propyl ether

$$CH_3CH_2CH_2OCH_3$$

$C_4H_{10}O$ **Mol. Wt.** 74.12 **CAS Registry No.** 557-17-5

Synonyms 1-methoxypropane; Metopryl; Neothyl

EINECS No. 209-158-7 **RTECS No.** KO 2280000

Uses Inhalation anaesthetic.

Physical properties

B. Pt. 38.8°C at 761 mmHg **Flash point** < -20°C **Specific gravity** 0.7356 at 13°C with respect to water at 4°C
Solubility Water: 50 ml l^{-1} at 25°C

Mammalian & avian toxicity

Acute data
LC_{50} (15 min) inhalation mouse 260 mg m^{-3} (1).

References

1. *Anesthesiology* 1950, **11**, 455

M292 methyl propyl ketone

$$CH_3C(O)CH_2CH_2CH_3$$

$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 107-87-9

Synonyms 2-pentanone; ethylacetone; pentan-2-one

EINECS No. 203-528-1 **RTECS No.** SA 7875000

Uses Solvent.
Occurrence Volatile emission product from a variety of foods including smoked meat (1).
Mammalian urinary product, particularly during starvation (2).

Physical properties

M. Pt. -78°C **B. Pt.** 102°C **Flash point** 7.22°C **Specific gravity** 0.809 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.91 **Volatility** v.p. 27 mmHg at 20°C ; v.den. 3.0
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

DE-MAK 200 ppm (710 mg m^{-3})
FR-VME 200 ppm (705 mg m^{-3})
UK-LTEL 200 ppm (716 mg m^{-3}) **UK-STEL** 250 ppm (895 mg m^{-3})
US-TWA 200 ppm (705 mg m^{-3}) **US-STEL** 250 ppm (881 mg m^{-3})

UN No. 1249 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3.7 g kg^{-1} (3).
LC_{50} (4 hr) inhalation rat 2000 ppm (3).
LD_{50} dermal rabbit 6.5 g kg^{-1} (4).
LD_{50} intraperitoneal rat 1.25 mg kg^{-1} (4).

Irritancy

Irritant to soft mucous tissues, including the lungs and upper respiratory tract (5-7).
Irritant to eyes (5).

Genotoxicity

Weak inducer of aneuploidy in *Saccharomyces cerevisiae* D61.M (8).

Other effects

Other adverse effects (human)

The defatting action on skin can lead to dermatitis (7).
Prolonged exposure can cause headache, drowsiness and ultimately death (7).

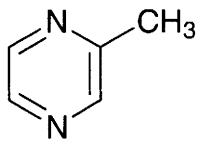
Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).

References

1. Wittkowski, R. et al *Food Chem.* 1990, **37**(2), 135-144.
2. Yancey, M. et al *J. Chromatogr.* 1986, **382**, 3-18.
3. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
4. *Raw Material Data Handbook* 1974, **1**, 83.
5. Douglas, R. B. et al *Ann. Occup. Hyg.* 1987, **31**(2), 265-267.
6. Abraham, M. H. *Quant. Struct.-Act. Relat.* 1990, **9**(1), 6-10.
7. *Material Safety Data Sheet* 1990, M and B Laboratory Products.
8. Zimmerman, F. K. et al *Mutat. Res.* 1985, **149**, 339.
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

M293 2-methylpyrazine



$C_5H_6N_2$ **Mol. Wt.** 94.12 **CAS Registry No.** 109-08-0

EINECS No. 203-645-8 **RTECS No.** UQ 3675000

Uses Chemical intermediate.

Occurrence In the aroma of a variety of cooked foods of vegetable and animal origin, including coffee (1) and boiled shrimps (2).
Formed by thermal pretreatment of sewage sludge (3).

Physical properties

M. Pt. -29°C **B. Pt.** 133°C at 737 mmHg **Flash point** 50°C **Specific gravity** 1.030 at 25°C
Solubility Water: miscible. Organic solvents: acetone, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} 30 min *Photobacterium phosphoreum* 430 ppm Microtox test (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1.8 g kg^{-1} (5).
LD_{50} intraperitoneal mouse 1.82 g kg^{-1} (6).
The compound has central depressant, weak hypnotic and anticonvulsant actions with hypnotic doses ~ 1.25 g kg^{-1} intraperitoneally in mice and anticonvulsant doses of 130-580 mg kg^{-1} intraperitoneally (6).

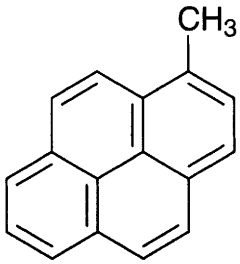
Genotoxicity

In mutagenicity tests with *Salmonella typhimurium* TA100 and TA102 methylpyrazine was judged not to contribute to the positive result seen with coffee (2).
Salmonella typhimurium TA100, TA98, TA1537 with and without metabolic activation negative. Induced chromosomal aberrations in Chinese hamster ovary cells with or without metabolic activation (7).

References

1. Shenderyuk, V. V. et al *Rybn. Khoz. (Moscow)* 1990, (1), 86-89 (Russ.) (*Chem. Abstr.* **112**, 177182t).
2. Aeschbacher, H. V. et al *Food Chem. Toxicol.* 1989, **27**(4), 227-232.
3. Pinnekamp, J. *Gewaesserschutz, Wasser, Abwasser* 1986, **85**, 331-358 (Ger.) (*Chem. Abstr.* **107**, 160853m).
4. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, 26(3), 361-431.
5. *Drug Chem. Toxicol. (1977)* 1980, **3**, 249.
6. *Toxicol. Appl. Pharmacol.* 1970, **17**, 244.
7. Stich, H. F. et al *Food Chem. Toxicol.* 1980, **18**, 581-584

M294 1-methylpyrene



$C_{17}H_{12}$ **Mol. Wt.** 216.28 **CAS Registry No.** 2381-21-7
EINECS No. 219-178-8 **RTECS No.** UR 2460000

Physical properties

M. Pt. 70-75°C **B. Pt.** 410°C

Ecotoxicity

Bioaccumulation

1-Methylpyrene enters the food chain, but is biotransformed. In the eider duck on the Baltic coast the distribution between tissues was gall bladder > adipose tissue > liver. Compound was also detected in seston and blue mussel, the latter a food source for the ducks (1).

Environmental fate

Adsorption and retention

1-Methylpyrene is retained by aquatic humic substances in lake water (2).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Newborn mouse bioassay, 42 mg kg^{-1} intraperitoneally for 3 days induced liver neoplasms (3).

Teratogenicity and reproductive effects

Compound is toxic to chick embryos (4).

Genotoxicity

Salmonella typhimurium TM677 with metabolic activation positive (5).
In vitro primary hepatocyte culture unscheduled DNA synthesis positive (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 $\mu g\ l^{-1}$ (6).

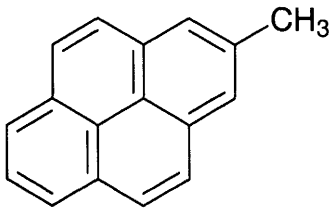
Other comments

In diesel exhaust and as air and water pollutant. Present in sediment of some urban waters (7).

References

1. Broman, D. et al *Environ. Toxicol. Chem.* 1990, **9**(4), 429-442.
2. Johnsen, S. et al *Sci. Total Environ.* 1987, **62**, 13-25.
3. Rice, J. E. et al *J. Toxicol. Environ. Health* 1987, **21**(4), 525-532.
4. Brunstroem, B. *Environ. Pollut.* 1990, **67**(2), 133-143.
5. *Cancer Res.* 1979, **39**, 4152.
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. Broman, D. et al *Bull. Environ. Contam. Toxicol.* 1987, **38**(6), 1020-1028.

M295 2-methylpyrene



$C_{17}H_{12}$ **Mol. Wt.** 216.28 **CAS Registry No.** 3442-78-2

EINECS No. 222-352-6

Occurrence Pollutant of soil, water and atmosphere. Present in sediment of some urban waters (1).

Physical properties

M. Pt. 142-144°C **B. Pt.** 410°C

Ecotoxicity

Bioaccumulation

2-Methylpyrene enters the food chain, but is biotransformed. It has been detected in eider ducks living on the Baltic coast and in their food source the seston and blue mussel. Tissue concentrations were gall bladder >adipose tissue >liver (2).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Compound has been included in a CASE-SAR analysis (3).

Teratogenicity and reproductive effects

Compound is toxic to chick embryos (4).

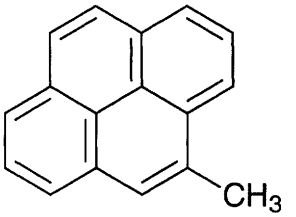
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 $\mu g\ l^{-1}$ (5).

References

1. Broman, D. et al *Bull. Environ. Contam. Toxicol.* 1987, **38**(6), 1020-1028.
2. Broman, D. et al *Environ. Toxicol. Chem.* 1990, **9**(4), 429-442.
3. Richard, A. M. et al *Mutat. Res.* 1990, **242(4)**, 285-303.
4. Brunstroem, B. et al *Environ. Pollut.* 1990, **67**(2), 133-143.
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

M296 4-methylpyrene



$C_{17}H_{12}$ **Mol. Wt.** 216.28 **CAS Registry No.** 3353-12-6

Physical properties

M. Pt. 222-225°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Compound has been included in a CASE-SAR analysis of potential carcinogenicity (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (2).

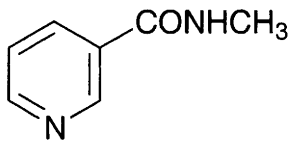
Other comments

Environmental pollutant. Present in sediment of some urban waters (3), and in topsoils polluted by synthetic-rubber manufacture (4).

References

1. Richard, A. M. et al *Mutat. Res.* 1990, **242**(4), 285-303.
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. Broman, D. et al *Bull. Environ. Contam. Toxicol.* 1987, 38(6), 1020-1028.
4. Nikiforova, E. M. et al *Pochvovedenie* 1989, (2), 70-78 (Russ.) (*Chem. Abstr.* **111**, 38455a).

M297 *N*-methyl-3-pyridinecarboxamide



$C_7H_8N_2O$ **Mol. Wt.** 136.15 **CAS Registry No.** 114-33-0

Synonyms *N*-methylnicotinamide; 3-(methylcarbamoyl)pyridine; nicotinic acid methylamide

EINECS No. 204-046-4

Occurrence Metabolite of nicotinamide and is a human metabolic product.
Product of tobacco smoke.

Physical properties

M. Pt. 104-105°C

Mammalian & avian toxicity

Teratogenicity and reproductive effects
Teratogenic in chickens at 5 and 10 mg kg^{-1} (1).

Metabolism and toxicokinetics
Catabolic metabolism is considered to occur constantly in humans consuming ordinary foods (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (3).
Weakly induced sister chromatid exchanges in UV irradiated human lymphocytes (4).

Other effects

Any other adverse effects
Inhibitor of poly(ADP-ribose) polymerase (5).

Legislation

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

References

1. Landover, W. et al *J. Exp. Zool.* 1967, **164**, 499.
2. Shibata, K. *Nippon Kasei Gakkaishi* 1990, **41**(10), 985-988.
3. Florin, I. et al *Toxicology* 1980, **18**, 219.
4. Honi, T. A. *Biochem. Biophys. Res. Commun.* 1981, **100**, 463.
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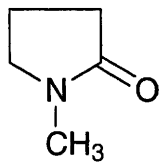
6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M298 *N*-methylpyrrolidone



C_5H_9NO **Mol. Wt.** 99.13 **CAS Registry No.** 872-50-4

Synonyms 1-methyl-2-pyrrolidinone; 1-methylpyrrolidone; M-pyrol

EINECS No. 212-828-1 **RTECS No.** UY 5790000

Uses Solvent.

Physical properties

M. Pt. -24°C **B. Pt.** 202°C **Flash point** 96°C (open cup) **Specific gravity** 1.027 at 25°C with respect to water at 4°C **Volatility** v.p. 0.133 kPa at 4°C, -1.22 kPa at 80°C ; v.den. 3.4
Solubility Water: miscible. Organic solvents: aliphatic hydrocarbons; miscible with benzene, chloroform, diethyl ether, ethanol, ethyl acetate, methanol

Occupational exposure

DE-MAK 20 ppm (80 mg m^{-3}) (vapour)
SE-LEVL 50 ppm (200 mg m^{-3}) **SE-STEL** 75 ppm (300 mg m^{-3})
UK-LTEL 100 ppm (412 mg m^{-3})
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 fire and/or explosion do not breathe fumes (S2, S41)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 3914, 5130 mg kg^{-1}, respectively (1,2).
LD_{50} dermal rabbit 8000 mg kg^{-1} (3).
LD_{50} intraperitoneal rat, mouse 2472, 3050 mg kg^{-1}, respectively (1,2).
LD_{50} intravenous mouse, rat 54,500, 80,500 μg kg^{-1}, respectively (4).

Sub-acute and sub-chronic data
Oral Crl:CDBr rats (28 days) 0, 2000, 6000, 18,000, 30,000 ppm *N*-methylpyrrolidone in feed. Mean body weight gains decreased in ♂ rats fed 18,000 ppm and both sexes fed 30,000 ppm. Clinical chemical changes indicating possible compound-related alterations in lipid, proteins, and carbohydrate metabolism occurred at 18,000 ppm in ♂s and 30,000 ppm in both sexes. No histopathological changes were judged to be directly related to *N*-methylpyrrolidone (NMP) exposure. The occurrence of mild to moderate leucopenia, hypocellular bone-marrow, testicular degeneration and atrophy, and thymic atrophy were judged to be secondary to nutritional and body weight effects in ♂ and/or ♀ rats at 30,000 ppm. Abnormal urine coloration was observed at 18,000 ppm and above. This discoloration was interpreted as a sign of systemic availability of NMP, but not as an adverse effect (5).
Oral B6C3F1 mice (28 days) 0, 500, 2500, 7500, or 10,000 ppm in feed. Cloudy swelling of the epithelia of the distal parts of the renal tubuli was observed in 4/5 ♂s and 3/5 ♀s at 10,000 ppm and in 2/5 ♂s at 7500 ppm. Abnormal urine coloration was observed, interpreted as a sign of systemic availability of NMP, but not as an adverse effect (5).

Teratogenicity and reproductive effects
Foetotoxic effects, namely resorption, stillbirth, low birth weight and delayed ossification in surviving young, have been demonstrated in animal studies after maternal exposure to *N*-methyl-2-pyrrolidone (NMPD) at levels which had a minimal to no adverse effect on the mother (6).

Irritancy
Irritant to the eyes and corneal lesions and moderate conjunctivitis has been reported in humans (7).
100 mg instilled into rabbit eye (72 hr) caused moderate irritation (8).

Genotoxicity

Found to induce aneuploidy in *Saccharomyces cerevisiae* (9).

Other effects

Other adverse effects (human)
A laboratory worker who had experienced sustained occupational exposure to *N*-methyl-2-pyrrolidone throughout the first 3 months of pregnancy experienced intra-uterine growth retardation and foetal death at 31 wk gestation; no other stress factors were apparent (6).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) and Schedule 6 (Release Into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology and workplace experience listed (1).

References

1. *Arzneim.-Forsch.* 1976, **26**, 1581.
2. *US EPA Report* No. 8EHQ-1087-0695, Office of Pesticides and Toxic Substances, US EPA, Washington, DC, USA.
3. *Raw Material Data Handbook, V. 1. Organic Solvents* 1974, 84, National Association of Printing Ink Research Institute, Francis McDonald Sinclair Memorial Laboratory, Lehigh University, Bethlehem, PA, USA.
4. *Iyakuhin Kenkyu* 1987, **18**, 922.
5. Malek, D. E. *Drug Chem. Toxicol.* 1997, **20**(1&2), 63-77.
6. Solomon, G. M. et al *J. Occup. Environ. Med.* 1996, **38**(7), 705-713.
7. Stasenara, K. P. et al *Toksikol Norykh. Prom. Khim. Veschester* 1965, **7**, 27-38.
8. *Food Chem. Toxicol.* 1988, **26**, 475.
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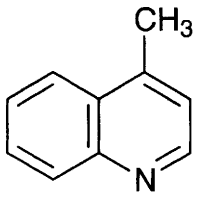
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M299 4-methylquinoline



$C_{10}H_9N$ **Mol. Wt.** 143.19 **CAS Registry No.** 491-35-0

Synonyms lepidine; cincholepidine; 4-lepidin; γ-methylquinoline

EINECS No. 207-734-2 **RTECS No.** OH 0316000

Occurrence In cigarette smoke (1).

Physical properties

M. Pt. 9-10°C **B. Pt.** 261-263°C **Flash point** >107°C **Specific gravity** 1.0826 at 20°C with respect to water at 4°C

Solubility Organic solvents: miscible with benzene, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 5.08 ppm Microtox test (2).

EC_{50} (48 hr) *Daphnia magna* 11 mg l^{-1} (3).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Structure-activity studies have predicted tumorigenic activity on mouse skin (4).

Assays in newborn ♂ mice show hepatocarcinogenicity (4).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (4).

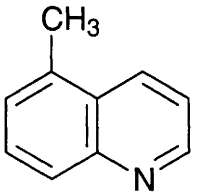
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. Dong, M. et al *Carcinog. – Compr. Survey* 1978, **37**, 97.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Herbes, S. E. et al *Bull. Environ. Contam. Toxicol.* 1977, **27**(1).
4. La Voie, E. J. et al *Carcinogenesis (London)* 1983, **12**(2), 217-220.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M300 5-methylquinoline



$C_{10}H_9N$ **Mol. Wt.** 143.19 **CAS Registry No.** 7661-55-4

EINECS No. 231-630-6 **RTECS No.** VC 0540000

Physical properties

M. Pt. 19°C **B. Pt.** 262.7°C **Specific gravity** 1.0832 at 20°C with respect to water at 4°C

Solubility Organic solvents: acetone; miscible with alcohol, diethyl ether

Ecotoxicity

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 0.991 ppm Microtox test (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

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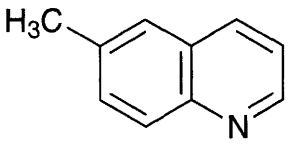
M301 6-methylquinoline



$C_{10}H_9N$ **Mol. Wt.** 143.19 **CAS Registry No.** 91-62-3

Synonyms *p*-methylquinoline; *p*-toluquinoline

EINECS No. 202-084-6 **RTECS No.** VC 0550000

Uses Fragrance.

Occurrence In coal liquefaction waste water. In whisky and tea (1).

Physical properties

B. Pt. 259°C **Flash point** >107°C **Specific gravity** 1.063 **Partition coefficient** log P_{ow} 2.57 (2)

Ecotoxicity

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 2.79 ppm Microtox test (3).

LC_{50} (48 hr) *Daphnia magna* 11 mg l^{-1} in a mixture with resorcinol (4).

LC_{100} (24 hr) *Tetrahymena pyriformis* 0.22 g l^{-1} (5).

Environmental fate

Degradation studies

Hydroxylated, but not degraded by *Pseudomonas aeruginosa* QP and *Pseudomonas putida* QP (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1260 mg kg^{-1} (1).

LD_{50} dermal rabbit 5000 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 386 mg kg^{-1} (1).

Carcinogenicity and chronic effects

In feeding studies in F344 rats at 0.05-0.1% for 104 wk, no indication of carcinogenicity (7).

Metabolism and toxicokinetics

Oxidised in dog to quinoline 6-carboxylic acid (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (1).

Sensitisation

No sensitisation in humans (1).

Genotoxicity

Salmonella typhimurium TA98, TA100 without metabolic activation negative, with metabolic activation positive (7,8).

Salmonella typhimurium TA100 with metabolic activation negative (9).

Other effects

Any other adverse effects

Increased rat liver aryl hydrocarbon hydroxylase activity when injected intraperitoneally (10).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).

References

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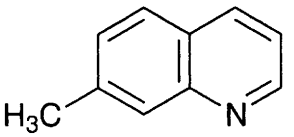
M302 7-methylquinoline



$C_{10}H_9N$ **Mol. Wt.** 143.19 **CAS Registry No.** 612-60-2

Synonyms *m*-toluquinoline

EINECS No. 210-316-2 **RTECS No.** VC 0560000

Occurrence Detected in water samples.

Physical properties

M. Pt. 35-37°C **B. Pt.** 258°C **Flash point** >110°C

Genotoxicity

Salmonella typhimurium TA98, TA100 without metabolic activation negative, with metabolic activation positive (1,2).

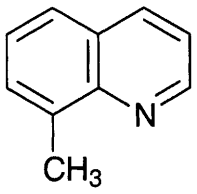
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Epler, J. L. et al *Environ. Health Perspect.* 1979, **30**, 174.
2. Nagao, M. et al *Mutat. Res.* 1977, **42**, 335.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M303 8-methylquinoline



$C_{10}H_9N$ **Mol. Wt.** 143.19 **CAS Registry No.** 611-32-5

EINECS No. 210-264-0 **RTECS No.** VC 0562000

Physical properties

M. Pt. –80°C **B. Pt.** 143°C at 34 mmHg **Flash point** 105°C **Specific gravity** 1.052

Partition coefficient log P_{ow} 2.60 (1)

Ecotoxicity

Fish toxicity

Anaesthetic concentration in sea water for sharks 7.16-21.48 mg l^{-1} (2).

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 9.03 ppm Microtox test (3).

LC_{100} (24 hr) *Tetrahymena pyriformis* 0.22 g l^{-1} (4).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse ~71.6-429.6 mg kg^{-1} (2).

Carcinogenicity and chronic effects

35.7, 71.5, 143.0 μg l^{-1} administered intraperitoneally to newborn CD-1 mice on day 1, 8, 15 of life for 1 yr caused no significant tumorigenic activity (4).

Newborn Sprague-Dawley rats administered 28.6 mg kg^{-1} by injection on day-1 of life and then 14.3 mg kg^{-1} wkly at wk 2-7 and 28.6 mg kg^{-1} at wk 8 exhibited no significant difference in tumorigenic activity compared with controls (5).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (6).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

References

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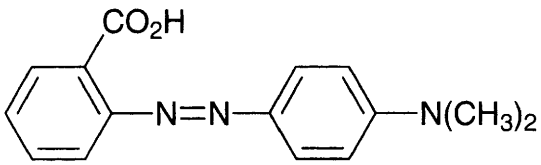
M304 Methyl Red



$C_{15}H_{15}N_3O_2$ **Mol. Wt.** 269.30 **CAS Registry No.** 493-52-7

Synonyms *o*[[*p*-(dimethylamino)phenyl]azo]benzoic acid; 2-carboxy-4'-(dimethylamino)azobenzene; 2-[(*p*-(dimethylamino)phenyl]azobenzoic acid; 4'-(dimethylamino)azobenzene-2-carboxylic acid; C.I. 13020; C.I. Acid Red 2

EINECS No. 207-776-1 **RTECS No.** DG 8960000

Uses Dyestuff. Indicator in chemical analysis.

Physical properties

M. Pt. 179-182°C

Solubility Water: almost insoluble. Organic solvents: acetic acid, chloroform, ethanol

Environmental fate

Degradation studies

Biodegradation by sewage sludge 100% after 9 days; 10% when treated with bacteria-free sludge (1).

Pseudomonas stutzeri, Bacillus subtilis (8 hr incubation) 10-43 μg l^{-1} dyestuff in buffered solution. Microbial degradation occurred via reductive cleavage of azo group with both growing cells and cell-free extracts. Cell permeability to dyestuff molecules is a factor in degradation processes (2).

Klebsiella pneumoniae RS-13 completely decolorised and degraded 100 mg l^{-1} methyl red in a culture medium under optimal aerobic conditions. *Acetobacter liquefaciens* S-1 also degraded methyl red, but less efficiently (3).

An *Enterobacter* sp. isolated from soil rapidly degraded methyl red under aerobic conditions to anthranilic acid and *N,N*-dimethyl-*p*-phenylenediamine (4).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

Oral ♂ and ♀ Wistar rats fed a diet containing 40 g methyl red kg^{-1} of diet for up to 2 yr. No tumours of the alimentary tract were observed (6).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation positive (7).

SOS-Chromotest with *Escherichia coli* PQ37 negative (8).

Chinese hamster ovary cell chromosomal aberration without metabolic activation negative (9).

Other comments

Methyl red is bound to bovine serum albumin (10).

Carcinogenic risk to man reviewed (11).

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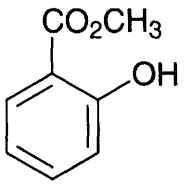
M305 methyl salicylate



$C_8H_8O_3$ **Mol. Wt.** 152.15 **CAS Registry No.** 119-36-8

Synonyms betula oil; methyl 2-hydroxybenzoate; sweet birch oil; teaberry oil; wintergreen oil

EINECS No. 204-317-7 **RTECS No.** VO 4725000

Uses Anti-inflammatory drug. In perfumery. Flavouring agent. UV-absorber in sunburn lotions.
Occurrence In plant oils.

Physical properties

M. Pt. –8 to –7°C **B. Pt.** 222°C **Flash point** 99°C (closed cup) **Specific gravity** 1.184 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 2.55 (1) **Volatility** v.p. 1 mmHg at 54°C ; v.den. 5.24
Solubility Water: ~670 mg l^{-1} at 20°C. Organic solvents: chloroform, diethyl ether, dimethyl sulfoxide, ethanol, glacial acetic acid

Ecotoxicity

Fish toxicity
Not toxic to stickleback and rainbow trout at 10 mg l^{-1} for 24 hr (sodium salt) (2).

Environmental fate

Degradation studies
BOD_5 55% ThOD (3).

Abiotic removal
Hydrolysis $t_{1/2}$ 12.1 hr at pH 9.2 and 25°C; and 3.2 hr at pH 11.26 and 24°C. $t_{1/2}$ ~22 days at pH 7.5 (4,5).
Photolysis $t_{1/2}$ 48 min in solution (absorption maximum 305 nm in methanol) (6,7).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 5.7 day (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig, rabbit, dog 700-2800 mg kg^{-1} (9,10).
LD_{Lo} subcutaneous guinea pig 1500 mg kg^{-1} (11).

Sub-acute and sub-chronic data

Inhalation rat (20 day) no-adverse-effect level 120 ppm for 7 hr day^{-1} (12).

Teratogenicity and reproductive effects

TD_{Lo} oral hamster 1750 mg kg^{-1} on day-7 of gestation (teratogenic effects on central nervous system) (13).
TD_{Lo} dermal hamster 5250 mg kg^{-1} on day-7 of gestation (teratogenic effects on central nervous system) (13).
TD_{Lo} intraperitoneal rat 400 mg kg^{-1} on day-12 of gestation (foetal mortality) (14).
TD_{Lo} intraperitoneal rat 500 mg kg^{-1} day^{-1} on days 11-12 of gestation (developmental effects on urogenital system) (14).

Metabolism and toxicokinetics

Undergoes rapid hydrolysis to salicylic acid, mainly in the liver. In some species, including the rabbit, partially excreted as sulfate or glucuronide conjugates (10,15).
Reported to cross the placental barrier (15).
Absorbed through the skin in humans (16).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (17).
500 mg instilled into rabbit eye for 24 hr caused mild irritation (18).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (19).

Other effects

Other adverse effects (human)

Lethal oral doses in man, 30 ml in adults, 10 ml in children. Symptoms of poisoning, which are similar to those for aspirin, include nausea, vomiting, acidosis, pulmonary oedema, pneumonia and convulsions (20).

Other comments

Autoignition temperature 454°C.

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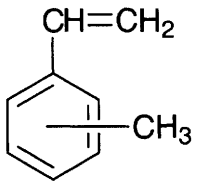
M306 methylstyrene



C_9H_{10} **Mol. Wt.** 118.18 **CAS Registry No.** 25013-15-4

Synonyms ethenylmethylbenzene; *ar*-methylstyrene; tolyl ethylene; vinyltoluene (mixed isomers)

EINECS No. 246-562-2 **RTECS No.** WL 5075000

Uses Manufacture of polymers. Solvent.

Occurrence In essential oil of some plants. Residues have been identified in natural waters and in drinking water (1,2).

Physical properties

M. Pt. –77°C **B. Pt.** 170-171°C **Flash point** 51.7°C **Specific gravity** 0.890 at 25°C with respect to water at 25°C **Volatility** v.p. 1.1 mmHg at 20°C ; v.den. 4.1

Solubility Organic solvents: acetone, carbon tetrachloride, diethyl ether, dimethyl sulfoxide, ethanol, methanol

Occupational exposure

DE-MAK 100 ppm (490 mg m^{-3})
FR-VME 50 ppm (240 mg m^{-3})
SE-LEVL 10 ppm (50 mg m^{-3}) **SE-STEL** 30 ppm (150 mg m^{-3})
UK-LTEL 100 ppm (491 mg m^{-3}) **UK-STEL** 150 ppm (736 mg m^{-3})
US-TWA 50 ppm (242 mg m^{-3}) **US-STEL** 100 ppm (483 mg m^{-3})

UN No. 2618 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Ecotoxicity

Bioaccumulation

Bioconcentration factor for goldfish 32-35 (3).

Environmental fate

Abiotic removal

Reaction with photochemically produced hydroxyl radicals and ozone in the atmosphere, estimated $t_{1/2}$ 6 hr (4,5). Estimated volatilisation $t_{1/2}$ 10 days from model pond water and 3.5 hr in model river water (6,7).

Adsorption and retention

Estimated K_{oc} 370 indicates the methylstyrene will adsorb moderately to soil and sediments (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2255, 3160 mg kg^{-1}, respectively (8,9).
LC_{50} (4 hr) inhalation mouse 3000 mg m^{-3} (exposure not specified) (9).
Inhalation rat (4 hr) 50 ppm induced leucopenia, without any change in differential or red blood cell counts (10).
LD_{Lo} dermal rat, mouse 4500 mg kg^{-1} (11).
LD_{50} intraperitoneal rat 2300 mg kg^{-1} (8).

Carcinogenicity and chronic effects

Inhalation rat, (2 yr) 0, 100 or 300 ppm, 6 hr day^{-1}, 5 days wk^{-1} for 103 wk. Mice were exposed to 0, 10 or 25 ppm under the same schedule. There was no evidence of carcinogenicity in ♂ and ♀ rats or mice (12).

Teratogenicity and reproductive effects

Intraperitoneal rat, lowest toxic dose 3800 mg kg^{-1} day^{-1} on days 1-15 of gestation, teratogenic effects (13).

Metabolism and toxicokinetics

Following inhalation exposure of rats, methylstyrene was metabolised to glutathione conjugates via the formation of electrophilic intermediates (14).

Irritancy

90 mg instilled into rabbit eye caused mild irritation (exposure not specified) (8).
Inhalation human, lowest irritant concentration 400 ppm (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (15).
In vitro mouse lymphoma L5178Y cells, tk^+/tk^- without metabolic activation positive (16).
In vivo mouse, ratio of polychromatic to normachromatic erythrocytes was slightly decreased. There was no increase in normochromatic cells with micronuclei (17).

Other effects

Other adverse effects (human)

Causes drowsiness and central nervous system depression. At high concentrations causes dizziness, drunkenness and anaesthesia (18).
Human volunteers noted that odour was detectable at 50 ppm, odour was strong and tolerable at 200 ppm, odour was strong and objectionable at 300 ppm, eye and nasal irritation occurred at 400 ppm (19).

Any other adverse effects

Intraperitoneal rat, mouse, Chinese hamster, single doses of up to 500 mg kg^{-1} caused a dose-dependent decrease in glutathione content in the liver and kidneys. In mice, the highest dose decreased microsomal cytochrome P_{450} content and 7-ethoxycoumarin *O*-deethylase activity acutely within 6 hr (20).

Legislation

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

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (22).
Autoignition temperature 490°C.
Usually occurs as a mixture of 50-70% 3-methylstyrene and 30-45% 4-methylstyrene.

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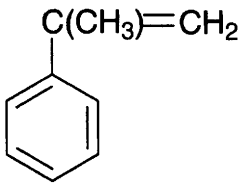
M307 α-methylstyrene



C_9H_{10} **Mol. Wt.** 118.18 **CAS Registry No.** 98-83-9

Synonyms (1-methylethenyl)benzene; isopropenylbenzene; α-methylstyrol; 2-phenylpropene

EINECS No. 202-705-0 **RTECS No.** WL 5075300

Uses Copolymer in speciality resin systems.

Physical properties

M. Pt. –96°C **B. Pt.** 152.4°C **Flash point** 45°C (closed cup) **Specific gravity** 0.862 at 20°C with respect to water at 4°C **Volatility** v.den. 4.08

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 100 ppm (490 mg m^{-3})

FR-VME 50 ppm (240 mg m^{-3}) **UK-STEL** 100 ppm (491 mg m^{-3})

US-TWA 50 ppm (242 mg m^{-3}) **US-STEL** 100 ppm (483 mg m^{-3})

UN No. 2303 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Supply classification irritant, dangerous for the environment
Risk phrases Flammable – Irritating to eyes and respiratory system – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R10, R36/37, R51/53)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid release to the environment. Refer to special instructions/safety sheet (S2, S61)

Mammalian & avian toxicity

Acute data
TC_{Lo} (duration unspecified) inhalation human 600 ppm (1).
LC_{Lo} (duration unspecified) inhalation rat 3000 ppm (2).
LC_{Lo} (duration unspecified) inhalation guinea pig 3000 ppm (1).

Sub-acute and sub-chronic data
Inhalation rats, guinea pigs, rabbits, mice and monkeys (6 month) 200 ppm, no adverse effects were reported (3). Inhalation rats, guinea pigs (27 day) 800 ppm, slight changes in liver and kidney weight and growth retardation occurred. Inhalation rats (3-4 day), 3000 ppm, fatal (3).

Irritancy
Dermal rabbit 100% caused moderate irritation, and 91 mg instilled into rabbit eye caused mild irritation (1). Strong eye irritation was reported in humans briefly exposed to 600 ppm, slight irritation occurred after 2 min exposure to 200 ppm (3).

Genotoxicity

Cultured human lymphocytes positive effect with sister chromatid exchanges (metabolic activation unspecified) (4).

Other effects

Other adverse effects (human)
Effects on blood clotting (5) and liver function have been reported (6).

α-Methylstyrene is irritating to the upper respiratory tract and prolonged exposure may cause central nervous system depression (7).

Any other adverse effects
The liquid caused slight conjunctival irritation in rabbit eye. The liquid caused erythema after application to rabbit skin (3).
Reversible skin damage was reported in an inhalation study on animals (8).

Other comments

Reviews on epidemiology, experimental toxicology, human health effects, physico-chemical properties and workplace experience listed (9).
Toxicity has been reviewed (10).

References

1. *Arch. Ind. Health* 1956, **14**, 387.
2. Gerarde, H. *Toxicology and Biochemistry of Aromatic Hydrocarbons* 1960, 131, Elsevier, New York, USA.
3. Wolf, M. A. et al *Arch. Ind. Health* 1956, **14**, 387-398.
4. Norppa, H. et al *Mutat. Res.* 1983, **116**(3-4), 379-387.
5. Netesa, V. A. et al *HSE Transl.* Jul-Sep 1985, **3**, 1.
6. Putalova, T. V. *HSE Transl.* Oct-Nov 1984, 1.
7. Proctor, N. H. et al *Chemical Hazards of the Workplace* 1991, Van Nostrand Reinhold, New York, USA.
8. Nikiforova, A. A. *HSE Transl.* Jul-Sep 1984, 3.
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.
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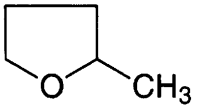
M308 2-methyltetrahydrofuran



$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 96-47-9

Synonyms tetrahydro-2-methylfuran; tetrahydrosylvan

EINECS No. 202-507-4 **RTECS No.** LU 2800000

Physical properties

B. Pt. 80°C **Flash point** −11/−12°C **Specific gravity** 0.853 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 5720 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat 6000 ppm (2).

LD_{50} dermal rabbit 4500 mg kg^{-1} (2).

Irritancy

500 g instilled into rabbit eye (24 hr) caused mild irritation (1).

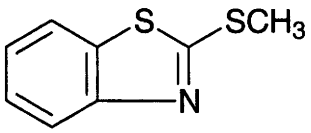
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
2. Deichmann, W. B. *Toxicology of Drugs and Chemicals* 1969, Academic Press, New York, USA.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M309 2-(methylthio)benzothiazole



$C_8H_7NS_2$ **Mol. Wt.** 181.28 **CAS Registry No.** 615-22-5

Synonyms 2-(methylmercapto)benzothiazole; methylcaptax

EINECS No. 210-417-1

Uses Defoliant. Used in the vulcanisation of rubber goods. In automobile antifreeze.

Physical properties

M. Pt. 43-46°C **Partition coefficient** log P_{ow} 5 (1)

Solubility Organic solvents: chloroform, ethanol

Ecotoxicity

Bioaccumulation

Average bioconcentration factors for the leeches *Dina dubia, Erpobdella punctata* and *Helobdella stagnalis* in a creek polluted industrially with 2-(methylthio)benzothiazole were 400, 200 and 100 ×, respectively (1).

Mammalian & avian toxicity

Metabolism and toxicokinetics

2-(methylthio)benzothiazole incubated with ^{35}S-labelled GSH and rat liver homogenate was oxidised to its corresponding methylsulfoxide and/or methylsulfone which becomes a substrate for GSH conjugation. The methylthio group is degraded to formaldehyde and sulfate (2).

Other effects

Any other adverse effects

Mutagenic (increased chromosomal aberrations) in *Gossypium barbadense* seeds (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
The log P_{ow} value exceeds the European Community recomended value level 3.0 (6th and 7th amendments) (5).

References

1. Metcalfe, J. L. et al *Environ. Monit. Assess.* 1988, **11**, 147-169.
2. Larsen, G. L. et al *Xenobiotica* 1988, **18**(3), 313-322.
3. Vesmanova, O. Y. et al *Tsitol. Genet.* 1988, **22**(2), 17-21 (Russ.) (*Chem. Abstr.* **109**, 106243r).
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 6th Amendment EEC Directive 79/831/EEC; 7th Amendment EEC Directive 91/32/EEC* 1991, HMSO, London, UK

M310 methyl thiocyanate

$$CH_3SCN$$

C_2H_3NS **Mol. Wt.** 73.12 **CAS Registry No.** 556-64-9

Synonyms methyl rhodanate; methyl sulfocyanate

EINECS No. 209-134-6 **RTECS No.** XL 1575000

Uses Insecticide.

Physical properties

M. Pt. -5°C **B. Pt.** 131°C **Flash point** 38°C **Specific gravity** 1.0678 at 25°C with respect to water at 4°C
Solubility Organic solvents: miscible with diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 60 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 23 mg kg^{-1} (2).
LD_{50} intravenous mouse 18 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Oral chicken 0.33% diet (duration unspecified) had no effect on thyroid size, but reduced egg iodine reduced food intake (4).

Metabolism and toxicokinetics

Liver enzymes liberate cyanide (species unspecified) (5).

Sensitisation

May cause allergic reaction (species unspecified) (6).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation negative (7).

Other effects

Other adverse effects (human)

May be fatal if inhaled, swallowed or absorbed through the skin. High concentrations are extremely destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin. Prolonged exposure may cause nausea, dizziness, headache, severe irritation or burns, lung irritation, chest pain and oedema, which may be fatal (6).

Legislation

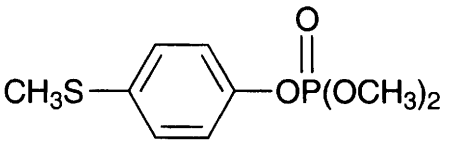
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (8).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

References

1. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, Prague, Czechoslovakia.
2. *Pestic. Biochem. Physiol.* 1972, **2**, 95.
3. *Report NX#02864*, US Army Armament Research and Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Aberdeen Proving Ground, MD21010, USA.
4. Papas, A. et al *Can. J. Anim. Sci.* 1979, **59**(1), 119.
5. Gosselin, R. E. et al (Eds.) *Clinical Toxicology of Commercial Products* 4th ed., **3**, 9, Williams & Wilkins, Baltimore, MD, USA.
6. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2446, Sigma-Aldrich, Milwaukee, WI, USA.
7. Yamaguchi, T. *Agric. Biol. Chem.* 1980, **44**(12), 3017.
8. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M311 4-(methylthio)phenyl dimethyl phosphate



$C_9H_{13}O_4PS$ **Mol. Wt.** 248.24 **CAS Registry No.** 3254-63-5

Synonyms phosphoric acid, dimethyl *p*-(methylthio)phenyl ester; Allied GC 5606; ENT 25734; GC 6506

RTECS No. TC 5075000

Uses Agricultural insecticide and acaricide.

Physical properties

B. Pt. 138-140°C at 0.1 mmHg

Occupational exposure

Supply classification very toxic

Risk phrases Very toxic in contact with skin and if swallowed (R27/28)

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

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 0.562 mg kg^{-1} (1).

LD_{50} oral rat, mouse 7, 18 mg kg^{-1}, respectively (2,3).

LD_{50} dermal rabbit 48 mg kg^{-1} (4).

Sub-acute and sub-chronic data

LD_{50} (3 day) oral deer mouse 50 mg kg^{-1} day^{-1} (5).

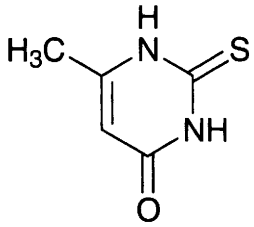
Legislation

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

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *Toxicol. Appl. Pharmacol.* 1972, **21**, 315.
3. *Arch. Toxicol.* 1975, **34**, 103.
4. Frear, E. H. (Ed.) *Pesticide Index* 1969, College Science Publications, State College, PA, USA.
5. *Environmental Properties of Chemicals* 1990, Research Report 91, Ministry of the Environment, Finland.
6. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

M312 6-methyl-2-thiouracil



$C_5H_6N_2OS$ **Mol. Wt.** 142.18 **CAS Registry No.** 56-04-2

Synonyms 2,3-dihydro-6-methyl-2-thioxo-4(1*H*)pyrimidinone; Alkiron; Metacil; Methiacil; MTU; Orcanon; Thiothymin

EINECS No. 200-252-3 **RTECS No.** YR 0875000

Uses Thyroid inhibitor.

Physical properties

M. Pt. 326-331°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2790 mg kg^{-1} (1).

LD_{Lo} oral rabbit 2500 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse, rat 200, 920 mg kg^{-1}, respectively (3,4).

Carcinogenicity and chronic effects

Thyroid adenomas with metastases in the lungs have been reported in rats and mice treated with methylthiouracil. Malignancy and metastases have been questioned. In further work, mice on an iodine-rich diet received methylthiouracil in drinking water as a 1% solution (1000 mg l^{-1}), and others on a low-iodine diet received 0.2-0.5% mixed in the food pellets. Thyroid adenomas and pulmonary nodules were seen but were not malignant. Hepatomas were also reported. Six months after treatment was discontinued no adenomas were present and pulmonary nodules of thyroid tissue were demonstrated (5).

Thyroid adenomas and carcinomas reported in rats fed 2.5 mg day^{-1} plus intraperitoneal injections of radioactive iodine (^{131}I) (6,7).

Legislation

Land disposal prohibited under U.S. Federal Resource Conservation and Recovery Act (8).

Other comments

Thyroid hyperplasia produced by administration of methylthiouracil to infant rats can be prevented by concurrent administration of thyroid hormone (9).

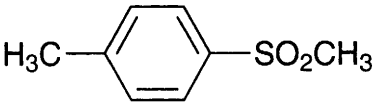
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (10).

References

1. *Farmaco, Ed. Sci.* 1952, **7**, 313.
2. *Merck Index* 11th ed., 1989, Merck & Co., Rahway, NJ, USA.
3. *NTIS Report* AD277-689, Natl. Tech. Inf. Ser., Springfield, VA, USA.
4. *Farmaco, Ed. Sci.* 1958, **13**, 882.
5. Jemec, B. *Cancer* 1977, **40**, 2188-2202.
6. Douiach, I. *Br. J. Cancer* 1953, **7**, 181-202.

7. Field, J. B. et al *Cancer Res.* 1959, **19**, 870-873.
8. *Fed. Regist.* 31 Jan 1991, **56**(21), 3864-3928.
9. Elphinstone, N. *Lancet* 27 Jun 1953, **1**, 1231-1233.
10. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

M313 methyl *p*-toluenesulfonate



$C_8H_{10}O_3S$ **Mol. Wt.** 186.23 **CAS Registry No.** 80-48-8

Synonyms 4-methylbenzenesulfonic acid, methyl ester; *p*-toluenesulfonic acid, methyl ester; methyl *p*-methylbenzenesulfonate; methyl toluene-4-sulfonate; methyl *p*-tosylate

EINECS No. 201-283-5 **RTECS No.** XT 7000000

Uses Methylating agent.

Physical properties

M. Pt. 27.5°C **B. Pt.** 144-145°C at 5 mmHg **Flash point** 152°C (open cup) (1) **Specific gravity** 1.230 at 25°C with respect to water at 25°C

Solubility Organic solvents: benzene, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 341 mg kg^{-1} (2).

LD_{50} subcutaneous rat 250 mg kg^{-1} (3).

Carcinogenicity and chronic effects

BD-strain rats administered methyl *p*-toluenesulfonate once a week developed local sarcomas. The number of tumours was dose dependent (4).

Subcutaneous BD rat single dose 50 mg kg^{-1}, 5/12 animals developed local tumours (5).

Irritancy

Dermal rabbit (24 hr) 500 mg caused severe erythema to slight eschar formation and severe oedema. 500 mg instilled into rabbit eye (24 hr) caused mild irritation (2).

Sensitisation

Positive allergic reactions, confirmed using patch tests, reported in patients reacting to dental impression materials (6).

Genotoxicity

Drosophila melanogaster negative when orally administered, positive when injected in sex-linked recessive lethal test. Fed in combination with inhibitors of cytochrome P_{450}, sufficient mutagen reached the gonads to produce significant genetic damage (7).

Other comments

Pollutant of drinking water wells in areas irrigated with sewage effluent (8).

Experimental toxicology and human health effects reviewed (9).

References

1. Bond, J. *Sources of Ignition: Flammability Characterisitics of Chemicals and Products* 1991, p.113, Butterworth- Heinemann, Oxford, UK.
2. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
3. *Z. Kinderheilkd.* 1970, **74**, 241.
4. Druckrey, H. et al *Z. Krebsforsch.* 1970, **74**(3), 241-273.
5. Preussman, R. *Food Cosmet. Toxicol.* 1968, **6**, 576-577.
6. van Groeningen et al *Contact Dermatitis* 1975, **1**, 373-376.
7. Zijlstra, J. A. et al *Mutat. Res.* 1988, **198**(1), 73-83.
8. Tu, J. et al *Huanjing Huaxue* 1986, **5**(5), 60-74 (Ch.) (*Chem. Abstr.* **106**, 22946x).
9. *BIBRA Toxicity Profile* 1991, British Industrial Biological Research Association, Carshalton, UK

M314 methyltrichlorosilane

$$CH_3SiCl_3$$

CH_3Cl_3Si **Mol. Wt.** 149.48 **CAS Registry No.** 75-79-6

Synonyms trichloromethylsilane

EINECS No. 200-902-6 **RTECS No.** VV 4550000

Uses Has been used to impart water repellency and wet strength to paper.

Physical properties

B. Pt. 66°C **Flash point** -15°C **Specific gravity** 1.273 **Volatility** v.p. 150 mm Hg at 25°C ; v.den. 5.17

Occupational exposure

UN No. 1250 **HAZCHEM Code** 4WE **Conveyance classification** flammable liquid, corrosive

Supply classification highly flammable, irritant

Risk phrases Highly flammable – Reacts violently with water – Irritating to eyes, respiratory system and skin (R11, R14, R36/37/38)

Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear eye/face protection (S2, S26, S39)

Mammalian & avian toxicity

Acute data

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

LC_{50} (4 hr) inhalation rat 450 ppm (2).

LC_{50} (2 hr) inhalation mouse 180 mg m^{-3} (3).

LD_{Lo} intraperitoneal rat 30 mg kg^{-1} (1).

Irritancy

Mild eye and severe skin irritant in rabbits (2).

Other comments

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

References

1. *J. Ind. Hyg. Toxicol.* 1948, **30**, 332.
2. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, Prague, Czechoslovakia.
3. *Toksikol. Nov. Prom. Khim. Veshchestv.* 1961, **3**, 23.
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

M315 methylurea

$$NH_2C(O)NHCH_3$$

$C_2H_6N_2O$ **Mol. Wt.** 74.08 **CAS Registry No.** 598-50-5

Synonyms *N*-methylurea; 1-methylurea

EINECS No. 209-935-0 **RTECS No.** YT 1750000

Physical properties

M. Pt. 101°C **B. Pt.** decomp. **Specific gravity** 1.205 at 20°C with respect to water at 20°C
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 500 mg kg^{-1} (1).

Teratogenicity and reproductive effects

Not teratogenic in rat or mouse *in vivo* (dose, duration and route unspecified). No degenerative effect reported on neuronal or non-neuronal foetal rat brain cells *in vitro* (2).

Irritancy

Non-irritating to skin (species unspecified) (3).

Genotoxicity

Salmonella typhimurium TA98, TA100 with or without metabolic activation negative. *Bacillus subtilis* TKJ5211 his^+ reversion without metabolic activation positive; his^+ met^+ double reversion without metabolic activation negative (4).

References

1. *Natl. Acad. Sci. Natl. Res. Council* 1953, **5**, 47.
2. Khera, K. S. et al *Toxicol. In Vitro* 1988, **2**(4), 257-273.
3. Han, S. K. et al *Arch. Pharmacol. Res.* 1991, **14**(1), 12-18.
4. Tanooka, H. *Mutat. Res.* 1977, **42**, 19-32

M316 2-methylvaleraldehyde

$$CH_3CH_2CH_2CH(CH_3)CHO$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 123-15-9

Synonyms 2-formylpentane; 2-methylpentanal; 2-methylvaleric aldehyde

EINECS No. 204-605-2

Uses Organic synthesis.

Occurrence In plant and animal oils.

Physical properties

M. Pt. –100°C **B. Pt.** 119-120°C **Flash point** 16°C **Specific gravity** 0.808 at 20°C **Volatility** v.den. 3.5

Solubility Water: miscible. Organic solvents: acetone, diethyl ether

Occupational exposure

UN No. 2367 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 190 mg l^{-1} (1).

Mammalian & avian toxicity

Irritancy

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

Other comments

Autoignition temperature 199°C.

References

1. Protic, A. et al *Aquat. Toxicol.* 1989, **14**(1), 47-64.
2. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**, 2460, Sigma-Aldrich, Milwaukee, WI, USA

M317 methyl vinyl ether

$$CH_3OCH{=}CH_2$$

C_3H_6O **Mol. Wt.** 58.08 **CAS Registry No.** 107-25-5

Synonyms methoxyethene; methoxyethylene; vinyl methyl ether; Agrisynth MVE; Agrimer VEMA-H-240

EINECS No. 203-475-4 **RTECS No.** KO 2300000

Uses Manufacture of polymers.

Physical properties

M. Pt. –123°C **B. Pt.** 5-6°C **Flash point** –51°C **Specific gravity** 0.7725 at 20°C with respect to water at 4°C
Volatility v.p. 1052 mmHg at 20°C ; v.den. 2.0
Solubility Water: 15 g l^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1087 **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
Calculated bioconcentration factor 2.7 indicates that environmental accumulation is unlikely (1).

Environmental fate

Abiotic removal
Reaction with photochemically produced hydroxyl radicals and ozone in the atmosphere, estimated $t_{1/2}$ 10 hr (2). Estimated volatilisation $t_{1/2}$ 42 hr from model pond water and 3.3 hr in model river water (1,3).

Adsorption and retention
Estimated soil K_{oc} 22 indicates that methyl vinyl ether will not adsorb to soil and sediments (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4900 mg kg^{-1} (4).
LD_{50} dermal rabbit >8000 mg kg^{-1} (5).

Other effects

Other adverse effects (human)
Inhalation exposure causes intoxication, blurred vision, headache, dizziness, excitation and loss of consciousness. The liquid or concentrated vapour is irritating to the eyes and causes frost bite to the skin. Aspiration of the liquid causes chemical pneumonitis (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).
Autoignition temperature 287°C.

References

1. Lyman, W. K. et al *Handbook of Chemical Property Estimation Methods Environmental Behaviour of Organic Compounds* 1982, McGraw-Hill, New York, USA.
2. Atkinson, R. et al *Chem. Rev. (Washington, D. C.)* 1984, **84**, 437-470.
3. *EXAMS II Computer Simulation* 1987, US EPA, Athens, GA, USA.
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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

M318 methyl vinyl ketone

$$CH_3C(O)CH=CH_2$$

C_4H_6O **Mol. Wt.** 70.09 **CAS Registry No.** 78-94-4

Synonyms acetylethylene; 3-buten-2-one; 1-buten-3-one; methylene acetone; δ-oxo-α-butylene

EINECS No. 201-160-6 **RTECS No.** EM 9800000

Uses Alkylating agent. Michael-acceptor. Organic synthesis. Manufacture of polymers.

Occurrence In fulvic acids. In various plants.

Physical properties

M. Pt. –7°C **B. Pt.** 81.4°C **Flash point** –6°C **Specific gravity** 0.8636 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 0.117 (calc.) (1) **Volatility** v.p. 84 mmHg at 25°C ; v.den. 2.41

Solubility Water: 10%. Organic solvents: acetone, diethyl ether, dimethyl sulfoxide, ethanol, glacial acetic acid, methanol

Occupational exposure

UN No. 1251 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity

EC_{50} *Selenastrum capricornutum* < 10 mg l^{-1} (exposure not specified) (2).

Bioaccumulation

Calculated bioconcentration factor 0.72 indicates that environmental accumulation is unlikely (1).

Environmental fate

Degradation studies

BOD_5 10% ThOD; COD 100% ThOD (3).

Abiotic removal

Photooxidation by UV light in aqueous medium at 50°C, 16.8% degradation to carbon dioxide after 24 hr (4).

Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 21 hr (5).

Estimated volatilisation $t_{1/2}$ 3.4 days from model river water and 37 days from model pond water (1,6).

Adsorption and retention

Estimated K_{oc} 28 indicates that adsorption to soil and sediments would not be significant (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 30-33 mg kg^{-1} (8,9).

LC_{50} (4 hr) inhalation rat 7 mg m^{-3} (9).

Metabolism and toxicokinetics

Readily absorbed through the skin (10).

Binds to protein sulfhydryl groups and GSH (11).

Sensitisation

Induced strong contact sensitivity in guinea pigs immunised with acrylate in Freund's complete adjuvant (12).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation negative, TA100 with metabolic activation positive, and without metabolic activation negative (13,14).

Other effects

Other adverse effects (human)

Skin irritant and lachrymator (15).

Suspected of causing conjunctivitis and injury to the corneal epithelium in occupational exposure study in former Czechoslovakia (10).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).

Autoignition temperature 491°C.

References

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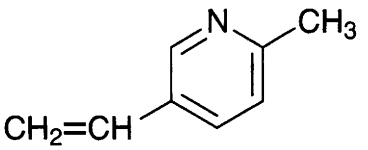
M319 2-methyl-5-vinylpyridine



C_8H_9N **Mol. Wt.** 119.17 **CAS Registry No.** 140-76-1

Synonyms 5-ethenyl-2-methylpyridine; 2-methyl-5-ethenylpyridine; 5-vinyl-2-picoline

EINECS No. 205-432-5 **RTECS No.** UT 2975000

Uses Manufacture of polymers. Oil additive. Flocculating agent. Chemical intermediate.

Physical properties

B. Pt. 181°C **Specific gravity** 0.980 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 2.04 (1)
Volatility v.p. 1.2 mmHg at 25°C
Solubility Water: 43 g l^{-1} at 25°C

Ecotoxicity

Bioaccumulation
The calculated bioconcentration factors are 3.1-46 (2).

Environmental fate

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 14 hr (3).
Reaction with ozone in the upper atmosphere, estimated $t_{1/2}$ 13 hr (4).
Estimated volatilisation $t_{1/2}$ 194 days from model pond water and from model river water 9 days (2,5).

Adsorption and retention
Estimated K_{oc} of 12-306 indicate that adsorption to soil and sediments would be insignificant (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 780, 1200 mg kg^{-1}, respectively (6,7).
LC_{50} (2 hr) inhalation rat, mouse 190, 210 mg m^{-3}, respectively (7).
LD_{50} dermal rabbit 720 mg kg^{-1} (6).
LD_{50} subcutaneous rat, mouse 530, 1300 mg kg^{-1}, respectively (7).

Sub-acute and sub-chronic data
Oral rat 300 mg day^{-1} $animal^{-1}$ for 10 days decreased the number of highly active cells in the hypothalamic/hypophyseal neurosecretory system, a decrease in the number of less active cells, a decrease in the diameter of cell nuclei, and induced the accumulation of neurosecretion in the nerve fibres and neurohypophysis (8).
Oral rat, 0.1 or 1.0 mg kg^{-1} for 120 days reversibly disturbed protein metabolism in the ganglion cell of the cerebral cortex, caused reversible chromatolysis, and inhibited glutamate dehydrogenase (9).

Teratogenicity and reproductive effects
Oral rat, 160 mg kg^{-1} day^{-1} throughout pregnancy caused disruption in the structure of the liver and skin in the offspring (10).

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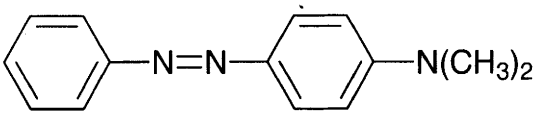
M320 Methyl Yellow



$C_{14}H_{15}N_3$ **Mol. Wt.** 225.29 **CAS Registry No.** 60-11-7

Synonyms C.I. Solvent Yellow 2; C.I. 11020; Butter Yellow; Brilliant Fast Oil Yellow; *N,N*-dimethyl-4-phenylazobenzenamine; 4-(dimethylamino)azobenzene; Dimethyl Yellow; Fat Yellow; Grasal Brilliant Yellow; Oil Yellow N; Petrol Yellow; Sudan Yellow GC

EINECS No. 200-455-7 **RTECS No.** BX 7350000

Uses Dyestuff. Analytical reagent.

Physical properties

M. Pt. 114-117°C (decomp.) **Partition coefficient** log P_{ow} 4.58 (1) **Volatility** v.p. 3.3×10^{-7} mmHg
Solubility Water: 13.6 mg l^{-1}. Organic solvents: benzene, chloroform, diethyl ether, ethanol, petroleum ether, vegetable oils

Ecotoxicity

Bioaccumulation
The estimated bioconcentration factor of 1780 indicates that environmental accumulation is likely (1).

Environmental fate

Nitrification inhibition
Not inhibitory to *Nitrosomonas* sp. at 100 mg l^{-1} (2).

Degradation studies
Degraded by the cell-free extract of *Aeromonas hydrophila* variant 24B. Aniline was the major metabolite (3). The microbial reduction of azo dyes was investigated. The reduction in the initial step of the microbial degradation of the dyes was microorganism specific or dye specific, because the reduction of the dyes was directly dependent not only on the presence of azoreductase in the microorganisms, but also on the permeation of the dye molecules into the cells. The cell permeability barrier of the dye molecules was observed for both sulfonated azo dyes and unsulfonated azo dyes. It was observed that microbial reductase exhibits a narrow specificity (4).

Abiotic removal
Reacts with photochemically produced hydroxyl radicals in the atmosphere, $t_{1/2}$ 7 hr (5).

Adsorption and retention
Calculated K_{oc} of 7390 indicates that adsorption to soil should occur. pK_a of 3.226 at 25°C, the extent of soil adsorption is pH dependent (5,6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 200, 300 mg kg^{-1}, respectively (7,8).
LD_{50} intraperitoneal rat, mouse 230 mg kg^{-1} (9).

Sub-acute and sub-chronic data
Oral marmoset (15 day) 56 mg kg^{-1} day^{-1}. Body weight decreased continuously and 2/15 treated animals died on day-10. Decreases in red blood cell counts, haemoglobin and haematocrit, and increases in mean corpuscular volume and white blood cell count were observed. Liver injury was indicated by changes in biochemical parameters (10).

Carcinogenicity and chronic effects

No adequate data for evaluation of carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (11).

Oral rat (2 yr) 5 mg day^{-1} for 40, 60, 100, 140 or 200 days caused liver carcinomas in 20, 26, 49, 80 and 81% of treated animals, respectively (12).

Gavage hamster (2 yr) 5-10 mg 3 × wk^{-1} for 42 wk. No excess of tumours was observed compared with controls (13).

Subcutaneous newborn mouse (1 yr) 0.2 mg on each of the first five days of life. Liver tumours were found in 26/28 ♂ compared with 3/31 in controls, and in 4/25 ♀ compared with 0/25 in controls. Lung adenomas were observed in 6/53 treated mice compared with 4/56 controls (14).

Dermal rat (90 wk) 1 ml of 2% solution applied 2 × wk^{-1} for life. All of six rats developed skin tumours compared with 0/6 controls (15).

Metabolism and toxicokinetics

Metabolism occurs via several pathways. In rats cleavage of the azo group by an azo reductase activity localised in the microsomal liver fraction occurs, requiring NADPH as an electron donor. Demethylation can occur before reduction of the azo linkage. Dimethylaminobenzene and its metabolites *p*-monomethylaminobenzene, aniline and *p*-phenylenediamine derivatives undergo ring hydroxylation mediated by microsomal mixed function oxidases centred on cytochrome P_{450}. *N*-hydroxylation may also occur in the rat liver. Phase II metabolites in the form of sulfates, glucuronides and acetyl derivatives accounting for 50-60% of the administered dose, have also been identified in the urine of rats (16).

Binding to proteins and DNA has been reported in the liver of rats and mice following intraperitoneal administration (17,18).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, T1535, with and without metabolic activation positive (19).

In vitro L5178 tk^+/tk^- mouse lymphoma cells with metabolic activation positive (20).

In vitro rat primary rat hepatocytes, unscheduled DNA synthesis positive (21).

Legislation

The log P_{ow} value exceeds the European Community recommended level of 3.0 (22).

Other comments

Physical properties, use, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (16).

Not permitted for use as food additive.

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M321 metiram

$C_{16}H_{33}N_{11}S_{16}Zn_3$ **Mol. Wt.** 1088.74 **CAS Registry No.** 9006-42-2

Synonyms zinc ammoniate ethylenebis(dithiocarbamate)-poly(ethylenethiuram disulfide); Polyram; Carbatene; Polikarbacin

RTECS No. TR 6250000

Uses Non-systemic foliar fungicide.

Physical properties

M. Pt. ~156°C (decomp.) **Specific gravity** 1.86 at 20°C **Partition coefficient** log P_{ow} 0.301 (pH 7)
Volatility v.p. $<7.25 \times 10^{-8}$ mmHg at 20°C
Solubility Water: practically insoluble. Organic solvents: pyridine (with decomposition)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) harlequin fish 17 mg l^{-1} (1).
LC_{50} (96 hr) rainbow trout, carp 1.1, 85 mg l^{-1}, respectively (1).

Invertebrate toxicity
LD_{50} contact, oral bee >16->40 μg bee^{-1} (1).

Environmental fate

Degradation studies
Degraded to derivatives of thiourea, thiuram monosulfide, thiuram disulfide and sulfur (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, mouse, rat 620-2850 mg kg^{-1} (2,3).
LC_{50} (4 hr) inhalation rat >5.7 mg l^{-1} (1).
LD_{50} dermal rat >2000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
No-effect level for rats in 2-yr feeding study 3.1 mg kg^{-1} (1).

Irritancy
Mild skin and eye irritant (species unspecified) (1).

Genotoxicity

Induced mitotic gene conversion in *Saccharomyces cerevisiae* D4 (4).

Other effects

Any other adverse effects

Attributed endocrine disruption effects in wildlife. Avian reproduction impaired, reduced egg production, reduced fertility, embryonic deaths (5).

Legislation

Included in Schedule 6 (Release Into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Zinc: guide level 100 μg l^{-1} (at outlets), 5000 μg l^{-1} (for consumer) (7).
WHO Toxicity Class Table 5 (8).
EPA toxicity class IV (1).
ADI 0.03 mg kg^{-1} body weight (9).
Community Right-To-Know List in the USA.

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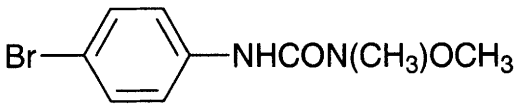
M322 metobromuron



$C_9H_{11}BrN_2O_2$ **Mol. Wt.** 259.10 **CAS Registry No.** 3060-89-7

Synonyms *N'*-(4-bromophenyl)-*N*-methoxy-*N*-methylurea; Patoran; 3-(4-bromophenyl)-1-methoxy-1-methylurea; Bromurex; Patonex

EINECS No. 221-301-5 **RTECS No.** YS 3325000

Uses Selective phenylurea herbicide.

Physical properties

M. Pt. 95-96°C **Specific gravity** 1.60 at 20°C **Partition coefficient** log P_{ow} 2.41 (1) **Volatility** v.p. 3×10^{-6} mmHg at 20°C

Solubility Water: 300 mg l^{-1} at 20°C. Organic solvents: acetone, chloroform, ethanol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) guppy 25.76 mg l^{-1} (2).

LC_{50} (96 hr) rainbow trout, crucian carp, bluegill sunfish, 36-40 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (96 hr) *Daphnia magna* 1.78 mg l^{-1} (2).

Low concentrations (0.05 mg l^{-1}) promoted growth of *Scenedesmus* sp. as indicated by dry weight, chlorophyll a content and the ratio of chlorophyll a:b; growth was inhibited at 0.1, 0.5 and 1.0 mg l^{-1} (3).

Bioaccumulation

Nile water algae accumulated metobromuron to a concentration of 0.75 mg g^{-1} in continuous culture (4).

Environmental fate

Degradation studies

In soil $t_{1/2}$ 30 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2000, 2100 mg kg^{-1}, respectively (5,6).

LC_{50} (4 hr) inhalation rat >1.1 mg l^{-1} air (1).

LD_{50} dermal rat, rabbit >3000, >10,200 mg kg^{-1}, respectively (1).

LD_{50} intraperitoneal rat, mouse 430, 850 mg kg^{-1}, respectively (6).

Carcinogenicity and chronic effects

No-effect level in dogs and rats in 2-yr feeding trials was 100 and 250 mg kg^{-1} diet, respectively (1).

Irritancy

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (8).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

WHO Toxicity Class Table 5 (10).

EPA Toxicity Class III (formulation) (11).

ADI 0.008 mg kg^{-1} body weight (11).

Other comments

Metabolic pathways reviewed (12).

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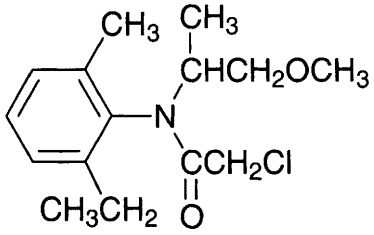
M323 metolachlor



$C_{15}H_{22}ClNO_2$ **Mol. Wt.** 283.80 **CAS Registry No.** 51218-45-2

Synonyms 2-chloro-6'-ethyl-*N*-(2-methoxy-1-methylethyl)acet-*o*-toluidide; 2-chloro-*N*-(2-ethyl-6-methylphenyl)-*N*-(2-methoxy-1-methylethyl)acetamide; Antigram; Dual; Duelor; Erbifos; Herbius

EINECS No. 257-060-8 **RTECS No.** AN 3430000

Uses Herbicide.

Physical properties

M. Pt. –62.1°C **B. Pt.** 100°C at 0.001 mmHg **Flash point** 190°C (1013 mbar) **Specific gravity** 1.12 at 20°C
Partition coefficient log P_{ow} 2.9 (25°C) (1) **Volatility** v.p. 1.3×10^{-5} mmHg at 20°C
Solubility Water: 488 mg l^{-1} at 25°C. Organic solvents: benzene, dimethylformamide, ethylene dichloride, miscible with methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, carp, bluegill sunfish 2-15 mg l^{-1} (1).

Environmental fate

Degradation studies
In soil $t_{1/2}$ 30 days (2).
Some (aerobic) metolachlor-degrading microbial population reported in sandy loam soil previously treated with metolachlor (3).
Microbial activity reported to be responsible for mineralisation of metolachlor in a soil perfusion system; degradation was enhanced in acclimated soils (4).
Metolachlor was transformed by *Streptomyces* sp. in a liquid medium and in Na_2CO_3 treated soil (5).
80% of added metolachlor (50 μg ml^{-1}) was absorbed and transformed by a stable bacterial community, suggesting seeding aquatic environments with a mixture of microorganisms rather than individual species may be advantageous in removal or detoxification of metolachlor (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral quail, rock dove, house sparrow, common grackle, starling 2.37, 5.6, 7.5, 23.7 and 31.6 mg kg^{-1}, respectively (7).

LD_{50} oral rat 2780 mg kg^{-1} (1).
LD_{50} dermal rat >3170 mg kg^{-1} (1).
LC_{50} (6 hr) rat >1.75 mg l^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail, mallard duck >10 g kg^{-1} diet (1).

Carcinogenicity and chronic effects
No-effect level in dogs, rats in 90-day feeding trials 500-1000 mg kg^{-1} diet (1).

Metabolism and toxicokinetics
In vitro transformation by rat liver enzymes is via conjugation with GSH and oxidation (8).

Irritancy
Mild skin irritant but non-irritating to eyes of rabbits (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1538 with and without metabolic activation negative (technical grade), positive (commercial grade) (9).
Saccharomyces cerevisiae D4 with or without metabolic activation negative (technical grade); without metabolic activation negative, with metabolic activation positive (commercial grade) (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 µg l^{-1} (10).
WHO guideline value for drinking water quality 10 µg l^{-1} (11).
WHO Toxicity Class III (12).
EPA Toxicity Class III (13).
ADI 0.1 mg kg^{-1} body weight (13).

Other comments

Six metabolites comprised 81% of the total [14C]metolachlor metabolised by the fungus *Cunninghamella elegans*. Two were identified as stereoisomers of 2-chloro-*N*-(2-ethyl-6-hydroxymethylphenyl)-*N*-(2-hydroxy-1-methylethyl)acetamide. Two others were tentatively identified as stereoisomers of 2-chloro-*N*-[2-(1-hydroxyethyl)-6-methyl-phenyl]-*N*-(2-methoxy-1-methylethyl)acetamide. The last two were identified as stereoisomers of 2-chloro-*N*-(2-ethyl-6-hydroxy-methylphenyl)-*N*-(2-methoxy-1-methylethyl)acetamide and 2-chloro-*N*-(2-ethyl-6-methylphenyl)-*N*-(2-hydroxy-1-methylethyl)acetamide (14).
Environmental fate reviewed (15).
Metabolic pathways reviewed (16).

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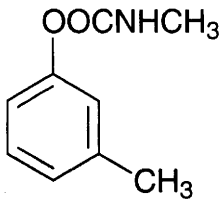
M324 metolcarb



$C_9H_{11}NO_2$ **Mol. Wt.** 165.19 **CAS Registry No.** 1129-41-5

Synonyms *m*-tolyl methyl carbamate; dicresyl; MTMC; 3-methylphenyl *N*-methylcarbamate

EINECS No. 214-446-0 **RTECS No.** FC 8050000

Uses Insecticide.

Physical properties

M. Pt. 76-77°C **Volatility** v.p. 1.09×10^{-3} mmHg at 25°C

Solubility Water: 2.6 g l^{-1} at 30°C. Organic solvents: cyclohexanone, 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

Low toxicity to fish (1).

Environmental fate

Degradation studies

Carbamates are readily degraded by soil microorganisms, and are photodecomposed in water by UV irradiation (2,3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 109-268 mg kg^{-1} (4,5).

LC_{50} inhalation rat 475 mg kg^{-1} (6).

LD_{50} dermal mouse 6000 mg kg^{-1} (7).

Genotoxicity

Induced chromosomal aberrations in Chinese hamster fibroblasts *in vitro* (metabolic activation unspecified) (8).

Other effects

Other adverse effects (human)

Most carbamates are active acetylcholinesterase activity inhibitors (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (9).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

WHO Toxicity Class II (11).

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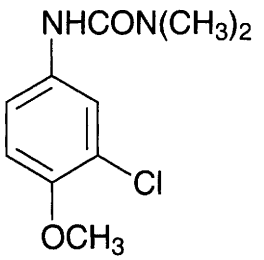
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

M325 metoxuron



$C_{10}H_{13}ClN_2O_2$ **Mol. Wt.** 228.68 **CAS Registry No.** 19937-59-8

Synonyms 3-(3-chloro-4-methoxyphenyl)-1,1-dimethylurea; *N,N*-dimethyl-*N'*-(4-methoxy-3-chlorophenyl)-urea; Dosanex

EINECS No. 243-433-2 **RTECS No.** YS 5775000

Uses Herbicide.

Physical properties

M. Pt. 126-127°C **Specific gravity** 0.8 at 20°C **Partition coefficient** log P_{ow} 1.60 at 23°C

Volatility v.p. 3.2×10^{-5} at 20°C

Solubility Water: 678 mg l^{-1} at 24°C. Organic solvents: acetone, acetonitrile, cyclohexanone, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, harlequin fish 20, 40 mg l^{-1}, respectively (1,2).

Invertebrate toxicity

LD_{50} oral bee 850 ppm (2).

Environmental fate

Degradation studies

Disappeared very quickly from loamy and clay loam soils via biodegradation, which was unaffected by supplying soil with ammoniacal nitrogen (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, mouse 1600, 2300, 2540 mg kg^{-1}, respectively (4-6).

Sub-acute and sub-chronic data

In 90-day feeding trials, rats receiving 1250 mg kg^{-1} diet, and dogs receiving 2500 mg kg^{-1} diet showed no ill-effects (1).

Genotoxicity

Salmonella typhimurium TA1535 with metabolic activation positive (7).
Inhibited testicular DNA synthesis (species unspecified (7).
Micronucleus test positive (species unspecified) (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (8).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).
WHO Toxicity Class Table 5 (10).

Other comments

Metabolic pathways reviewed (11).

References

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2. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
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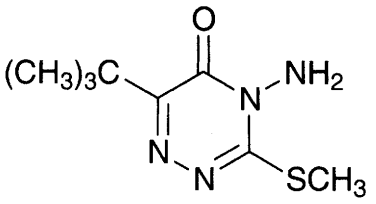
9. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
10. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
11. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

M326 metribuzin



$C_8H_{14}N_4OS$ **Mol. Wt.** 214.29 **CAS Registry No.** 21087-64-9

Synonyms 4-amino-6-*tert*-butyl-3-(methylthio)-1,2,4-triazin-5(4*H*)-one; 4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4*H*)-one

EINECS No. 244-209-7 **RTECS No.** XZ 2990000

Uses Herbicide.

Physical properties

M. Pt. 125-126°C **Specific gravity** 1.31 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.602 (1) **Volatility** v.p. 4.35×10^{-7} mmHg at 20°C

Solubility Water: 1.05 g l^{-1} at 20°C. Organic solvents: acetone, cyclohexane, chloroform, dimethylformamide

Occupational exposure

FR-VME 5 mg m^{-3}

US-TWA 5 mg m^{-3}

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) harlequin fish 140 mg l^{-1} (2).

LC_{50} (96 hr) rainbow trout, bluegill sunfish 76-80 mg l^{-1} (1).

Invertebrate toxicity

LD_{50} oral bee, 35µg bee^{-1} (3).

Environmental fate

Degradation studies

Degraded in soil via deamination, with further degradation to water-soluble conjugates. $t_{1/2}$ 1-2 months (1). $t_{1/2}$ in pond water 7 days (1).

Surface accumulation of crop residue in no-tillage soil inhibited metribuzin mineralisation compared with conventional tillage soils (4).

Abiotic removal

Undergoes non-biological degradation in four dry Manitoba soils at 15°C, the rate law describing this degradation was somewhat less than first order. $t_{1/2}$ 90-115 days, at an application rate of 1.8 ppm $t_{1/2}$ longer at higher application rate (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail 164 mg kg^{-1} (1).
LD_{50} oral rat 1936-1986 mg kg^{-1} (6).
LD_{50} oral guinea pig, mouse 250, 711 mg kg^{-1}, respectively (1).
LD_{50} dermal rat 2000 mg kg^{-1} (6).

Sub-acute and sub-chronic data

LC_{50} (5 day) diet bobwhite quail, mallard duck >4000 mg kg^{-1} (1).
Liver damage in guinea pigs followed administration (dose unspecified) directly into gastric lumen 6 × wk^{-1} for 30 or 90 days (7).

Carcinogenicity and chronic effects

No-effect level for rats and dogs in 2-yr feeding trials 100 mg kg^{-1} (1).

Metabolism and toxicokinetics

In mammals 90% of oral dose eliminated via urine and faeces, within 96 hr equally (1).

Genotoxicity

Escherichia coli SOS chromotest negative (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).
WHO Toxicity Class Table 5 (11).
EPA Toxicity Class III (3).
ADI 0.013 mg kg^{-1} body weight (3).

Other comments

Metabolic pathways reviewed (12).

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3. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
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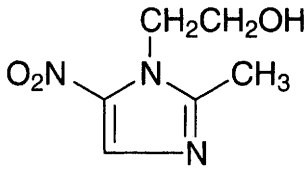
10. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
11. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
12. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

M327 metronidazole



$C_6H_9N_3O_3$ **Mol. Wt.** 171.16 **CAS Registry No.** 443-48-1

Synonyms 2-methyl-5-nitroimidazole-1-ethanol; 1-(2-hydroxyethyl)-2-methyl-5-nitroimidazole; 1-(β-ethylol)-2-methyl-5-nitro-3-azapyrrole

EINECS No. 207-136-1 **RTECS No.** NI 5600000

Uses Antiprotozoal used in treatment of *Trichomonas vaginalis, Entamoeba histolytica* and *Giardia lamblia* infection.

Physical properties

M. Pt. 158-160°C

Solubility Water: 10 g l^{-1} at 20°C. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 3.0, 3.8 g kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal, subcutaneous mouse 3, 3.6 g 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 (3).

Significantly increased incidence of lung tumours after oral administration to ♀ and ♂ mice, and of lymphomas in ♀ mice and of mammary, pituitary, testicular and liver tumours in rats. Increased incidence of colonic tumours induced in rats by subcutaneous administration of 1,2-dimethylhydrazine (3).

Administration by gavage of 2 mg day^{-1} for 100 days caused a significant increase in lung tumours in ♂ mice and of lymphomas in ♀ mice (4).

Administration by gavage of 2 mg day^{-1}, 5 days wk^{-1}, every alternate wk for life resulted in a significant increase in overall tumour incidence in ♀ but not ♂ mice. Increased tumour incidence was observed in F_1 but not F_2 generation (5).

Excess lung cancer (but no significant increase overall in cancer-related morbidity ormortality) reported in a follow-up study of 771 patients in Rochester, Minnesota given metronidazole. No increase in lung cancer was observed in a follow-up of 2460 San Franciscan patients (6).

Some excess cervical cancer reported in women treated with metronidazole, although this neoplasm has risk factors in common with vaginal trichomoniasis, the main indication in women for treatment with the drug (3).

Studies in mice imply prolonged treatment with metronidazole may predispose to photocarcinogenesis (7).

Teratogenicity and reproductive effects

Crosses the placenta, is excreted in breast milk and its use in pregnancy is controversial. Its use during the first trimester is contra-indicated by the manufacturer and the U.S. Centers for Disease Control. In the 2nd and 3rd trimester use of trichomoniasis may be acceptable if alternatives have failed, but it should not be given as a single dose (6).

Administration by gavage to Swiss strain mice of 2 mg day^{-1}, 5 days wk^{-1}, every alternate wk in a multigeneration study not teratogenic (5).

Metabolism and toxicokinetics

Readily absorbed after oral administration and bioavailability approaches 100%; peak plasma concentrations of

5-10 μg ml^{-1} occur 1 hr after single doses of 250-500 mg. Bioavailability from rectal suppositories is 60-80%, with peak plasma levels about half that of oral doses occurring after 4 hr. It is widely distributed and appears in most body tissues and fluids in concentrations similar to plasma. Metabolised in liver by side-chain oxidation and glucuronide formation. Principal oxidative metabolites are 1-(2-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole and 2-methyl-5-nitroimidazole-1-acetic acid, with small amounts of acetamide and *N*-(2-hydroxyethyl)oxamic acid. Excretion, mainly as metabolites, is via urine. Plasma elimination $t_{1/2}$ 8 hr, but longer in neonates and patients with liver disease (6).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive; TA1537, TA1538, TA98 with and without metabolic activation negative (8).
Escherichia coli with metabolic activation positive (8).
Did not induce sex-linked recessives in *Drosophila melanogaster* (8).
Did not induce sister chromatid exchanges in human lymphocytes or in Chinese hamster cells *in vitro* without metabolic activation (8).
Did not induce micronuclei in bone marrow cells of mice or rats (8).
In vivo mouse bone marrow micronucleus test positive (9).
Did not induce chromosomal aberrations in human lymphocytes *in vitro* without metabolic activation (8).
No increased incidence of chromosomal aberrations in lymphocytes or bone marrow of treated patients (8).
Human lymphocytes from metronidazole-treated patients (3×500 to 3×750 mg day^{-1} for 5-8 days). Induction of DNA strand breaks negative (10).

Other effects

Other adverse effects (human)
Gastro-intestinal disturbances are the most common adverse effects, including nausea and an unpleasant metallic taste. Headache, anorexia, vomiting, diarrhoea, dry mouth, furred tongue, glossitis and stomatitis may occur. High doses or prolonged treatment may cause peripheral neuropathy and epileptiform seizures. Leucopenia, skin rash, urethral discomfort, dark urine, raised liver enzyme values and thrombophlebitis may occur. Bone marrow aplasia, deafness, myopia, pancreatitis and gynaecomastia have been reported (6).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (11).

References

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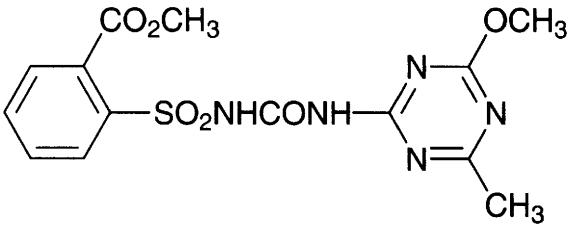
M328 metsulfuron-methyl



$C_{14}H_{15}N_5O_6S$ **Mol. Wt.** 381.37 **CAS Registry No.** 74223-64-6

Synonyms 2-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonylamino]sulfonyl]benzoic acid, methyl ester; Ally; Brush-off; Escort; Granstar; Gropper; Express; Jubilee; Lorate

RTECS No. DH 3563000

Uses Sulfonylurea herbicide.

Physical properties

M. Pt. 158°C **Specific gravity** 1.47 **Partition coefficient** log P_{ow} –1.74 at pH 7 (1) **Volatility** v.p. 2.5×10^{-12} mmHg at 25°C

Solubility Water: 550 mg l^{-1} at 25°C at pH 5; 2.79 mg l^{-1} at 25°C and pH 7.0. Organic solvents: acetone, dichloromethane, ethanol, methanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish >12.5 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* >150 mg l^{-1} (1).

Environmental fate

Degradation studies

Degraded by non-chemical hydrolysis (especially at low soil pH) and by soil microorganisms. $t_{1/2}$ 20 to >150 days, depending on soil type. Degradation decreased with increasing soil depth (2).

$t_{1/2}$ 1-4 wk. Breakdown is quicker at higher temperatures, higher levels of soil moisture and at lower soil pH (1).

Adsorption and retention

Adsorption was negatively correlated with soil pH and positively correlated with soil organic matter content. Because adsorption is weak at high pH, leaching can occur after high rainfall (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >5000 mg kg^{-1} (1).

LD_{50} oral ♂, ♀ rat >5000 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation ♂, ♀ rat >5 mg l^{-1} air (1).

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

Sub-acute and sub-chronic data

NOEC for rats and dogs was 50 and 200 mg kg $diet^{-1}$, respectively, in 2-yr feeding study (1).

Metabolism and toxicokinetics

Excreted predominantly unchanged by mammals (species unspecified) following oral administration. The sulfonylurea and methoxy carbonyl groups are only partly degraded by *O*-demethylation and hydroxylation (1).

Irritancy
Moderate rabbit eye irritant (reversible). Mild guinea pig skin irritant (1).

Sensitisation
Not a sensitiser of guinea skin (1).

Genotoxicity

Non-mutagenic in Ames test (details unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class Table 5 (5).
EPA Toxicity Class IV (formulation) (6).
ADI 0.0125 mg kg (6).

Other comments

Non-toxic to bees (1).
Metabolic pathways reviewed (7).

References

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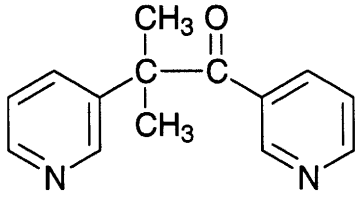
6. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
7. Roberts, T. R. et al (Eds.) *Metabolic Pathways of Agrochemicals. Part 1: Herbicides and Plant Growth Regulators* 1998, The Royal Society of Chemistry, Cambridge, UK

M329 metyrapone



$C_{14}H_{14}N_2O$ **Mol. Wt.** 226.28 **CAS Registry No.** 54-36-4

Synonyms 2-methyl-1,2-di-3-pyridyl-1-propanone; methapyrapone; 2-methyl-1,2-bis(3-pyridyl)-1-propanone; 2-methyl-1,2-di-3-pyridinyl-1-propanone

EINECS No. 200-206-2 **RTECS No.** UC 3050000

Uses Diagnostic aid in pituitary function; an adrenal 11-β hydroxylase inhibitor which blocks endogenous glucocorticoid synthesis.

Physical properties

M. Pt. 50-51°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 520 mg kg^{-1} (1).

LD_{Lo} intraperitoneal mouse 300 mg kg^{-1} (2).

Teratogenicity and reproductive effects

Decreased lung tissue disaturated phosphatidylcholine, disaturated phosphatidylcholine/total phospholipids, superoxide dismutase, catalase and glutathione peroxidase reported in offspring of rats given 45 mg kg^{-1} 2 × day^{-1} for 3 days prior to delivery (3).

Not teratogenic in rats (dose, duration and route unspecified); thymidine/sulfate ratio 0.76 in mouse limb bud micromass assay (proposed preliminary screen for developmental toxins) (4).

References

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M330 mevinphos

$$CH_3C[OP(O)(OCH_3)_2]=CHCO_2CH_3$$

$C_7H_{13}O_6P$ **Mol. Wt.** 224.15 **CAS Registry No.** 7786-34-7

Synonyms 2-methoxycarbonyl-1-methylvinyl dimethyl phosphate; 3-[(dimethoxyphosphinyl)oxy]-2-butenoic acid methyl ester; Phosdrin; methyl 3-(dimethoxyphosphinyloxy)crotonate

EINECS No. 232-095-1 **RTECS No.** GQ 5250000

Uses Acaricide and insecticide.

Physical properties

M. Pt. *E*-isomer, 21°C; *Z*-isomer, 6.9°C **B. Pt.** 99-103°C at 0.3 mmHg **Specific gravity** 1.24 at 20°C
Partition coefficient log P_{ow} 0.127 **Volatility** v.p. 1.28×10^{-4} mmHg at 20°C
Solubility Water: completely miscible. Organic solvents: miscible with acetone, benzene, chloroform, carbon tetrachloride, toluene

Occupational exposure

DE-MAK 0.01 ppm (0.093 mg m^{-3})
FR-VME 0.01 ppm (0.1 mg m^{-3})
UK-LTEL 0.01 ppm (0.09 mg m^{-3}) **UK-STEL** 0.03 ppm (0.28 mg m^{-3})
US-TWA 0.09 mg m^{-3} **US-STEL** 0.27 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 vapour – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves –

In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S28, S36/37, S45)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) rainbow trout, bluegill sunfish 0.034-0.041 mg l^{-1} (1,2).

LC_{50} (96 hr) American eel, mummichog, striped killifish, bluehead, striped mullet, Atlantic silverside, northern puffer 65-800 μg l^{-1} (3).

LC_{50} (96 hr) bluegill sunfish, largemouth bass 70-100 μg l^{-1} (2).

Invertebrate toxicity

LC_{50} (96 hr) *Daphnia pulex, Simocephalus serrulatus, Gammarus fasciatus* 0.16-2.8 μg l^{-1} (4,5).

LC_{50} (96 hr) sand shrimp, grass shrimp, hermit crab 11-69 μg l^{-1} (6).

LC_{50} (96 hr) *Palaemonetes kadiakensis, Asellus brevicaudus* 12-56 μg l^{-1} (5).

LC_{50} (96 hr) *Gammarus lacustris* 130 μg l^{-1} (7).

LD_{50} *Bufo arenarum* 880 mg kg^{-1} (8).

Environmental fate

Degradation studies

$t_{1/2}$ 13 days in silty clay acid and sandy clay neutral soils (9).

Degradation rate in surface and groundwater samples from 50 to 0.1 μg l^{-1}, 164 days (10).

Abiotic removal

50% hydrolysis occurs in 120 days at pH 6; 35 days at pH 7; 3 days at pH 9; and 1.4 hr at pH 11 (11).

Mammalian & avian toxicity

Acute data

LD_{50} oral blackbird, duck 3-4.6 mg kg^{-1} (12).

LD_{50} oral house sparrow, starling, common grackle, rock dove, quail 1.8, 3.8. 4.2, 4.2, 23.7 mg kg^{-1}, respectively (13).

LD_{50} oral rat 3 mg kg^{-1} (12).

LC_{50} (1 hr) inhalation rat 14 ppm (14).

LD_{50} dermal rat, duck 4.2 and 11 mg kg^{-1}, respectively (12,15).

LD_{50} intraperitoneal rat, mouse 1.35, 2 mg kg^{-1}, respectively (16,17).

LD_{50} intravenous, subcutaneous mouse 680 1180 μg kg^{-1}, respectively (18).

Carcinogenicity and chronic effects

No-adverse-effect level in rats and dogs in 2-yr feeding trials 4-5 mg kg^{-1} diet (11).

Metabolism and toxicokinetics

Eliminated as metabolites (unspecified) in urine and faeces in 3-4 days after oral administration to mammals (11).

Irritancy

Mild irritant to skin and eyes of rabbits (11).

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).

EEC maximum residue limit stone or citrus fruit 0.2 ppm, leaf vegetables 0.5 ppm, other fruit and vegetables 0.1 ppm (11).

Reportable quantity regulated under U.S. Federal Comprehensive Environmental Response, Compensation and Liability Act (21).

WHO Toxicity Class Ia (22).

EPA Toxicity Class I (23).

ADI 0.0015 mg kg^{-1} body weight (11).

Other comments

Toxicity and environmental effects of organophosphates reviewed (24).
Commercial product is a mixture of the *cis*- and *trans*-isomers, the former being 100 × more insecticidally active.

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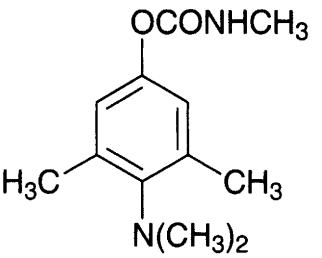
M331 mexacarbate



$C_{12}H_{18}N_2O_2$ **Mol. Wt.** 222.29 **CAS Registry No.** 315-18-4

Synonyms 4-(dimethylamino)-3,5-xylyl-*N*-methylcarbamate; 4-(dimethylamino)-3,5-dimethylphenol methylcarbamate (ester); Zectran

EINECS No. 206-249-3 **RTECS No.** FC 0700000

Uses Superseded insecticide and molluscicide.

Physical properties

M. Pt. 85°C **Volatility** v.p. <0.1 mmHg at 139°C
Solubility Water: 0.01% at 25°C. Organic solvents: acetone, acetonitrile, methylene chloride, ethanol, benzene

Occupational exposure

Supply classification very toxic
Risk phrases Harmful in contact with skin – Very toxic if swallowed (R21, R28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, coho salmon, yellow perch, brown trout, Atlantic salmon, fathead minnow 0.6-23.7 mg l^{-1} (1).
LC_{50} (96 hr) coho salmon, perch, brown trout, rainbow trout, yellow perch 1.73-20 mg l^{-1} (2-4).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia pulex* 0.1 mg l^{-1} (5).
LC_{50} (96 hr) *Gammarus fasciatus* 0.04 mg l^{-1} (6).
LC_{50} (2 day) *Pycnopsyche* sp., *Simulium venustum*, *Ophiogomphus* sp. 0.099-0.492 mg l^{-1} (7).
LOEC *Oscillatoria terebriformis*, *Synechococcus lividus*, *Navicula pelliculosa*, *Scenedesmus quadricauda* 1-10 mg l^{-1} (8).
LC_{50} (96 hr) *Lymnaea acuminata* 1.7 mg l^{-1} (9).
LC_{50} (96 hr) crayfish 8.8 μg ml^{-1}; behavioural abnormalities occurred at levels >1.0 μg ml^{-1} but as duration of exposure increased, animals recovered (10).

Bioaccumulation
Bioconcentration factor in mosquito larvae 0-8 (at 5.5-10.8 ppb in water), in brine shrimp 18 (at 5 ppb in water), in silverside fish 45 (at 4.7 ppb in water) (11).

Environmental fate

Degradation studies
Presence of 4-methylamino and 4-amino-3,5-xylyl methylcarbamate, and 4-dimethylamino-3,5-xylenol in water and aquatic plants following aerial spraying showed demethylation and hydrolytic routes are major metabolic pathways for degradation of mexacarbate (12).
Carbamates are readily degraded by soil microorganisms and are photodecomposed in water by UV radiation (13).

Mammalian & avian toxicity

Acute data
LD_{50} oral duck, chicken, pigeon 3-5.6 mg kg^{-1} (14).
LD_{50} oral mouse, rat, dog, rabbit 12, 14, 22, 37 mg kg^{-1}, respectively (15-17).
LD_{50} dermal mouse 107 mg kg^{-1} (18).
LD_{50} intraperitoneal mouse 7.8 mg kg^{-1} (19).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (20).
The USA National Toxicology Program tested mexacarbate via feed, negative in ♂ and ♀ rats and mice (21).

Metabolism and toxicokinetics
An oral dose in dogs was eliminated in urine as 4-dimethylamino-3,5-xylenol, predominantly in the conjugated form, as conjugated forms of the 2,6-dimethyl hydroquinone and as small amounts of 2,6-dimethyl-*p*-benzoquinone (2).
Carbamates do not accumulate in mammals (13).

Genotoxicity

Bacillus subtilis without metabolic activation positive (22).
Induction of sister chromatid exchanges in Chinese hamster ovary cells are predicted by a CASE study (23).

Other effects

Other adverse effects (human)
Most carbamates are active acetylcholinesterase inhibitors (13).
A fatal case of poisoning was reported 4 hr after ingestion of 55 g; the victim suffered bradycardia and heart failure (13).
Classical signs of cholinesterase poisoning, progressing to paralysis of the extremities was reported in an aerial spray plane pilot overexposed to mexacarbate via a leaking pump line (13).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (24).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (25).

Other comments

Metabolism reviewed (26).

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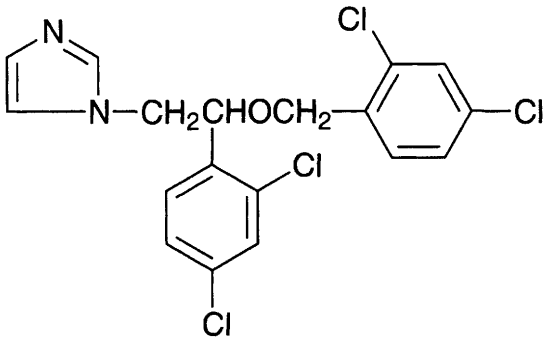
M332 miconazole



$C_{18}H_{14}Cl_4N_2O$ **Mol. Wt.** 416.13 **CAS Registry No.** 22916-47-8

Synonyms 1-[2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)methoxy]ethyl]-1*H*-imidazole

EINECS No. 245-324-5 **RTECS No.** NI 4770000

Uses Topical antifungal. Administered intravenously for severe fungal infections.

Physical properties

Solubility Organic solvents: acetone, diethyl ether, 2-propanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 872 mg kg^{-1} (1).

LD_{50} intraperitoneal rat, mouse 350, 450 mg kg^{-1}, respectively (1).

Teratogenicity and reproductive effects

No effect on mortality, growth or incidence of external, visceral or skeletal abnormalities reported in foetuses of rats given 30 mg kg^{-1} intravenously on days 6-18 of pregnancy (2).

Metabolism and toxicokinetics

Incompletely absorbed from the human gut; peak plasma concentrations of 1 μg ml^{-1} 4 hr after a 1 g dose. Doses >9 mg kg^{-1} by intravenous infusion usually produce plasma concentrations >1 μg ml^{-1}. It diffuses well into infected joints but penetration into cerebrospinal fluid and sputum is poor. >90% is bound to plasma proteins. Metabolised in the liver to inactive metabolites. 10-20% of an oral or intravenous dose is excreted in urine as metabolites. 50% of an oral dose is excreted mainly unchanged in faeces. Elimination pharmacokinetics after intravenous infusion are triphasic with $t_{1/2}$ of 0.4, 2.5 and 24 hr. Little is absorbed dermally (3).

Sensitisation

Sensitisation to miconazole nitrate reported in the guinea pig maximisation test (4).

Genotoxicity

Disturbed normal cell division by altering chromosome distribution and lead to mitotic non-disjunction in *Aspergillus nidulans* (5).

Micronucleus test in mice negative (6).

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M333 mineral oil

CAS Registry No. 8012-95-1

Synonyms adepsine oil; crystosol; oil mist, mineral; paraffin oil

EINECS No. 232-384-2 **RTECS No.** PY 8030000

Uses Mainly as lubricating oils.
Occurrence Petroleum crude oil refinery process streams.

Physical properties

Specific gravity 0.838
Solubility Organic solvents: benzene, diethyl ether, chloroform

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 22 g kg^{-1} (1).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity of untreated or mildly treated mineral oils in humans and animals, IARC classification group 1. Inadequate evidence for carcinogenicity of highly refined mineral oils in humans and animals, IARC classification group 3 (2).
Mineral oils exposure has been associated strongly and consistently with some squamous cell cancers, especially of the scrotum; excesses of gastro-intestinal, sinonasal, oral, bladder and lung cancers have been reported in many groups of workers exposed to mineral oils in many different industries including metal workers, toolmakers and printers (2).

Teratogenicity and reproductive effects
Used crankcase oil was embryolethal and teratogenic when applied at 1-15 µl to mallard duck and quail eggs (3).

Metabolism and toxicokinetics
5 hr after oral administration of 0.66 ml kg^{-1} to rats 1.5% was absorbed unchanged and 1.5% found as non-mineral oil substances. The liver, spleen, kidney, brain and fat contained mineral oil. Within 2 days 0.3% remained in the animals (3).
Mineral oil [class 5] is poorly absorbed from the gut, but was found in lungs, liver, lymph and spleen of a man who ingested considerable amounts over many years (3).

Irritancy
Mild skin and eye irritant in rabbits (4,5).
Neither paraffinic nor naphthenic base stock caused primary eye irritation in rabbits (3).
Several light mineral oils caused hypertrophy, hyperplasia, hyperkeratosis and dilipidation after application to guinea pigs' skin; skin damage increased with increasing molecular size (3).
Occupational exposure causes eczematous dermatitis, contact dermatitis, oil acne, folliculitis, lipid granuloma and melanosis (3).

Sensitisation

Neither paraffinic nor naphthenic base stock caused skin sensitisation in guinea pigs (3).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation positive for vacuum distillates, hydrotreated oil and used steel-hardening oil, negative for white oil and unused steel-hardening oil (3).

Salmonella typhimurium TA1537, TA1538, TA98, TA100 with and without metabolic activation positive for used crankcase oils; both positive and negative results reported for unused crankcase oils (3).

Urine of workers occupationally exposed to mineral oils [class 8] and iron oxide was mutagenic in *Salmonella typhimurium* TA98, TA100 with metabolic activation (3).

Two insulation oils from highly-refined mineral-base oils induced transformation of Syrian hamster embryo cells and enhanced transformation of mouse cells; unused new, re-refined and used crankcase oils induced transformation of Syrian hamster embryo cells (6).

Increased frequency of chromosomal aberrations reported in peripheral lymphocytes of glass workers exposed to mineral oil mists (6).

Other effects

Other adverse effects (human)

Occupational ingestion, aspiration or inhalation exposure causes lipid pneumonia and lipid granuloma of the lung (3).

Legislation

White mineral oil is approved by the US FDA for use as a direct additive to food for human consumption; mineral oil is approved, with some limitations, for use as an animal feed additive and in materials in contact with food.

UK Mineral Hydrocarbons in Food Regulations 1966 prohibits use in food composition or preparation (3).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (7).

PAH content of petroleum-derived lubricants may increase during use, and used petrol engine oils can contain up to 1% lead (3).

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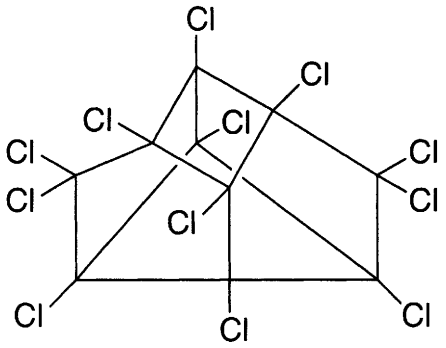
M334 mirex



$C_{10}Cl_{12}$ **Mol. Wt.** 545.54 **CAS Registry No.** 2385-85-5

Synonyms 1,1a,2,2,3,3a,4,5,5,5a,5b,6-dodecachlorooctahydro-1,3,4-metheno-1*H*-cyclobuta[*cd*]pentalene; dechlorane; hexachlorocyclopentadiene dimer

EINECS No. 219-196-6 **RTECS No.** PC 8225000

Uses Superseded insecticide. In flame-retardant coatings.

Physical properties

M. Pt. 485°C (decomp.) **Partition coefficient** log P_{ow} 5.28 **Volatility** v.p. 3×10^{-7} mmHg at 25 °C
Solubility Water: 0.2 mg l^{-1} at 24°C. Organic solvents: tetrahydrofuran, carbon disulfide, chloroform, benzene

Occupational exposure

Supply classification harmful, dangerous for the environment
Risk phrases Harmful in contact with skin and if swallowed – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment – Possible risk of impaired fertility – Possible risk of harm to the unborn child – May cause harm to breastfed babies (R21/22, R40, R50/53, R62, R63, R64)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Wear suitable protective clothing and gloves – If swallowed seek medical advice immediately and show this container or label – 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, S13, S36/37, S46, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, goldfish, bluegill sunfish 0.2-30 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (96 hr) *Gammarus fasciatus* 0.3 mg l^{-1} (2).
LC_{50} (96 hr) *Daphnia magna* 0.6 mg l^{-1} (3).
LC_{50} (120 hr) grass shrimp 190 μg l^{-1} (4).
LC_{65} (48 hr) juvenile crayfish 0.1 μg l^{-1} (4).

Bioaccumulation
Bioconcentration factor in mussels 34,200-73,700; crustaceans 16,860-71,400; algae 12,000 (5).
Tissue concentration in skunk and fox rose rapidly after spraying. Concentrations in aquatic ecosystems did not rise until 1 yr after spraying (6).

Bioaccumulates at all trophic levels and is biomagnified through food chains. Following application to land, residues were 10 μg l^{-1} in water and were 0 to 0.07 mg kg^{-1} in sediment. Concentrations increased significantly up the food chain; birds, 0-0.17 mg kg^{-1} and mammals 0-4.4 mg kg^{-1}. Accumulates to high levels in insectivorous birds with reported levels of 1-10 mg kg^{-1} (4).

Environmental fate

Degradation studies

Microbial biodegradation does not occur except occasionally under anaerobic conditions, and even then slowly; dechlorination to a monohydro derivative by anaerobic microbial action in sewage sludge (4).

Abiotic removal

Photodegraded to toxic products, chlordecone monohydromirex and dihydromirex (6).
Slow photodegradation under UV to photomirex (4).
Environmental $t_{1/2}$ is many years (4).
$t_{1/2}$ 48.4 hr in water under intense UV radiation at 90-95°C (4).
Photodegradation products include: 10-monohydromirex, 8-monohydromirex, 5,10-dihydromirex, chlordecone, and 2,8-dihydromirex (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral duck 2400 mg kg^{-1} (7).
LD_{50} oral Japanese quail 10,000 mg kg^{-1} (4).
LD_{50} oral starling, pheasant 562, 1600 mg kg^{-1}, respectively (4,8).
LD_{50} oral rat 235 mg kg^{-1} (7).
LD_{50} dermal rabbit, rat 800, 2000 mg kg^{-1}, respectively (4,7).

Sub-acute and sub-chronic data

LC_{50} (8 day) oral ring-necked pheasant, bobwhite quail, Japanese quail, mallard duck 1540->5000 mg kg^{-1} diet (4).

Carcinogenicity and chronic effects

No adequate data on carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC group 2B (9).
US National Toxicological Program evaluated mirex via feed, clear evidence of carcinogenicity in ♂, ♀ rat, inducing increased incidence of benign neoplastic nodules in liver in ♂ and ♀, as well as adrenal gland pheochromocytomas and transitional cell papillomas of the kidney in ♂, and mononuclear cell leukaemia in ♀ (10).
Increased incidence of hepatomas reported in mice fed 26 mg kg^{-1} for 70 wk. Increased incidence of reticulum cell sarcomas in mice given 1000 mg kg^{-1} subcutaneously (4).

Teratogenicity and reproductive effects

Reduced litter size in mice fed 5 mg kg^{-1} diet for 30 days before mating. Cessation of mating occurred in mice fed 17.8 mg kg^{-1} for 3 months. Reduced litter size, neonatal viability and cataracts in neonates reported in rats fed 25 mg kg^{-1}. Rats fed 6 mg kg^{-1} day^{-1} on days 8-15 gestation gave birth to dead, oedematous foetuses. Visceral foetal anomalies, reduced foetal weight and survival reported at maternally toxic levels of 12.5 mg kg^{-1} day^{-1} administered orally on gestation days 6-15 in rats (4).
Reduced viability of neonates in an *in vivo* mouse teratology screen (11).

Metabolism and toxicokinetics

Absorbed via the gut, by inhalation and skin. Not metabolised in any animal species investigated; $t_{1/2}$ in the body is several months, being stored in adipose tissue because it is lipophilic. It crosses the placenta and is excreted in breast milk. Excretion is via faeces as unchanged mirex (4).

Genotoxicity

Salmonella typhimurium (strain unspecified) with and without metabolic activation negative (4).
Dominant lethal test in rats negative (4).
Microscreen phage-induction assay with or without metabolic activation positive (12).

Other effects

Any other adverse effects

Toxicity in oral short-term studies is characterised by reduced body weight, hepatomegaly, induction of mixed function oxidases, morphological changes in liver cells and occasionally death (4).

Legislation

Regulated by US OSHA under its Air Contaminants Standard 1989 (13).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (14).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).
Included in the UN Banned and Severely Restricted list (16).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (17).

Other comments

Biodegradation of chlorinated organic compounds by *Phanerochaete chrysosporium* reviewed (18).
Hazards reviewed (19).
Toxicity reviewed (20).
Aquatic toxicity reviewed (4).

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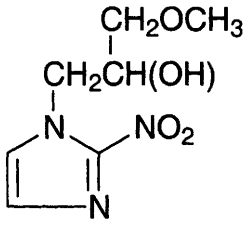
M335 misonidazole



$C_7H_{11}N_3O_4$ **Mol. Wt.** 201.18 **CAS Registry No.** 13551-87-6

Synonyms α-(methoxymethyl)-2-nitro-1*H*-imidazole-1-ethanol; α-(methoxymethyl)-2-nitroimidazole-1-ethanol; SR 1354

EINECS No. 236-931-6 **RTECS No.** NI 5572000

Physical properties

M. Pt. 110-111°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1869 and 2131 mg kg^{-1}, respectively (1,2).

LD_{50} subcutaneous mouse 1414 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 1340 mg kg^{-1} (4).

Metabolism and toxicokinetics

[^{3}H]Misonidazole was injected into ♂ and ♀ (lactating) mice at doses of 75 or 750 mg kg^{-1}. At the higher dose groups radiolabel was detected in meibomian gland ducts > oesophagus keratinised layer >liver periportalzone >hair bulb (5).

[^{3}H]-, [^{14}C]-Misonidazole (24 hr) intravenous tumour-bearing mice. The 24 hr tissue retention (highest to lowest) was oesphageal epithelium, liver, foot pad, eyelid, lung, subcutaneous lung tumour (A110), oesphageal wall, uterus, eyeball, blood, salivary gland, spleen, voluntary muscle, pancreas and inguinal fat (6).

In vitro sciatic nerves of CH3/He mice show an apparent biological $t_{1/2}$ correlated to hydrophilicity (7).

Genotoxicity

*Escherichia coli uvr*ABC excinuclease-proficient and -deficient strains grown under oxic and hypoxic conditions showed some induction of the SOS response (8).

Other effects

Any other adverse effects

Has increased cytotoxicity towards hypoxic compared with oxic cells. DNA is considered to be the target for cytotoxic activity (8).

Under anaerobic conditions both rat liver microsomes and cytosol catalysed the reductive metabolism and DNA binding of misonidazole (9).

Unspecified species, high-dose and short-term treatment induced oedematous or necrotic changes in the cerebellar and vestibular nuclei (10).

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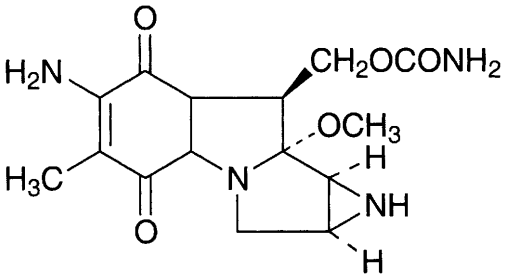
M336 mitomycin



$C_{15}H_{18}N_4O_5$ **Mol. Wt.** 334.33 **CAS Registry No.** 50-07-7

Synonyms mitomycin C; 6-amino-8-[[(aminocarbonyl)oxy]methyl]-1,1a,2,8,8a,8b-hexahydro-8a-methoxy-5-methylazirino[2',3':3,4]pyrrolo[1,2-*a*]indole-4,7-dione, [1a*S*-(1aα,8β,8aα,8bα)]-; azirino [2',3':3,4]pyrrolo[1,2-*a*]indole-4,7-dione, 6-amino-1,1a,2,8,8a,8b-hexahydro-8-(hydroxymethyl)-8a-methoxy-5-methyl, carbamate(ester); Ametycine; Mutamycin

EINECS No. 200-008-6 **RTECS No.** CN 0700000

Uses Antibiotic, acting as a bioreductive alkylating agent, used in the treatment of malignant neoplasms.
Occurrence Produced by the growth of *Streptomyces caespitosus*.

Physical properties

M. Pt. >360°C
Solubility Organic solvents: acetone, butyl acetate, cyclohexanone

Ecotoxicity

Invertebrate toxicity
EC_{50} (5, 10 or 20 min) *Photobacterium phosphoreum* >15.3 ppm Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 23, 30 mg kg^{-1}, respectively (2).
LD_{50} oral redwing blackbird, starling, quail 7.5->17.8 mg kg^{-1} (3).
LD_{50} subcutaneous rat, mouse 3250 and 7800 mg kg^{-1}, respectively (4).
LD_{50} intraperitoneal rat, mouse 2-4 mg kg^{-1} (5,6).
LD_{50} intravenous dog, rat, mouse 1-4 mg kg^{-1} (2,6,7).

Sub-acute and sub-chronic data

Intravesicular instillation rat wkly long-term experiment (dose and duration unspecified). Effects on the bladder included high percentage of pyuria and microscopic haematuria with submucosal/muscular fibrosis and severe dysplastic changes in the urothelium (8).

Intraperitoneal (5 wk) rat 1.7 mg kg^{-1} wkly. Caused lung changes characterised by a decrease in aminopeptidase excretion, alveolar septal congestion, tubular damage with acute enzyme leakage from cells followed by enzyme depletion (9).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (10).

Dose estimated to induce tumours in 50% of a group of animals was calculated to be ♀ rat 1.1 mg kg^{-1} day^{-1}, ♂ rat 0.73 mg kg^{-1} day^{-1} (11).

Subcutaneous (66 wk) mice (strains BTK, C57BL, C3H, DDO) 0.2 μg in saline 2 × wkly for 35 wk, followed by 31-wk observation. All BTK and 2/10 C57BL mice developed local sarcomas within 39-54 wk. No tumours were noted in the other two strains or any of the controls (12).

Intraperitoneal (18 month) Charles River CD rats 0.038 or 0.15 mg kg^{-1} 3 × wkly for 6 month and then observed for a further 12 months. Peritoneal sarcomas developed in 30/31 ♀ and 27/29 ♂ (13).

Intravenous (lifetime) ♂ BR46 rats 0.52 mg kg^{-1} 5 × within 2 wk. 79/96 survived to the time of the appearance of the 1st tumour (average time for tumour onset was 18 months). 34% developed malignant tumours which included lymphosarcomas, abdominal polymorphic-cell sarcomas, mammary carcinomas and sarcomas, subcutaneous fibrosarcomas and squamous-cell carcinomas. Three developed benign tumours. Malignant tumours were observed in 6.2% of the controls (7).

Teratogenicity and reproductive effects

Intraperitoneal ICR mice day 1, 2 or 3 of pregnancy 1.5-5 mg kg^{-1} (single dose) dose-dependent increase in foetal mortality and a decrease in the number of implants, foetal weight and the number of ossified sacral and caudal vertebrae. 5 mg kg^{-1} caused an increase in the incidence of external malformation umbilical hernia (14).

In vitro morula-stage mouse embryo 0.004-0.5 μg ml^{-1} caused a decrease in the number of inner cell mass cells at the blastocyst stage and a decrease in the tropectoderm population at the highest dosage only. Post-blastocyst development was retarded: fewer embryos formed trophoblastic outgrowths and the inner cell mass was poorly developed. Embryo-transfer experiments showed that the reduction in inner cell mass cells diminished the potential of embryogenesis and successful implantation (15).

Metabolism and toxicokinetics

Intravenous injection humans rapidly disappears from the blood, and is widely distributed but does not cross the blood-brain barrier. Metabolised mainly in the liver, about 10% is excreted unchanged in the urine, small amounts are also found in the bile and faeces (16).

Intravenous Wistar rat 2 mg kg^{-1}, 18% was collected unchanged in urine within 24 hr. 8 mg kg^{-1}, 35% was recovered in urine but none in faeces or tissues (17).

Intravenous guinea pig 8 mg kg^{-1}, after 30 min the drug was found concentrated in the kidneys and excreted in urine. Traces were detected in blood. It was not detected in the liver, spleen or brain (18).

Sensitisation

Patients receiving intravesical mitomycin C can develop severe eczematous symptoms which appear to be due to a hypersensitivity reaction (19).

Genotoxicity

Saccharomyces cerevisiae D5 induction of mitotic crossing over positive (20).

Escherichia coli K-12 without metabolic activation negative (21).

In vitro human whole-blood and separated-lymphocyte cultures without metabolic activation, micronuclei positive (22).

In vitro Chinese hamster ovary K1 cells with and without 1-β-D-arabinofuranosylcytosine induced sister-chromatid exchanges and chromosomal aberrations in s-phase synchronised cells (23).

In vitro human lymphocytes, micronuclei and chromosome nondisjunction positive (24).
In vivo rat liver and bone marrow cells chromosomal aberrations positive (25).
In vivo adult ♂ grasshopper injected with 0.2 ml of 0.01% mitomycin C caused an increase in chromosomal aberrations in the late spermatocytes. The induced aberration frequency was calculated to be ~20% (26).
In vivo intraperitoneal (5 day) ♂ rats 5-50 mg kg^{-1} day^{-1} percentage aberrant sperm heads increased four-fold (27).

Other effects

Other adverse effects (human)

Main adverse effects are delayed cumulative bone-marrow suppression. Profound leucopenia and thrombocytopenia occurs after 4 wk with recovery ~8-10 wk after a dose (16).

Any other adverse effects

Subconjunctival injection rabbit eye cornea 0.4 mg ml^{-1}, cytotoxic in intact and lesioned eye (28).
Intravesical instillation rats, 1 dose, short-term experiment (dose unspecified). Effects on the bladder included increased weight, oedematous changes in the muscle layer, congestion of the mucosa and infiltration of polymorphonuclear cells 3 days after instillation. These local changes had disappeared within 10 days (8).
Intraperitoneal rat 2.5 mg kg^{-1}, rats were examined after 5 days, alanine aminopeptidase:creatinine ratio increased compared with the control group (9).
Forelimb buds from 14-day-old rat foetuses were cut into pieces and transplanted subcutaneously into athymic (nude) mice. The mice were treated with mitomycin C on days 7, 9 and 11 after grafting and were examined on day-20, the differentiation of the grafts was inhibited compared with the controls (29).

Other comments

Pharmacokinetics, clinical pharmacology and antitumour mechanism reviewed (30,31).
Nephrotoxicity reviewed (32).

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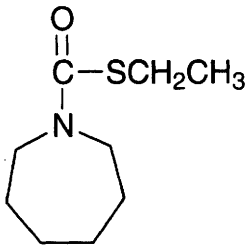
M337 molinate



$C_9H_{17}NOS$ **Mol. Wt.** 187.31 **CAS Registry No.** 2212-67-1

Synonyms hexahydro-1*H*-azepine-1-carbothioic acid, *S*-ethyl ester; *S*-ethyl azepine-1-carbothioate; *S*-ethyl perhydroazepine-1-carbothioate; *S*-ethyl perhydroazepine-1-thiocarboxylate; Ordram

EINECS No. 218-661-0 **RTECS No.** CM 2625000

Uses Herbicide used primarily for weed control in rice culture.

Physical properties

B. Pt. 202°C at 10 mmHg **Specific gravity** 1.063 at 20°C **Partition coefficient** log P_{ow} 2.8808 (1)
Volatility v.p. 5.6×10^{-3} mmHg at 25°C
Solubility Water: 88 mg l^{-1} (20°C). Organic solvents: miscible with acetone, benzene, ethanol, kerosene, methanol, 4-methylpentan-2-one, 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) – Avoid contact with the skin (S2, S24)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) bluegill sunfish 0.48 mg l^{-1} (2).
LC_{50} (96 hr) mosquito fish 16.4 mg l^{-1} (3).
LC_{50} (21 day) carp 0.18 mg l^{-1} (4).
Newly hatched fathead minnow larvae were exposed for 4 days to molinate at levels approximating to half the LC_{50} and to a much lower level similar to that experienced by minnow in the waters of the Colusa Basin Drain. The higher level caused reduction in swimming capacity, an increased sensitivity to electric shock, a reduction in upper lethal temperature, and a reduction in acetylcholinesterase activity. The lower level of exposure caused no measurable effect (5).
In vitro disposition and biotransformation by whole blood of the common carp. Accumulation by erythrocytes was nearly complete by 4 hr. Oxidised by erythrocytes to its sulfoxide and cleaved to form the mercapturic acid in both erythrocytes and plasma (6).

Invertebrate toxicity

Anabaena sphaerica 5-50 μg ml^{-1} significantly inhibited growth in a dose-dependent manner. 50 μg ml^{-1} stimulated protein and chlorophylla synthesis but inhibited biliprotein formation. These effects were greater under 3000 lx illumination than under 300 lx (7).

LC_{50} (48 hr) *Asellus brevicaudus, Daphnia magna* 0.4-0.6 mg l^{-1} (2).

LC_{50} (96 hr) prawn, scud, crayfish 1.0-5.6 mg l^{-1} (8,9).

Environmental fate

Degradation studies

Degraded by *Streptomyces, Mycobacterium* and *Flavobacterium* species isolated from soil (10).

Nocardia sp., *Micrococcus* sp. isolated from garden soils and rice field drains degraded molinate completely to various hydroxy and oxidised products (11,12).

Metabolites of microbial breakdown in soil include ethyl mercaptan, carbon dioxide and dialkylamine (1).

In soil $t_{1/2}$ ~2-5 wk (1).

Abiotic removal

[^{14}C]Molinate added to tap water decreased to 40% of original concentration in 14 days, this loss was primarily due to volatilisation. Major metabolites were molinate sulfoxide, 3- and 4-hydroxymolinate, 4-ketomolinate and ketohexamethyleneimine (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 369 and 530 mg kg^{-1}, respectively (13,14).

LC_{Lo} inhalation rat, cat 200 mg kg^{-1} (duration unspecified) (15).

LD_{50} dermal rabbit 3536 mg kg^{-1} (16).

LD_{50} subcutaneous rat 1167 mg kg^{-1} (14).

Sub-acute and sub-chronic data

LC_{50} (5 day) mallard duckling >9300 ppm in diet (17).

LC_{50} (9 wk) quail >1000 ppm in diet (17).

Metabolism and toxicokinetics

Oral rat rapidly metabolised within 72 hr; 50% eliminated as carbon dioxide, 25% is excreted in urine and 5-20% in faeces (1).

Irritancy

Dermal (48, 72 hr) human, 1% caused no irritation or sensitisation (18).

Moderate irritation to rabbit eye with iris and corneal dullness, all effects were gone by 5 days (8).

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).

WHO Toxicity Class II (21).

EPA Toxicity Class IV (13).

Other comments

Effect on fish reproduction disorders reviewed (22).

Cucumbers germinated and grown in soil which had previously been used to grow rice treated with molinate showed no adverse effects (23).

Metabolic pathways reviewed (24).

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M338 molybdenum

Mo

Mo **Mol. Wt.** 95.94 **CAS Registry No.** 7439-98-7

EINECS No. 231-107-2 **RTECS No.** QA 4680000

Uses Tungsten production. Lubricant additive in colloidal form. In the ferromolybdenum form for manufacturing special steels used in tools, rifle barrels, propeller shafts etc.

Occurrence In the ores molybdenite and Wulfenite. Occurence in earth's crust 1-1.5 ppm.

Physical properties

M. Pt. 2622°C **B. Pt.** 4825°C **Specific gravity** 10.28

Occupational exposure

DE-MAK 4 mg m^{-3} (inhalable fraction of aerosol)
SE-LEVL 10 mg m^{-3} (total dust); 5 mg m^{-3} (respirable dust)
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) barb 550 mg l^{-1} (as ammonium molybdate) (1).

LC_{100} (96 hr) barb 650 mg l^{-1} (as ammonium molybdate) (1).

Symptoms produced in barb include fin erosion, impaired swimming ability, dark colour and surfacing behaviour (1).

LC_{50} (96 hr) swim-up, advanced fry of chinook salmon, coho salmon >100 mg l^{-1} (form unspecified) (2).

Bioaccumulation

In analysis of plankton, molluscs and marine plants molybdenum was only detected in marine plant tissues (3).

Found in *Calyptogena* sp., *Mytilus edulis, Ridgeia pisceae, Riftia pachyptila, Paravinella palmiformis, Munidopsis* sp. collected from hydrothermal springs in Juna de Fuca and the Gulf of California (4).

Deep-sea macroinvertebrates (mussels and limpets) from submarine thermal springs accumulated molybdenum at levels corresponding to the levels discharged from the springs (5).

Three microorganism species were able to biosorb molybdenum from dilute solutions (6).

Mammalian & avian toxicity

Acute data

LD_{50} (route unspecified) mouse, rabbit 300, 700 mg kg^{-1}, respectively, as ammonium molybdate (7).

LD_{100} (route unspecified) sheep 1000 mg kg^{-1} (as ammonium molybdate) (7).

LD_{Lo} intraperitoneal rat 114 mg kg^{-1} (form unspecified) (8).

LD_{Lo} intraperitoneal rabbit 70 mg kg^{-1} (form unspecified) (9).

Acute symptoms in mouse, rabbit and sheep included general depression anaemia, decreased blood haemoglobin levels and alkaline phosphatase activity and increased xanthine oxidase in the liver and uric acid in the serum. Accumulation was highest in the kidney, liver and lungs (7).

Oral sheep 1000 mg kg^{-1} (form unspecified) developed symptoms of poisoning 1-15 hr after administration and death 5-6 hr later. Levels: kidneys, 530-550 mg kg^{-1}; lungs, 480-500 mg kg^{-1}; liver, 250-370 mg kg^{-1}; and muscles, 100-105 mg kg^{-1} (10).

Sub-acute and sub-chronic data

Sheep, rabbit chronic studies (duration, dose unspecified) resulted in weight reduction of liver and spleen, decreased haemoglobin levels, change in hepatic xanthine oxidase activity and uric acid level in the serum. Accumulation was highest in the liver (7).

Oral (3 month) rabbits, 1-10 mg kg^{-1} (as ammonium molybdate) did not cause any changes to health or physiological indexes. Levels accumulated in the tissues and organs were dose dependent and the majority of accumulation was in the liver (10).

Oral (duration unspecified) rats 0.1% as ammonium molybdate in diet caused significant anaemia and marked cardiac hypertrophy and copper deficiency (11).

Teratogenicity and reproductive effects

The air sacs of chick eggs were injected with various doses of a molybdenum salt on day-2 of incubation. On day-14 the developing embryos were examined. LD_{50} 333 μg egg^{-1}. Teratogenic effects were observed (12).

Genotoxicity

Escherichia coli PQ37, PQ35 SOS Chromotest with and without metabolic activation negative (as molybdenum chloride) (13).

Salmonella typhimurium TA1535, TA1537, a correlation was observed between toxicity and mutagenicity (14).

In vivo rats administered 0.0125 mg kg^{-1} (maximum level allowed in water drinking water) not mutagenic (form unspecified) (15).

Other effects

Other adverse effects (human)

There is a correlation between levels in soil and age-adjusted incidences of heart disease and cancer death rates (16).

Concentrations in soil and food relate inversely to the significantly higher than national average rates of human stomach and oesophageal cancers in China (17).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (18).

Other comments

Toxicity, biokinetics (including tissue distribution and metabolism), environmental effects reviewed (19-21).
Heavy metal toxicity to *Azotobacter chroococcum* described (22).
Has been detected in roe deer and mallard kidney and liver tissues (23).
Did not have a significant genotoxic effect on *Drosophila melanogaster* cells (form unspecified) (24).
Until two nitrogenases were isolated from *Azobacter* that lacked molybdenum, the element was considered indispensable for catalytic function in nitrogen fixation (25).
Analysis of lung tissue from 21 workers previously employed in metal refining showed levels of 0.037 $\mu g\ g^{-1}$ wet weight lung, whilst control groups showed 0.03 $\mu g\ g^{-1}$ (26).
Reviews on human health effects, workplace experience, epidemiology and experimental toxicology listed (27).

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M339 molybdenum trioxide

MoO_3

MoO_3 **Mol. Wt.** 143.94 **CAS Registry No.** 1313-27-5

Synonyms molybdena; molybdenum(VI) oxide; molybdic acid anhydride; molybdic anhydride

EINECS No. 215-204-7 **RTECS No.** QA 4725000

Uses Reagent for chemical analysis.

Physical properties

M. Pt. 795°C **B. Pt.** 1155°C **Specific gravity** 4.696 at 26°C with respect to water at 4°C

Solubility Water: 0.49 g l^{-1} at 28°C

Occupational exposure

DE-MAK 5 mg m^{-3} (inhalable fraction of aerosol)

FR-VME 5 mg m^{-3} (as Mo)

SE-LEVL 10 mg m^{-3} (total dust); 5 mg m^{-3} (respirable dust)

UK-LTEL 5 mg m^{-3} (as Mo) **UK-STEL** 10 mg m^{-3} (as Mo)

US-TWA 5 mg m^{-3} (as Mo)

Supply classification harmful

Risk phrases Irritating to eyes and respiratory system – Harmful: danger of serious damage to health by prolonged exposure through inhalation and if swallowed (R36/37, R48/20/22)

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

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 125 mg kg^{-1} (1).

LD_{50} subcutaneous mouse 4 mg kg^{-1} (2).

LD_{Lo} intraperitoneal guinea pig 400 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Inhalation rat, mouse 1, 33, 100 mg m^{-3} under investigation by The National Toxicology Program, National Institute of Environmental Health Sciences (4).

Teratogenicity and reproductive effects

Inhalation (13 wk) ♂ B6C3F_1 mice 10-100 ppm, no change in reproductive organ weight or sperm motility, density or morphology (5).

Inhalation (13 wk) ♂ F344 rat 10-100 mg m^{-3}, statistically significant reduction in epididymis weight and an increase in the number of abnormal sperm was observed. Testis and cauda weight and sperm motility and sperm density were not significantly different from controls (5).

Legislation

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

Other comments

Reviews on hazards reviewed (7).

Human health effects, epidemiology, workplace experience and experimental toxicology listed (8).

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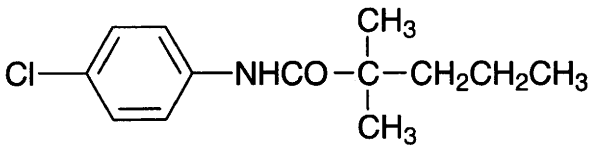
M340 monalide



$C_{13}H_{18}ClNO$ **Mol. Wt.** 239.74 **CAS Registry No.** 7287-36-7

Synonyms *N*-(4-chlorophenyl)-2,2-dimethylpentanamide; 4'-chloro-2,2-dimethylvaleranilide; Potablan

EINECS No. 230-712-9 **RTECS No.** YV 6010000

Uses Superseded herbicide for post-emergence control of broad-leaved weeds.

Physical properties

M. Pt. 87-88°C **Volatility** v.p. 1.8×10^{-6} mmHg at 25°C

Solubility Water: 22.8 mg l^{-1} at 23°C. Organic solvents: cyclohexanone, petroleum ether, xylene

Ecotoxicity

Fish toxicity

LC_{50} (duration unspecified) guppy >100 mg l^{-1} (1,2).

Environmental fate

Degradation studies

In compost soil at pH 4.85, 5.2, 10.8; $t_{1/2}$ 726, 1161, 1412 hr, respectively (3).

The decomposition product 4-chloroaniline was isolated from soil (3).

Abiotic removal

Decomposition in buffer solutions using two methods with slightly different pH ranges; pH 1.1-11.0 and pH 1.8-10.9. Regardless of the method used, decomposition was fastest in acid media, with decomposition in alkaline media being slower and slowest under neutral conditions. At pH 7, $t_{1/2}$ 80-372 wk, depending on the method of determination used (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2600 mg kg^{-1} (4).

LD_{50} dermal rabbit 2600 mg kg^{-1} (5).

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

Sub-acute and sub-chronic data
NOEL (28 day) rat 150 mg kg^{-1} day^{-1} (1,2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).
WHO Toxicity Class Table 5 (8).
EPA Toxicity Class III (1).

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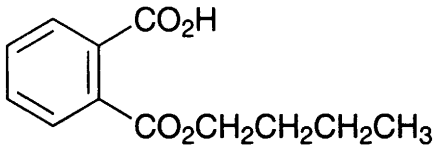
M341 monobutyl phthalate



$C_{12}H_{14}O_4$ **Mol. Wt.** 222.24 **CAS Registry No.** 131-70-4

Synonyms 1,2-benzenedicarboxylic acid, monobutyl ester; phthalic acid, monobutyl ester; phthalic acid, butyl ester; butyl hydrogen phthalate; mono-*n*-butyl phthalate

EINECS No. 205-036-2 **RTECS No.** TI 2475000

Physical properties

Specific gravity 1.105 at 81°C
Solubility Organic solvents: ethanol

Occupational exposure

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

Mammalian & avian toxicity

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

Sub-acute and sub-chronic data

Oral (34-36 day) ♂ Wistar rat 0.5 or 5% in diet. The higher dose group showed growth depression, liver enlargement, testicular atrophy, decrease of succinate and pyruvate dehyrogenase activities in liver mitochondria and changes in liver and testis biochemistry and histology (2).

Oral (1 wk) ♂ rat 0.8 g kg^{-1} day^{-1} caused severe testicular injury (3).

Other comments

Reviews on human health effects and experimental toxicology listed (4).

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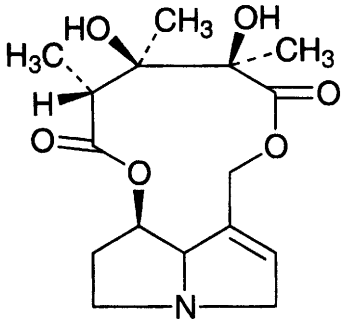
M342 monocrotaline



$C_{16}H_{23}NO_6$ **Mol. Wt.** 325.36 **CAS Registry No.** 315-22-0

Synonyms (13α,14α)-14,19-dihydro-12,13-dihydroxy-20-norcrotalanan-11,15-dione; monocrotalin

RTECS No. QB 3140000

Uses In Africa and India crushed roots of *Crotalaria* sp. are used for a colic remedy, fever relief, remedy for haemoptysis and in the treatment of childhood malaria.

Occurrence Pyrrolizidine alkaloid which is the major toxic constituent of *Crotalaria spectabilis* Roth. Leguminosae (1).

Physical properties

M. Pt. 197-198°C (decomp.)

Solubility Water: 1.2%. Organic solvents: chloroform, ethanol

Occupational exposure

UN No. 2811

Ecotoxicity

Fish toxicity

Non-toxic to trout, bluegill sunfish, yellow perch, goldfish (24 hr) at 5 ppm. Test conditions: pH 7.0; dissolved oxygen content 7.5 ppm; total hardness (soap method) 300 ppm; methyl orange alkalinity 310 ppm; free carbon dioxide 5 ppm; and temperature 12.8°C (2).

Three-spine stickleback, steelhead trout, sockeye salmon (24 hr) no fish death or loss of equilibrium 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 (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 166-261 mg kg^{-1} (4,5).

LD_{50} oral rat 66-71 mg kg^{-1} (6).

LD_{Lo} subcutaneous rat 60 mg kg^{-1} (7).

LD_{50} intravenous rat 92 mg kg^{-1} (8).

LD_{50} intravenous mouse 261 mg kg^{-1} (9).

LD_{Lo} intraperitoneal rat 130 mg kg^{-1} (10).

LD_{50} intraperitoneal mouse 259 mg kg^{-1} (11).

LD_{50} intraperitoneal ♂, ♀ rat 178-189 mg kg^{-1} (12).

Guinea pig (route unspecified) 240 mg kg^{-1} (4 times LD_{50} for rats) showed no clinical or pathological effects (13).

Sub-acute and sub-chronic data

Gavage (14 day) ♀ C57B1/6 mice 0-150 mg kg^{-1}. Dose-dependent suppression in the antibody response to sheep red blood cells, cytotoxic T-lymphocyte response was decreased (38% of control), the number of cytotoxic T-lymphocytes $spleen^{-1}$ was reduced to 12% of control and the antibody titres were dose dependently suppressed (14).

Oral (6 wk) ♂ mice 2.4, 4.8 or 24.0 mg kg^{-1} day^{-1} in drinking water continuously. Pulmonary endothelial function was investigated. A dose-dependent decrease in lung angiotensin converting enzyme and plasminogen activator activity, indicative of endothelial dysfunction, was found. However, these responses were only significant at the highest dose. Microscopy revealed dose-dependent pulmonary inflammation and exudative reactions (15).

Oral (6 month) rat 0.1 LD_{50} 2 × wkly in drinking water, lesions in the lungs, liver, kidneys and heart. Two ♀ rats developed preneoplastic lesions in the liver (16).

Subcutaneous infant stumptail monkeys 30 mg kg^{-1} followed by 60 mg kg^{-1} during the 2, 4, 6 months of the experiment produced severe lung lesions and cardiac hypertrophy, but little liver damage. The same doses given to adolescent monkeys caused severe hepatic veno-occlusive lesions (17).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (18).

Gavage (72 wk) ♂ Sprague-Dawley (CD) rat 25 mg kg^{-1} wk^{-1} for 4 wk then 8 mg kg^{-1} wk^{-1} for 38 wk followed by observation until 72 wk. 42/72 rats survived until the appearance of the 1st tumour (55 wk). Of these, 10 developed liver cell carcinomas. Lung metastases were also observed (19).

Gavage (72 wk) ♂ Sprague-Dawley (CD) rats fed a diet marginally deficient in lipotrophes 25 mg kg^{-1} wk^{-1} for 4 wk and then 8 mg kg^{-1} wk^{-1} for 38 wk followed by observation up to 72 wk. 35/50 survived until the appearance of the 1st tumour at 46 wk and, of these, 14 developed liver cell carcinomas. Lung metastases were also observed (19).

Teratogenicity and reproductive effects

Oral rat 0.5 LD_{50} in feed during pregnancy and lactation, toxic effects studied in newborn rats for up to 18 months after lactation. Toxic effects detected in lungs, liver, spleen and kidneys of newborns during early stages. These toxic effects were more severe in rats exposed during pregnancy and lactation than in rats only exposed during lactation (20).

Metabolism and toxicokinetics

The major metabolite excreted in rat urine is an *N*-acetylcysteine conjugate of (±)-6, 7-dihydro-7-hydroxy-1-hydroxymethyl-5*H*-pyrrolizine (21).

[^{14}C]Monocrotaline (60 mg kg^{-1}, 200 μCi kg^{-1}) applied to rats subcutaneously. At 4 hr the distribution in tissues was 27.7, 24.1, 21.8, 11.7, 2.6 μg g^{-1} of tissue for red blood cells, liver, kidney, lung and plasma, respectively. At 24 hr the distribution in tissues was 15.9, 8.1, 2.9, 3.3, 0.7 μg g^{-1} of tissue for red blood cells, liver, kidney, lung and plasma, respectively (22).

Kinetic studies of [^{14}C]monocrotaline (60 mg kg^{-1}, 10 μCi kg^{-1}) intravenously to rats demonstrated rapid elimination of radioactivity with ~ 90% recovery of injected radioactivity in urine and bile by 7 hr. The plasma level of radioactivity dropped from 36.76 μg g^{-1} to 3.58 μg g^{-1} by 7 hr, red blood cell levels decreased from 46.85 μg g^{-1} to 26.35 μg g^{-1} by 7 hr. Intravenous rat with cannulated bile duct [^{14}C]monocrotaline; 83% of the dose was excreted in urine within 7 hr and 12% of the dose was found in bile (22).

Genotoxicity

In vitro human embryo kidney cell cultures irreversibly inhibited DNA synthesis (23).

In vivo ♂ *Drosophila melanogaster* injected into abdomen sex-linked recessive lethals positive (24).

In vivo after intraperitoneal injection of 0-30 mg kg^{-1} caused DNA-DNA interstrand cross-linking in a dose-dependent manner in rat liver cells (25).

Other effects

Other adverse effects (human)

In vitro human embryo kidney cell culture inhibited carbohydrate synthesis and the cellular utilisation of carbohydrates. Formation of lactate was decreased and the intracellular pH markedly increased (23).

Consumption of *Crotalaria* sp. containing monocrotaline can lead to veno-occlusive disease (26).

Other comments

Pulmonary effects reviewed (27).

Reviews on human health effects and experimental toxicology listed (28).

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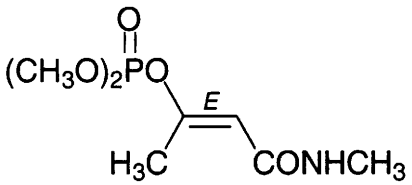
M343 monocrotophos



$C_7H_{14}NO_5P$ **Mol. Wt.** 223.17 **CAS Registry No.** 6923-22-4

Synonyms (*E*)-dimethyl 1-methyl-3-(methylamino)-3-oxo-1-propenyl phosphate; (*E*)-3-dimethoxyphosphinoyloxy-*N*-methylisocrotonamide; Azodrin; Agrofos; Aimocron; Balwan; Crisodrin; Eritox; Nuvacron

EINECS No. 230-042-7 **RTECS No.** TC 4375000

Uses Systemic insecticide. Acaricide.

Physical properties

M. Pt. 25-30°C (commercial solid product), 54-55°C (crystals) **B. Pt.** 125°C at 0.0005 mmHg
Specific gravity 1.33 at 20°C **Partition coefficient** K_{ow} 0.60 (calculated) **Volatility** v.p. 7×10^{-6} mmHg at 20°C
Solubility Water: 1 kg kg^{-1} at 20°C. Organic solvents: acetone, ethanol

Occupational exposure

FR-VME 0.25 mg m^{-3}
US-TWA 0.25 mg m^{-3}
Supply classification very toxic, dangerous for the environment
Risk phrases Toxic in contact with skin – Very toxic if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24, R28, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe 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) snakehead fish 10 ppm (1).
Snakehead fish (15-120 day) 1 ppm. Fish at 15 day were hypoglycaemic and hypolactaemic, after 30 days anaerobic metabolism prevailed over aerobic metabolism, after 60 and 120 days both aerobic and anaerobic pathways were impaired (1).
LC_{50} (acute exposure) rainbow trout 4.9 mg l^{-1} (2).

LC_{50} (96 hr) harlequin fish 450 mg l^{-1} (3).
LC_{100} (96 hr) cichlid 18.6 mg l^{-1} (4).

Invertebrate toxicity

Two successive applications at field doses to flooded rice soil decreased significantly the population size of soil algae and also altered the species composition of the native algal flora (5).
LC_{50} (96 hr) marine edible crab 0.577 ppm (6).
Sublethal concentrations were greatly deleterious to the midgut of the freshwater crab *Paratelphusa masoniana*, causing significant histopathological changes (7).
LC_{50} (48, 96 hr) shrimp 4.46, 1.59 mg l^{-1}, respectively (8,9).
LC_{50} (96 hr) oarfooted crustacean 0.24 mg l^{-1} (10).

Toxicity to other species

Clawed frog embryos, caused dose-dependent developmental defects (dose unspecified) including abnormal pigmentation, abnormal gut development, notochordal defects and reduced growth (11).

Environmental fate

Nitrification inhibition

≥5 μg ml^{-1} inhibited nitrogen fixation activity of *Nostoc linckia* (12).

Degradation studies

20-day incubation in flooded rice soil decreased levels to trace amounts. In flooded rice soil that had been autoclaved monocrotophos persisted, indicating microbiological action was important in degradation (5).
Soils treated 5 × 15 day intervals and isolated algae were then incubated with the monocrotophos 5-50 ppm for 30 days. All 5 algal species degraded the insecticide. Degradation was almost complete by 30 days (13).
$t_{1/2}$ in aqueous environment at 25°C; pH 3 131 day; pH 9 26 day. Hydrolysis followed 1st-order kinetics and the major hydrolytic degradation products were *N*-methylacetoacetamide and *O*-demethylmonocrotophos (14).
Soil metabolism studies showed rapid and extensive decomposition, eventually to carbon dioxide and unextractable residues. The intermediate degradation products were *N*-methylacetoacetamide, *N*-(hydroxymethyl)monocrotophos and 3-hydroxy-*N*-methylbutyramide (14).

Abiotic removal

Degradation did not occur in the absence of light (15).
Photodegradation was greater on soil surfaces than on glass. Photodegradation: alluvia <black <red loamy >laterite soil. Photolysis was greater on flooded moist soils than dry loam soil (15).
UV light was more effective at degradation than sunlight. Rate of photodegradation in tap water was twice that in distilled water (15).
River water in a sealed jar under sunlight and artificial light 0.01 mg l^{-1} initial concentration, 100% remained after 8 wk (16).

Adsorption and retention

Mobile in soil under test conditions (14).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 8-15 mg kg^{-1} (17,18).
LD_{50} oral rat ♂ 17, ♀ 20 mg kg^{-1} (19).
LD_{50} oral northern bobwhite, quail, duck 0.8-3.4 mg kg^{-1} (20,21).
LD_{50} oral redwing blackbird, house sparrow, redbilled quelea, common grackle, common pigeon, quail, starling 1-5.62 mg kg^{-1} (22).
LD_{50} oral mallard 42.2 mg kg^{-1} (22).
LC_{50} (4 hr) inhalation rat 63 mg m^{-3} (23).
LD_{50} dermal rat ♂ 126, ♀ 112 mg kg^{-1} (19).
LD_{50} dermal duck 30 mg kg^{-1} (24).

LD_{50} subcutaneous rat, mouse 6964-8710 μg kg^{-1} (25,26).
LD_{Lo} intraperitoneal rat 20 mg kg^{-1} (27).
LD_{50} intraperitoneal mouse 3800 μg kg^{-1} (28).
LD_{50} intravenous rat, mouse 9200 μg kg^{-1} (26,29).

Sub-acute and sub-chronic data
Intragastric (2 wk) rat 0.3-2.4 mg kg^{-1} day^{-1} showed dose-, time-, and sex-related changes in blood chemistry and body and organ weights (30).
Oral (13 wk) ♂, ♀ Wistar-derived rats 0, 0.1, 0.25, 0.5, 2.0, 8.0 ppm in diet to animals in each treatment group. Half the animals in each treatment group were killed after 8 wk and the remainder were killed after 13 wk. No clinical symptoms or deaths due to the treatment were observed. There was a slight reduction of body weight in both sexes at the 8 ppm dose level. At all doses there was a dose-related decrease of plasma, erythrocyte and brain cholinesterase activities. The inhibition of brain cholinesterase was biologically significant in the 2.0 and 8.0 ppm dose groups. Cholinesterase activity was almost completely recovered by 5 wk post-treatment (31).

Carcinogenicity and chronic effects
Oral (104 wk) ♂, ♀ CD mice 1, 2, 5 or 10 ppm in diet. No evidence of treatment-related oncogenic effects at any of the dose levels (31).
Oral (24 month) ♂, ♀ Wistar-derived rats 0.01, 0.03, 0.1, 1.0 or 10 ppm in diet. No evidence of treatment-related oncogenic effects at any of the dose levels (31).

Teratogenicity and reproductive effects
Oral ♂, ♀ rats (5-wk-old at start of study) 0, 0.1, 1, 3 or 10 ppm in diet for at least 15 wk (F_0 generation) these were mated and the progeny (F_1) were fed the same diet for 18 wk prior to mating to produce an F_2 generation. Significantly lower (6-9% lower) body weights were seen in the ♂ F_0 and F_1. No effects on sperm count were seen in the ♂ F_0 or ♂ F_1. Mating performance, fertility index and gestation index were not different among the F_0 groups. 10 ppm F_1 ♂ mating index was lower and fewer litters were produced compared with controls. Mean litter size, viability index and lactation index were significantly reduced at 10 ppm for both F_1 and F_2 generations and the viability index of 3 ppm F_2 was also reduced. Mean pup weights were reduced for the F_1 at 10 ppm and the F_2 at 10 and 3 ppm. There were 3 total litter losses at F_1, F_2 at 10 ppm and 1 at F_2 at 3 ppm. The no-effect level in this reproduction study was 1 ppm (31).
Gavage (days 6 to 15 of gestation) ♀ rat 0, 0.3, 1.0 or 2.0 mg kg^{-1} day^{-1}. At the 2.0 mg kg^{-1} mean body weight and crown rump length of the foetuses were significantly lower. At 1.0, 2.0 mg kg^{-1} the mean percentage of runt foetuses was increased. At 2 mg kg^{-1} the percentage of foetuses with non-ossified sternebrae was doubled compared with the controls. Malformed and/or misshapen brain was observed in foetuses at 0.3, 1 and 2 mg kg^{-1}; this type of malformation is uncommon to this strain of rat (31).

Metabolism and toxicokinetics
Oral mammals 60-65% excreted within 24 hr, mostly in urine (32).

Genotoxicity

Escherichia coli SOS Chromotest with and without metabolic activation negative (33).
Salmonella typhimurium TA98, TA100, TA102, TA1535, TA1537, TA1538 with and without metabolic activation *TA100* positive, all others negative (31,34).
Saccharomyces cerevisiae D3, D7 with and without metabolic activation positive (31).
In vitro primary rat tracheal epithelial cells, Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges positive (35).
In vitro Chinese hamster ovary cells with and without metabolic activation clastogenesis positive (36).
In vitro human lymphocytes time- and concentration-dependent increases of chromosome damage and sister chromatid exchanges (37).
In vivo rat bone marrow cells chromosomal aberrations equivocal (38).
In vivo mice 0.9, 1.8, 3.6 mg kg^{-1} increased the number of abnormal sperm to 2.12, 3.20, 5.36%, respectively, control 2.09% (39).

Other effects

Other adverse effects (human)

Occupationally exposed pesticide sprayers had significantly increased numbers of sister chromatid exchanges and chromosomal aberrations, at all durations of exposure, compared with unexposed controls. They also showed cell cycle delay and a decrease in the mitotic index (40,41).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (42).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (43).
WHO Toxicity Class Ib (44).
EPA Toxicity Class I (45).
ADI 0.0006 mg kg^{-1} body weight (45).

Other comments

Pesticide Suitability Rating (calculated to indicate suitability for use in the household) designates monocrotophos to be just above the acceptable limit (46).

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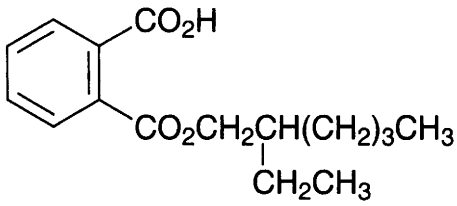
M344 mono(2-ethylhexyl) phthalate



$C_{16}H_{22}O_4$ **Mol. Wt.** 278.35 **CAS Registry No.** 4376-20-9

Synonyms 1,2-benzenedicarboxylic acid, mono(2-ethylhexyl) ester; phthalic acid, mono(2-ethylhexyl) ester; 2-ethylhexyl hydrogen phthalate

EINECS No. 224-477-1 **RTECS No.** TI 2500000

Physical properties

M. Pt. 14-16°C

Occupational exposure

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

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1340 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse, rat 240 and 415 mg kg^{-1}, respectively (2).

LD_{50} intravenous rat, mouse 150 and 208 mg kg^{-1}, respectively (2).

Sub-acute and sub-chronic data

Oral ♂ Chinese hamster, ♂ Syrian hamster (14 day) 0.5% in diet caused an increase in liver size and an induction of peroxisomal enzyme activity. The effects were more pronounced in Chinese hamsters (3).

Oral ♂ rat (>21 day) various doses, doses ≥1000 ppm caused peroxisomal proliferation (4).

Gavage ♂ cyanomologus monkeys (>21 day) up to 500 mg kg^{-1} day^{-1} did not cause peroxisomal proliferation (4).

Teratogenicity and reproductive effects

♂ Rat single dose (route unspecified) 0.8 g kg^{-1} induced testicular atrophy which was age-dependent with only prepubertal rats being susceptible. Testicular zinc levels were affected to varying degrees, dependent on treatment (5).

Oral mice (6-13 day gestation) 545 mg kg^{-1} day^{-1}. Mice were allowed to deliver litters and the pups were studied for 3 days. The number of viable litters was significantly reduced, 2/33 pregnancies compared with the control of 34/38. Of the viable litters there was no significant decrease in live born per litter, percentage survival, birth weight or weight gain (6).

Designated negative for developmental toxicity in rabbits, positive for mice, with a predicted negative developmental toxicity for humans (7).

Metabolism and toxicokinetics

In vitro cultures of ♂ rat hepatocytes, Sertoli cells, Leydig cells, incubated with [^{14}C]mono(2-ethylhexyl) phthalate for up to 24 hr caused no significant reduction in viability. Hepatocytes extensively metabolised [^{14}C]mono-(2-ethylhexyl) phthalate to a variety of products within 1 hr; Sertoli cells and Leydig cells showed no significant metabolism in 24 hr. Hepatocytes were much more efficient at uptake than Sertoli or Leydig cells (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 with and without metabolic activation negative (9,10).

In vitro Chinese hamster cells DNA amplification negative (9).

In vitro rat, hamster hepatocytes DNA damage negative (9).

In vitro rat hepatocytes unscheduled DNA synthesis negative (11).

Other effects

Any other adverse effects

In vitro rat, human hepatocyte cell cultures induced enzymes indicative of peroxisomal proliferation (12).

Other comments

Reviews on human health effects and experimental toxicology listed (13).

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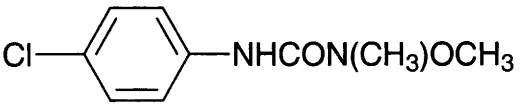
M345 monolinuron



$C_9H_{11}ClN_2O_2$ **Mol. Wt.** 214.65 **CAS Registry No.** 1746-81-2

Synonyms *N'*-(4-chlorophenyl)-*N*-methoxy-*N*-methylurea; 3-(*p*-chlorophenyl)-1-methoxy-1-methylurea; Aresin; Arezin; Arezine; Monorotox

EINECS No. 217-129-5 **RTECS No.** YS 6425000

Uses Herbicide.

Physical properties

M. Pt. 80-83°C **Specific gravity** 1.3 at 20°C **Partition coefficient** log P_{ow} 2.2041 (1)
Volatility v.p. 1.5×10^{-4} mmHg
Solubility Water: 0.735 g l^{-1} at 25°C. Organic solvents: acetone, chloroform, diethyl ether, dioxane, 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} (96 hr) brown trout (non-migratory), common carp, cichlid, snakehead fish, 3.1, 12.9, 54, 105 mg l^{-1}, respectively (2,3).

Invertebrate toxicity
LC_{50} (96 hr) *Daphnia magna* 1.3 mg l^{-1} (2).
LOEC (duration unspecified) *Microcystis aeruginosa* 0.14 mg l^{-1} (4).
LC_{50} (96 hr) mosquito larvae 24.2 mg l^{-1} (2).
LD_{50} oral bee >296.3 μg g^{-1} body weight (5).

Environmental fate

Degradation studies
In soils $t_{1/2}$ ~45-60 day (1).
Breakdown in soil involves cleavage of the methyl and methoxy groups on the terminal nitrogen atom, with simultaneous ring hydroxylation and formation of 3-(2-hydroxy-4-chlorophenyl)urea and the corresponding 3-hydroxy compound (1).

Abiotic removal
Major decomposition product after photochemical exposure was 3-phenyl-1-methylurea (6).

Adsorption and retention
Soil adsorption K_{oc} 250-500 (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck >500 mg kg^{-1} (1,5).
LD_{50} oral bobwhite quail, Japanese quail 1260, >1690 mg kg^{-1}, respectively (1,5).

LD_{50} intragastric duck, mouse, chicken, rabbit 0.38-1.80 g kg^{-1}. Affected the nervous system, heart function and blood composition. Accumulation was mainly in the liver, kidneys, lungs and heart (7).
LD_{50} oral dog, rat 500, 1800 mg kg^{-1}, respectively (8,9).

Carcinogenicity and chronic effects
In a 2-yr feeding study, no-effect level for rats was 250 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} (10).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (11).
WHO Toxicity Class Table 5 (12).
ADI 0.005 mg kg^{-1} body weight (5).

Other comments

Behaviour in soils predicted (13).
Metabolic pathways reviewed (14).

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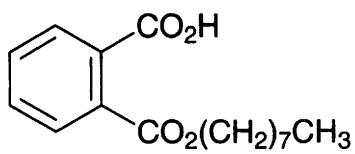
M346 monooctyl phthalate



$C_{16}H_{22}O_4$ **Mol. Wt.** 278.35 **CAS Registry No.** 5393-19-1

Synonyms 1,2-benzenedicarboxylic acid, monooctyl ester; phthalic acid, monooctyl ester; octyl hydrogen phthalate

RTECS No. CZ 4320000

Physical properties

M. Pt. 21.5-22.5°C (crystallised from petroleum ether)

Occupational exposure

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

Mammalian & avian toxicity

Metabolism and toxicokinetics

It inhibited the state 3 oxygen consumption in mitochondrial function of rat testis, to a concentration as low as 18 mg l^{-1} (1).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

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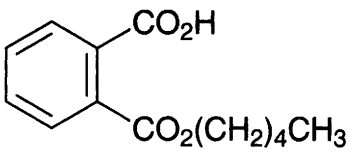
M347 monopentyl phthalate



$C_{13}H_{16}O_4$ **Mol. Wt.** 236.27 **CAS Registry No.** 24539-56-8

Synonyms 1,2-benzenedicarboxylic acid, monopentyl ester; phthalic acid, monopentyl ester; monoamyl phthalate; mono-*n*-pentyl phthalate

Physical properties

M. Pt. 75.4-75.6°C in petroleum ether

Occupational exposure

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

Other effects

Any other adverse effects

Produced ultrastructural changes in Sertoli cells in primary co-cultures of rat seminiferous tubules; were in the configuration of the plasma membrane, in microfilament distribution and in an increased density of ribosomes, smooth endoplasmic reticulum and the Golgi body (1).

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M348 monothiuram

$$(CH_3)_2NC(S)SC(S)N(CH_3)_2$$

$C_6H_{12}N_2S_3$ **Mol. Wt.** 208.37 **CAS Registry No.** 97-74-5

Synonyms carbamic acid, dimethyldithioanhydrosulfide; tetramethyl thiodicarbonic diamide tetramethylthiurammonium sulfide; 1,1'-thiobis(*N*,*N*-dimethylthio)formamide; bis(dimethylthiocarbamoyl) sulfide

EINECS No. 202-605-7 **RTECS No.** WQ 1750000

Uses Component of bird repellent (1).
Antioxidant in resin manufacture. Vulcanisation accelerator. Fungicide.

Physical properties

M. Pt. 104°C **Partition coefficient** log P_{ow} 1.17 (2)
Solubility Organic solvents: chloroform, ethanol

Occupational exposure

Supply classification harmful, danagerous for the environment
Risk phrases Harmful if swallowed – May cause sensitisation by skin contact – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R43, R51/53)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves – Avoid release to the environment. Refer to special instructions/safety data sheet (S24, S26, S37, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) guppy 5.3 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 2.9 mg l^{-1} (2).

Bioaccumulation
EC_{50} (96 hr) *Chlorella pyrenoidosa* 1.0 μg l^{-1} (2).

Environmental fate

Nitrification inhibition
The minimum inhibiting concentration (3 hr) for *Nitrosomonas* and *Nitrobacter* spp. is 32 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 500 mg kg^{-1} (3).
LD_{50} oral mouse 818 mg kg^{-1} (4).
LD_{Lo} oral cat 100 mg kg^{-1} (5).
LD_{Lo} oral guinea pig 10 mg kg^{-1} (6).
LD_{50} intraperitoneal mouse 300 mg kg^{-1} (7).

Carcinogenicity and chronic effects
TD_{Lo} subcutaneous mouse 100 mg kg^{-1} reported equivocal tumorigenic effects (8).

Teratogenicity and reproductive effects
TD_{Lo} (6-14 days) subcutaneous pregnant mouse 900 mg kg^{-1} reported reproductive effects (9).

Day-3 chicken embryos were injected and testing continued to day-14 of incubation. Embryotoxicity was observed, most common malformations were eye defects and open coeloms (10).

Irritancy

1% concentration caused a positive patch-test reaction in 11-34% of cases evaluated (11).

Genotoxicity

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

Other effects

Any other adverse effects

Rats, pretreated by gavage with two doses of 3.3 mg kg^{-1} or 53 mg kg^{-1} at 90 min or 18 hr before intraperitoneal administration of 2 g kg^{-1} in ethanol showed significant increases in blood acetaldehyde. Oral 3.3 mg kg^{-1} dose could be detected up to 48 hr after administration (13).

Administration oral ♀ rat 26 mg kg^{-1} caused prolongation of the hexobarbital sleeping time, related to inhibition of microsomal oxygenases. Decrease in erythrocytes and Hb count in blood (4).

Inhibited lipid peroxidation in rat hepatic microsomes (14).

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M349 montmorillonite

CAS Registry No. 1318-93-0

Synonyms Arcillite; Bentolite; Deriton; Walkerde Flygtol GA

EINECS No. 215-288-5

Uses In industrial chromatography techniques. In the petroleum industry. Catalyst carrier.

Occurrence A clay forming the principal constituent of bentonite and Fuller's Earth.

Environmental fate

Nitrification inhibition

Increasing the concentration of montmorillonite in a soil enhanced the rate of nitrification (1).

Other effects

Any other adverse effects

Potential health risk due to exposure to montmorillonite dust can be excluded. Scanning electron microscopic investigations did not reveal fibrous particles (2).

Other comments

A constituent of Fuller's Earth, used in the treatment of paraquat poisoning (3).

Montmorillonite clay is a good adsorber of ammonium but a poor absorber of potassium (4).

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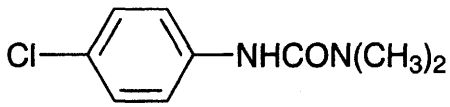
M350 monuron



$C_9H_{11}ClN_2O$ **Mol. Wt.** 198.65 **CAS Registry No.** 150-68-5

Synonyms *N'*-(4-chlorophenyl)-*N,N*-dimethylurea; 3-(*p*-chlorophenyl)-1,1-dimethylurea; Telvar; Karmex Monuron Herbicide; Telvar Monuron Weed Killer; Karmex W. monuron herbicide

EINECS No. 205-766-1 **RTECS No.** YS 6300000

Uses Superseded herbicide.

Physical properties

M. Pt. 170.5-171.5°C **Specific gravity** 1.27 at 20°C with respect to water at 20°C

Partition coefficient log P_{ow} 2.13 (1) **Volatility** v.p. 5×10^{-7} mmHg at 25°C, 1.78×10^{-3} mmHg at 100°C

Solubility Water: 230 ppm at 25°C. Organic solvents: acetone, ethanol, methanol

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed – Possible risk of irreversible effects (R22, R40)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) coho salmon 110 mg^{-1} (2).

Invertebrate toxicity

Microalgae, cyanobacteria minimum inhibitory concentration to growth >17.1 μg ml^{-1} (3).

EC_{50} (5 min) *Photobacterium phosphoreum* 228 ppm Microtox test (4).

EC_{50} (duration unspecified) *Phaeodactylum tricornutum* 90 mg l^{-1} affected photosynthesis (5).

LOEC (duration unspecified) *Dunaliella euchlora, Phaeodactylum tricornutum* 1.0 mg l^{-1} affected reproduction (6).

Environmental fate

Nitrification inhibition

In soil 40.0 ppm did not inhibit nitrification (7).

Degradation studies

In soils 75-100% disappeared in 10 months (8).

Abiotic removal

Acetone solutions of monuron injected into water samples and exposed to natural and artificial light at room temperature. 40, 30, 20 and 0% remained after 1, 2, 4 and 8 wk, respectively (9).

160 mg l^{-1} activated carbon will reduce 5 mg l^{-1} to 0.1 mg l^{-1}; 29 mg l^{-1} activated carbon will reduce 1 mg l^{-1} to 0.1 mg l^{-1} (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1053-3700 mg kg^{-1} (11,12).

LD_{Lo} oral guinea pig 670 mg kg^{-1} (13).

LD_{50} intraperitoneal mouse 1000 mg kg^{-1} (14).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (15).

Oral (2 yr) rat 25 mg kg^{-1} day^{-1} no toxic effects, 250 mg kg^{-1} day^{-1} caused slight toxic effects (16).

National Toxicology Program tested rats and mice via feed (maximum dose rats 1500 ppm, mice 10,000 ppm) no evidence for carcinogenicity in ♂, ♀ mice and ♀ rats. Positive evidence for carcinogenicity in ♂ mice: tumours found were kidney tubular cell adenocarcinoma (1/50), kidney tubular cell adenoma (2/50) and liver neoplastic nodules/carcinoma (6/49) (17).

Oral (78 wk) ♂, ♀ mice (strains (C57BL/6XC3H/Anf) F_1, (C57BL/6XAKR) F_1) 215 mg kg^{-1} body weight in 0.5% gelatin via gavage at 7 days of age daily for up to 4 wk and then 517 mg kg^{-1} in diet for the rest of the experimental period. A significant tumour incidence was seen for lung adenomas in ♂ of the 2nd strain only (18,19).

Gavage (13 month) random bred and C57BL mice 6 mg $animal^{-1}$. 13/23 random bred mice developed tumours and 7/25 C57BL mice developed tumours compared with the controls of 0 and 1, respectively. Tumour sites included: stomach, lung, and kidney in mice and intestine, liver, lung and kidney in rats. Survival of the controls was unspecified (20).

Metabolism and toxicokinetics

Oral rat 875 mg kg^{-1} peak blood concentration 2 hr after administration. Distribution was even throughout the body. Monuron-related products were secreted in milk of lactating animals and excreted in urine. Oral rat 175 mg kg^{-1} day^{-1} for 60 days or 0.1-0.2 mg kg^{-1} day^{-1} for 6 months showed tissue retention of monuron-related substances of lungs >heart >liver, brain, kidneys >milk, bone marrow, thyroid gland (21).

In mammals metabolised by oxidative *N*-demethylation, hydroxylation of the aromatic nucleus and fission of the urea residue to give chloroaniline derivatives. The principal urinary metabolites were: *N*-(4-chlorophenyl)urea, *N*-(2-hydroxy-4-chlorophenyl)-*N'*-methylurea, *N*-(2-hydroxy-4-chlorophenyl)urea and *N*-(3-hydroxy-4-chlorophenyl)urea, accounting for 14.5, 1.5, 6.5 and 2.2% of the initial dose, respectively (22,23).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (24).

In vitro Chinese hamster ovary cells with and without metabolic activation, sister chromatid exchanges positive; chromosomal aberrations negative without metabolic activation and positive with metabolic activation (25).

Legislation

As of July 1973 no longer registered for use on agricultural crops in the US (26).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (27).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (28).

Other comments

Hazards reviewed (29).

Accumulation of pesticides and their association with fish fertility disorders reviewed (30).

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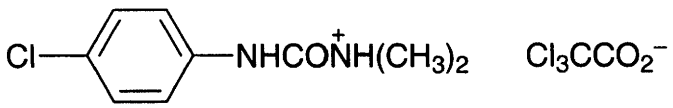
M351 monuron-TCA



$C_{11}H_{12}Cl_4N_2O_3$ **Mol. Wt.** 362.04 **CAS Registry No.** 140-41-0

Synonyms trichloroacetic acid, compound with *N'*-(4-chlorophenyl)-*N,N*-dimethylurea (1:1); GC 2996; Urox; Urox 379

RTECS No. AJ 8050000

Uses Superseded herbicide. Inhibitor of photosynthesis.

Physical properties

M. Pt. 78-81°C

Occupational exposure

Supply classification harmful
Risk phrases Irritating to eyes and skin – Possible risk of irreversible effects (R36/38, R40)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2300 mg kg^{-1} (1).
LD_{50} subcutaneous rabbit 1000 mg kg^{-1} (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).

Other comments

It is toxic to beans for 5 or 12 months, respectively, after application in March at 20 or 50 kg ha^{-1}, and for 12 months (at both application levels), when applied in July (5).

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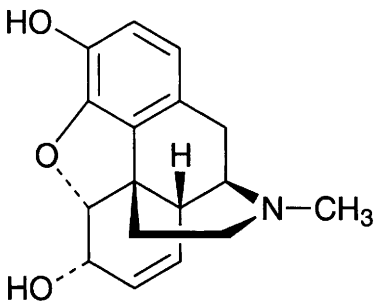
M352 morphine



$C_{17}H_{19}NO_3$ **Mol. Wt.** 285.34 **CAS Registry No.** 57-27-2

Synonyms (5α,6α)-7,8-didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol; Duromorph; Morphia; (–)-morphine; Morphium; Ospalivina

EINECS No. 200-320-2 **RTECS No.** QC 7875000

Uses Narcotic analgesic.
Occurrence Principal alkaloid of opium.

Physical properties

M. Pt. 197°C metastable phase; 254°C (decomp.) **B. Pt.** sublimes at 190-200°C at 0.2 mmHg
Solubility Water: 1 g in about 5000 ml. Organic solvents: chloroform, cresols, ethanol, phenol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 335, 524 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous mouse 220 mg kg^{-1} (3).
LD_{50} intravenous rat 140 mg kg^{-1} (4).
LD_{50} intraperitoneal rat, mouse 160, 140 mg kg^{-1}, respectively (5,6).

Teratogenicity and reproductive effects
Oral rat 10, 35 or 70 mg kg^{-1} day^{-1}. The pregnancy rate was reduced at the intermediate and high doses to 57 and 6%, respectively. No teratogenic effects were observed at any dosage, but growth retardation was present at the intermediate dose (7).
Infusion lambs (10 day) 3 mg hr^{-1} did not affect foetal survival or the response of foetal breathing movements to hypercapnia. Respiratory effects were observed which may be related to accumulation of morphine-3-β-D-glucuronide. Higher doses 10 and 30 mg hr^{-1} caused seizures and decreased foetal survival (8).

Metabolism and toxicokinetics
Morphine salts are well absorbed from the gastro-intestinal tract in humans but have poor oral bioavailability since they undergo first-pass metabolism in the liver and gut. It is conjugated with glucuronic acid in the liver and gut to produce morphine-3-glucuronide which is inactive, whereas the active metabolite is morphine-6-glucuronide. Other active metabolites are normorphine, codeine and morphine ethereal sulfate. It is distributed throughout the body but mainly in the kidneys, liver, lungs and spleen with lower concentrations in the brain and muscles. Mean plasma elimination $t_{1/2}$ 1.7 hr. Up to 10% of a dose may eventually be excreted, as conjugates, through the bile into the faeces. The remainder is excreted in the urine mainly as conjugates. ~90% is excreted in 24 hr with traces in urine ≥48 hr (9).
It was well absorbed from rat gastro-intestinal tract in the order jejunum>duodenum>ileum>middle intestine>rectum, but it was poorly adsorbed from the stomach (10).
Microsomal cytochrome P_{450} linked metabolism plays a minor role in the hepatic toxicity of morphine in rats, whilst mophine-6-dehydrogenase plays a major part in this toxicity (11).

Other effects

Other adverse effects (human)
Nausea, vomiting, constipation, drowsiness and confusion occurs with normal doses. Tolerance generally develops with long-term use. Larger doses produce respiratory depression and hypotension with circulatory failure and deepening coma. Pulmonary oedema after overdosage is a common cause of fatalities among opiate addicts. Rhabdomyolysis progressing to renal failure has been reported in overdosage (9).
A report of severe rectovaginal spasm following intrathecal administration. The spasms were successfully controlled with midazolan (12).
Adult human hepatocytes incubated with morphine. Cytotoxic effects were observed at ~100 times the plasma concentration required to produce analgesia. 285 mg l^{-1} reduced the glycogen content by 50% and 228 mg l^{-1} inhibited albumen synthesis by ~50% after 24 hr of pretreatment. Intracellular glutathione was reduced by 50% after 2-3 hr of incubation with 570 mg l^{-1}, opiate doses during tolerance or abuse may be a cause of liver dysfunction (13).

Any other adverse effects

0.002-1.0 mg injected into the cerebral ventricles of unanaesthetised cats evoked vomiting, lasting for 1-7 minutes. Number of vomitings induced ranged from 2-5 (14).

Intraperitoneal 5-, 10- and 20-day old rats 10 mg kg^{-1}, overt sedation in all three age groups and induced catalepsy which was particularly apparent in the 5- and 10-day-old animals (15).

It has no direct peripheral effects on heart rate or blood vessel tone, nor has it any effect on norepinephrine and epinephrine release from the sympathetic nerves and the adrenal medulla in the rat (16).

Subcutaneous mice 20 mg kg^{-1} showed renal elimination of phenol red in mice, tolerance was more readily induced to the effects of narcotics on venal blood flow and tubular function than the reduction of glomerular function (17).

♂/♀ deer mice 10 mg kg^{-1} produced maximum analgesic responses in adults. There are significant sex and population differences in opiate-induced analgesia in young and adult deer mice (18).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (19).

Restricted drug (9).

Other comments

In acute oral poisoning the stomach should be emptied. A laxative may be given to aid peristalsis (20).

Metabolism reviewed (21).

Abuse leads to habituation or addiction (9).

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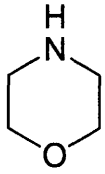
M353 morpholine



C_4H_9NO **Mol. Wt.** 87.12 **CAS Registry No.** 110-91-8

Synonyms diethylene imidoxide; diethylene oximide; tetrahydro-*p*-oxazine; tetrahydro-1,4-oxazine; Drewamine

EINECS No. 203-815-1 **RTECS No.** QD 6475000

Uses Rubber accelerator. Solvent. Organic synthesis. Additive to boiler water. Waxes and polishes. Corrosion inhibitor. Optical brightener for detergents.

Physical properties

M. Pt. –7 to –5°C **B. Pt.** 128.9°C **Flash point** 35°C (open cup) **Specific gravity** 1.007 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –1.08 (1) **Volatility** v.p. 10 mmHg at 23°C ; v.den. 3.00
Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol, 2-hexanone

Occupational exposure

DE-MAK 10 ppm (36 mg m^{-3})
FR-VME 20 ppm (70 mg m^{-3}) **FR-VLE** 30 ppm (105 mg m^{-3})
SE-LEVL 20 ppm (70 mg m^{-3}) **SE-STEL** 30 ppm (110 mg m^{-3})
UK-LTEL 20 ppm (72 mg m^{-3}) **UK-STEL** 30 ppm (109 mg m^{-3})
US-TWA 20 ppm (71 mg m^{-3})

UN No. 2054 **HAZCHEM Code** 2W **Conveyance classification** flammable liquid
Supply classification corrosive
Risk phrases Flammable – Harmful by inhalation, in contact with skin and if swallowed – Causes burns (R10, R20/21/22, 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} (96 hr) bluegill sunfish, static bioassay in fresh water at 23°C, 350 ppm (2).
LC_{50} (96 hr) bluegill sunfish, static bioassay in synthetic seawater at 23°C, 400 ppm (2).

Invertebrate toxicity
EC_{50} (5, 15 or 30 min) *Photobacterium phosphoreum* concentration 60, 51 or 57 mg l^{-1}, respectively, Microtox test (3).
Cell multiplication inhibition test *Pseudomonas putida* 310 mg l^{-1}, *Microcystis aeruginosa* 1.7 mg l^{-1}, *Entosiphon sulcatum* 12 mg l^{-1} (4,5).
LC_{50} (24 hr) *Daphnia magna* 119 mg l^{-1} (6).

Environmental fate

Degradation studies
BOD_5: 0.9% ThOD (7).
BOD_{15}: 4.0% ThOD (7).
BOD_{20}: 5.1% ThOD (8).

No biodegradation of morpholine 10, 50 and 100 mg l^{-1} was observed after 14 days incubation at 20°C in media inoculated with river mud (9).
Mycobacterium MorG, enzymes for ethanolamine, glycolate and pyrrolidine catabolism were strongly induced. Catabolised initially by an analogous route to pyrrolidine, producing 2-(2-aminoethoxy)acetate which can be oxidatively cleaved to give rise directly to glycolate and indirectly to ethanolamine (10).

Abiotic removal
Computer estimated $t_{1/2}$ (4 hr) for the reaction of morpholine with hydroxyl radicals in the atmosphere (11).

Adsorption and retention
The estimated soil sorption coefficient is 8. This indicates that morpholine will not adsorb strongly to soil (12).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♀ rat 1.05 g kg^{-1} (13).
LD_{50} oral guinea pig 0.9 g kg^{-1} (14).
LC_{50} (1 hr) inhalation rat 22.2 mg l^{-1} (15).
Inhalation lethality (8 hr) rats >8000 ppm (16).
LD_{50} dermal rabbit 0.5 ml kg^{-1} (15).

Sub-acute and sub-chronic data
Oral (4 wk) ♂ rats 323 mg kg^{-1} day^{-1} indicated an increase in weight of adrenal glands and a lower mean body weight gain. Lower concentrations 27.6 and 93.1 mg kg^{-1} day^{-1} had no apparent effects. Histopathology was not mentioned, but no gross lesions were found (17).
Dermal (30 day) guinea pigs 0.9, 0.18 or 0.27 g kg^{-1} no lesions were observed, the skin was thickened at the application site (18).

Carcinogenicity and chronic effects
In the stomach the reaction of morpholine with sodium nitrite produces *N*-nitrosomorpholine, which is a known carcinogen causing stomach, liver and lung tumours (19-21).

Metabolism and toxicokinetics
It is not readily metabolised in rat, dog and rabbit (22-27).
It is metabolised extensively in guinea pigs via *N*-methylation and *N*-oxidation (24).
87% of an administered dose was excreted in the urine of rats within 24 hr (23).
Intraperitoneal rat, hamster and guinea pig 125 mg kg^{-1} blood plasma $t_{1/2}$ 115, 120 and 30 min, respectively. In all three species ~80% was excreted in urine within 24 hr (24).

Irritancy
In rabbit eyes, it has caused corneal conjuctivitis, clouding and general conjunctivitis (dose and duration unspecified) (28).
A 40% solution instilled into rabbit eyes caused severe corneal necrosis (duration unspecified), undiluted morpholine caused necrosis within 24 hr (29).
In humans it is a skin, eye and mucous membrane irritant and a skin sensitiser (30).

Sensitisation
10% did not cause sensitisation in guinea pigs (31-33).

Genotoxicity

Salmonella typhimurium (activation and strain unspecified), negative (34).
Salmonella typhimurium TA98, TA100 and TA1530 with or without metabolic activation negative (35).
No increase in the number of chromosomal aberrations in the blood cells of workers exposed to 0.54-0.93 or 0.74-2.14 mg m^{-3} (36).

Other effects

Any other adverse effects

Inhalation rabbit 250 ppm induced enzyme changes in pulmonary lavage fluids that may be related to pulmonary damage (37).

Inhalation rabbit 250 ppm for 33 exposures, maximum induction of α-mannosidase and acid phosphatase activities in ♀ rabbit was 1.7-fold and 2-fold, respectively, and in ♂ rabbit, 3-fold and unchanged, respectively (38).

In rats, high concentrations of vapours have caused death due to lung congestion, with degeneration, fatty changes and cellular necrosis of the liver and kidneys (39).

Sub-chronic inhalation studies on rats at 25, 100 and 250 ppm for 6 hr day^{-1} 5 day wk^{-1} for 13 wk indicated salivation and nasal damage at the two higher concentrations, although no haematological or organ weight changes were noted (40).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (41).

Other comments

Morpholine concentration in cigarette smoke condensate was 0.08 μg cigarette (42).

Reviews on human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels, epidemiology and workplace exposure listed (43).

Autoignition temperature 310°C.

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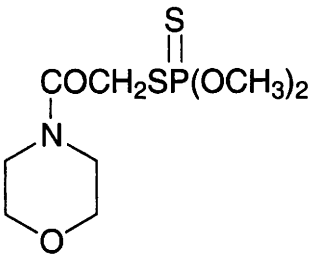
M354 morphothion



$C_8H_{16}NO_4PS_2$ **Mol. Wt.** 285.33 **CAS Registry No.** 144-41-2

Synonyms phosphorodithoic acid, *O,O*-dimethyl *S*-[2-(4-morpholinyl)-2-oxoethyl] ester; *O,O*-dimethyl *S*-(morpholino-carbonylmethyl) phosphorodithioate; *O,O*-dimethyl *S*-[2-(4-morpholinyl)-2-oxoethyl] phosphorodithioate; phosphorodithioic acid, *O,O*-dimethyl ester, *S*-ester with 4-(mercaptoacetyl)morpholine; Ekatin F; Ekatin M; Morphotox

EINECS No. 205-628-0 **RTECS No.** TE 1400000

Uses Superseded pesticide.

Physical properties

M. Pt. 65°C

Solubility Organic solvents: acetone, acetonitrile, 1,4-dioxane

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) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S13, S45, S60, S61)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat, rabbit 130-190 mg kg^{-1} (1,2).

LD_{50} dermal rat 283 mg kg^{-1} (3).

Legislation

Included in Schedule 4 (Release Into Air: 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).

Other comments

Environmental aspects reviewed (6).

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M355 MSMA

$$CH_3As(=O)(OH)ONa$$

CH_4AsO_3Na **Mol. Wt.** 161.95 **CAS Registry No.** 2163-80-6

Synonyms monosodium acid methanearsonate; sodium hydrogen methylarsonate; Ansar 170; Daconate; Gepiron

EINECS No. 218-495-9 **RTECS No.** PA 2625000

Uses Herbicide.

Physical properties

M. Pt. 113-116°C (sesquihydrate);132- 139°C(hexahydrate) **Specific gravity** 1.535 at 25°C **Partition coefficient** log P_{ow} <0

Solubility Water: 1.4 kg kg^{-1} at 20°C (anhydrous salt). Organic solvents: methanol

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) bluegill sunfish >1000 mg l^{-1} (1).

Invertebrate toxicity

Mixed culture of *Citrobacter freundii, Aeromonas* sp. and *Klebsiella* sp. isolated from soil LC_{50} (96 hr) 220 mg l^{-1}, LC_{50} (48 hr) 60 mg l^{-1} and LC_{50} (24 hr) 27 mg l^{-1} (2).

LC_{50} juvenile cray fish and adult crayfish 101 and 1019 ppm, respectively (3).

LD_{50} 68μg bee^{-1}; NOEL 36μg bee^{-1} (4).

Environmental fate

Degradation studies

Degradation via oxidative demethylation by microbial population. Degradation rate is reduced at high clay contents, high adsorptive capacity for monosodium methanearsonate, and at low clay content, lower microbial population. 30°C at 20 and 150% field capacity the $t_{1/2}$ ranged from 88-178 and 25-178 days, respectively (5).

Adsorption and retention

It is adsorbed by clay soils (6).

It is fixed by iron and aluminium in the soil (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 700 mg kg^{-1} (7).

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

LD_{50} oral rabbit 102 mg kg^{-1} caused constipation, diarrhoea, oligourea, generalised weakness and the loss of appetite (9).

LD_{50} (route unspecified) snowshoe hare 173 mg kg^{-1} (10).

Metabolism and toxicokinetics

Oral rabbit (12 wk) 54% was eliminated in urine 46% in faeces (10).

Dermal ♀ rat young and adult (dose unspecified) significantly reduced skin penetration in young animals; parallel dose-absorption curves in young and adult rats indicated a lack of significant dose effect (11).

Irritancy

Dermal rabbit 54 mg, uncovered, caused mild irritation. Instilled into the eye of a rabbit 34 mg caused mild irritation (12).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 and TA1535 with or without metabolic activation, negative (13).

Allium cepa root meristems (1 hr), a marked clastogenic effect (14).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Maximum admissible concentration 50 μg As l^{-1} (16).

EPA Toxicity Class III (formulation) (4).

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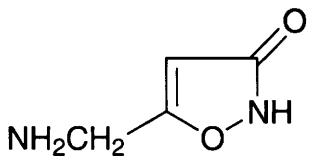
M356 muscimol



$C_4H_6N_2O_2$ **Mol. Wt.** 114.10 **CAS Registry No.** 2763-96-4

Synonyms 5-(aminomethyl)-3(2*H*)-isoxazolone; Agarin; Agarine; Pantherine

EINECS No. 220-430-4 **RTECS No.** NY 3325000

Uses Molecular probe to study γ-aminobutyric acid receptors. Sedative. Antiemetic.

Occurrence Hallucinogenic agent found in poisonous mushrooms.

Physical properties

M. Pt. 175°C (decomp.)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 17, 45 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous mouse 3800 μg kg^{-1} (1).
LD_{50} intravenous rat 4500 μg kg^{-1} (1).
LD_{50} intravenous mouse 5620 μg kg^{-1} (3).
LD_{Lo} intravenous rabbit 10 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 2500 μg kg^{-1} (2).

Teratogenicity and reproductive effects

Muscimol binding by membranes of neocortex synaptosomes from 2-month-old rats exposed in utero (days 5-20 of pregnancy) was 27% higher than in controls. Impaired γ-aminobutyric acid system may be the cause of behavioural teratogenicity of rats with induced alcoholism (4).

Other effects

Other adverse effects (human)

Adverse effects usually occur within 2 hr of ingestion, symptoms include ataxia, euphoria, delirium and hallucinations. Fatalities are rare (5).

Legislation

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

References

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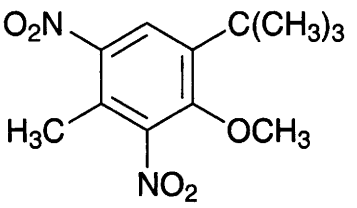
M357 musk ambrette (synthetic)



$C_{12}H_{16}N_2O_5$ **Mol. Wt.** 268.27 **CAS Registry No.** 83-66-9

Synonyms 1-(1,1-dimethylethyl)-2-methoxy-4-methyl-3,5-dinitrobenzene; 6-*tert*-butyl-3-methyl-2,4-dinitroanisole; Amber musk

RTECS No. BZ 8575000

Uses Perfumery.

Occurrence *Moschus moschiferus.*

Physical properties

M. Pt. 84-85°C **B. Pt.** 185°C at 165 mmHg **Volatility** v.p. 5.9×10^{-5} to 7.3×10^{-3} mmHg at 30.3 to 72.3 °C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 339 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (2).

Sensitisation

Guinea pig photoallergy model, 6 exposures over 2 wk period, contact photoallergy was detected (3).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation, positive (4).
Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation, negative (5).
Induced a significant number of micronuclei in polychromatic erythrocytes of mouse bone marrow, and also induced chromosomal aberrations (4).

Other effects

Other adverse effects (human)

Causes photoallergic reactions in humans (6).

Any other adverse effects
Neurotoxic and causes testicular atrophy in rats (7).

Legislation

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

Other comments

Toxicity reviewed (9).

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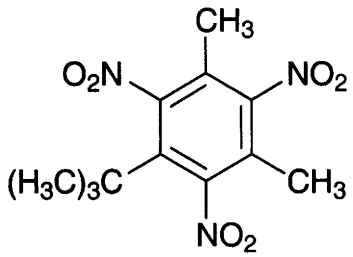
M358 musk xylene



$C_{12}H_{15}N_3O_6$ **Mol. Wt.** 297.27 **CAS Registry No.** 81-15-2

Synonyms 5-*tert*-butyl-2,4,6-trinitro-*m*-xylene; 1-(1,1-dimethylethyl)-3,5-dimethyl-2,4,6-trinitro-benzene; 1-*tert*-butyl-3,5-dimethyl-2,4,6-trinitrobenzene; 2,4,6-trinitro-1,3-dimethyl-5-*tert*-butyl-benzene; musk xylol

EINECS No. 201-329-4 **RTECS No.** CZ 7210000

Uses Ingredient in hand lotions, soaps and perfume.

Occupational exposure

UN No. 2956 **Conveyance classification** flammable solid

Ecotoxicity

Fish toxicity
Rainbow trout exposed to 1000 mg l^{-1} for 96 hr showed no mortality or clinical symptoms (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >10 g kg^{-1} (2).
LD_{50} dermal rabbit >15 g kg^{-1} (2).

Sub-acute and sub-chronic data

Dermal rat (90 day) 240 mg kg day^{-1} caused some organ weight changes but no associated histopathological changes in any tissue. No-effect level was ♂ 75 mg kg^{-1} and ♀ 24 mg kg^{-1} (3).
Oral B6C3F1 mouse (17 weeks) both sexes 0-0.6% in diet enlargement and irregularity of hepatocytes at 0.15% (4).

Metabolism and toxicokinetics

After oral administration to Wistar rats 76% of dose was eliminated in faeces and 10% in urine within 7 days (5).
Oral Long Evans rats fed 0.001-0.1 g kg^{-1} food pellets for 10 wk before mating and during pregnancy and lactation. Dose-dependent accumulation in offspring was at levels 1/2-3/4 of adult ♀ or 3-4 × adult ♂ body fat levels (at 0.1 mg kg^{-1} food) at days 1 and 14. Milk levels were comparable with adult ♀ adipose tissue. Rats fed musk xylene in adulthood accumulated highest levels in adipose tissue with significant amounts in other organs. Tissue levels in adult ♀s were 3.7-6.8 × higher than in adult ♂s (6).

Irritancy

Dermal human (48 hr) 5 mg caused mild irritation (7).

Sensitisation

A study using the Colworth guinea pig photoallergy test suggests that Musk xylene could cause a weak photoallergic reaction in humans (8).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation negative (9).
SOS chromotest with and without metabolic activation negative (9).
Chinese hamster ovary cells assay, mouse lymphoma assay, *in vitro* unscheduled DNA synthesis in primary rat hepatocytes assay and *in vivo* unscheduled DNA synthesis assay, all negative (10).

Other effects

Any other adverse effects

Musk xylene causes an increase in total hepatic cytochrome P450 in the rat, with CYPIA1 and IA2 proteins being specifically elevated (11).

Other comments

The lack of genotoxicity of musk exylene suggests that it induces mouse liver tumours by another mechanism (10).
Environmental data on musk ketone and musk xylene reviewed. The data form the basis for an initial environmental risk assessment for these compounds (12).

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M359 mustard gas

$$S(CH_2CH_2Cl)_2$$

$C_4H_8Cl_2S$ **Mol. Wt.** 159.08 **CAS Registry No.** 505-60-2

Synonyms 1,1'-thiobis[2-chloroethane]; bis(β-chloroethyl) sulfide; kampstaff Lost; senfgas; sulfur mustard; yperite

RTECS No. WQ 0900000

Uses In chemical warfare.

Physical properties

M. Pt. 13-14°C **B. Pt.** 215-217°C **Flash point** 105°C **Specific gravity** 1.2741 at 20°C with respect to water at 4°C **Volatility** v.p. 9.0×10^{-2} mmHg at 30°C ; v.den. 5.4

Solubility Water: 0.68 g l^{-1} at 25°C. Organic solvents: soluble in fat solvents and common organic solvents

Mammalian & avian toxicity

Acute data

LC_{50} (10 min) inhalation rat, mouse 100, 120 mg m^{-3}, respectively (1).

LC_{50} (10 min) inhalation dog, monkey 70, 80 mg m^{-3}, respectively (1).

LC_{Lo} (10 min) inhalation human 1500 mg m^{-3} (2).

LD_{Lo} dermal human 64 mg kg^{-1} (3).

LD_{50} dermal rat 5 mg kg^{-1} (4).

LD_{50} dermal rabbit 40 mg kg^{-1} (1).

Time-related histopathological responses were observed when 50 µl was applied to clipped rabbit skin. The extracellular matrix (ECM) underwent significant structural changes with the induction of oedema, infiltration of polymorphonuclear cells and cell destruction. Injury appeared to be most severe on day-3 after application when the thickness of the skin registered the maximum change. Recovery was observed on day-6 and continued thereafter (5).

LD_{50} subcutaneous rat 1500 µg kg^{-1} (4).

LD_{50} subcutaneous mouse 20 mg kg^{-1} (1).

LD_{50} intravenous dog 200 µg kg^{-1} (1).

Sub-acute and sub-chronic data

LC_{50} (14 days) inhalation mouse 42.5 mg m^{-3}. RD_{50} inhalation mouse (the concentration that depresses respiration 50%) 27.4 mg^{-3} (6).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 1 (7).

The estimated potency factor for mustard gas is 1.3 relative to benzo[a]pyrene (8).

Inhalation 80 ♂/♀ mice 12.5 cm^3 l^{-1} for 15 min. After 11 months all animals were killed, 33 of mice had lung tumours. Number of tumours $mouse^{-1}$ was 0.66 (9).

Subcutaneous 40 mice 0.05 ml wk^{-1} for 5.6 wk. At natural death 4 fibrosarcomas were found at site of injection. Mammary tumours were found in 10 animals (10).

Intravenous 30 ♂/♀ mice 4 injections of 0.25 ml. All survivors killed at the age of 6 month, 14/15 mice had pulmonary tumours (11).

3354 humans who had worked in manufacture of mustard gas were traced for mortality to the end of 1984. Large and highly significant excesses were observed as compared with national death rates for deaths from cancer of the larynx, pharynx and all other buccal cavityand upper respiratory sites combined. For lung cancer, a highly significant but more moderate excess was observed (12).

Teratogenicity and reproductive effects

Intragastric intubation rats and rabbits. Rats were dosed 6-15 days of gestation with 0, 0.5, 1.0 or 2.0 mg kg^{-1}, rabbits were dosed 6-19 days of gestation with 0, 0.4, 0.6 or 0.8 mg kg^{-1}. At necropsy in rats, reduction in body weight was observed in maternal animals and their ♀ foetuses at the lowest dose, incidence of foetal malformations were not increased. In rabbits the highest dose induced maternal mortality and depressed body weight measures, but did not affect foetal developments. It is not teratogenic in rats and rabbits since foetal effects were observed at maternally toxic doses only (13).

Oral ♂/♀ rat 0.5 mg kg^{-1}, then mating between treated and untreated rats. An increase in early foetal resorptions and preimplantation losses and decrease of total live embryo implants; a significant increase in the percentage of abnormal sperm was detected in ♂ exposed to 0.5 mg kg^{-1} (14).

Metabolism and toxicokinetics

Intravenous rabbit 5 mg kg^{-1} body weight of ^{35}S-labelled mustard gas, it was rapidly diffused throughout the body, 20% radioactivity was excreted in the urine within 12 hr and excretion via the bile was noted. Main organs of retention were the liver, lungs and kidneys (15).

The main urinary metabolites were thiodiglycol and conjugates (15%), glutathione-bis-(β-chloroethyl)sulfide conjugates (45%), glutathione-bis-(β-chloroethyl) sulfone conjugates (7%) and bis-β-chloroethylsulfone and conjugates (8%) (16).

Mustard gas reacts *in vivo* with proteins and nucleic acids of the lung, liver and kidneys of A/J mice (17).

The perfusion of lungs isolated from dogs showed that equilibrium between the blood and tissues was reached after 5 min and that 14% of the radioactivity was retained in the lung (18).

Irritancy

10 µl of a 0.01 to 1.00% dilution was applied to an epidermis explant for 18 hr at 36°C, causing increased amounts of histamine, plasminogen-activating activity and prostaglandin E_2 (19).

Dermal (1 hr) pigs, high dose. After 72 hr the pigs exhibited microvesicle formations of varying intensities (20).

Genotoxicity

Salmonella typhimurium uvrB+G46, (metabolic activation unspecified) positive (20).

In vitro mouse bone marrow induced micronuclei (21).

At low concentrations inhibited DNA synthesis in *Escherichia coli*, in L-cells and in HeLa and Chinese hamster cells (22-26).

It was the first chemical reported to induce mutation and chromosome rearrangement in *Drosophila melanogaster* (27).

Induced chromosomal aberrations in cultured rat lymphosarcoma cell lines (28).

Dominant lethal mutations in adult ♂ virgin rat were induced after exposure to 0.1 mg m^{-3} for 52 wk (29).

Of 1700 mustard gas factory workers examined, variants were detected in 85 and 6 cases by electrophoresis and enzyme activity measurement, respectively. All of the 66 cases in which parents could also be examined were genetic variants. In 62,747 equivalent locus tests made by electrophoresis, the mutation rate was $0\text{-}4.77 \times 10^{-5}$ $locus^{-1}generation^{-1}$, showing no significant difference from the spontaneous mutation rate (30).

Other effects

Other adverse effects (human)

Causes conjunctivitis, blindness within 12 hr, cough, oedema of eyelids, erythema of skin, severe pruritus. May cause oedema, ulceration, necrosis of respiratory tract and exposed skin. Ingestion may cause nausea and vomiting (31).

Eleven cases of exposure in fishermen who retrieved leaking gas shells from underwater dumps are reported. All 11 had very inflamed skin, in the axillary and genitofemoral regions, yellow blisters on the hands and legs, painful irritation of the eyes and transient blindness. Two developed pulmonary oedema. There was evidence of a mutagenic effect and in view of the increased risk of lung cancer in soldiers and workers exposed to the gas, it can be assumed that the fishermen heavily exposed also had an increased cancer risk (32).

Most patients exposed to mustard gas recover completely and only a small proportion will have long term eye and lung damage (33), although death from respiratory, renal and bone-marrow failure may occur (34).

Any other adverse effects

Mustard gas applied topically to guinea pigs was hepatotoxic, causing severe steatosis and biochemical changes. Significant increase in the levels of glutamic oxaloacetic and transaminase and glutamic pyruvate transaminase occurred after exposure. Liver damage appeared to be at a maximum on day-3 after exposure and recovery had begun by day-6 (35).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (36).

Other comments

Mustard gas inhibited the carcinogenic action of coal tar on mouse skin (37).
Pharmacokinetics and toxicology reviewed (38,39).

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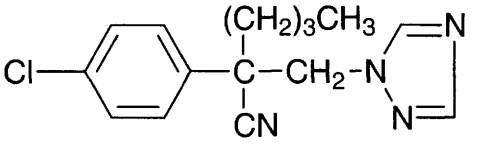
M360 myclobutanil



$C_{15}H_{17}ClN_4$ **Mol. Wt.** 288.78 **CAS Registry No.** 88671-89-0

Synonyms α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile; Nova; Nu-Flow M; Rally; Systhane 6Flo

RTECS No. XZ 5257000

Uses Fungicide.

Physical properties

M. Pt. 63-68°C **B. Pt.** 202-208°C at 1.0 mmHg **Partition coefficient** log P_{ow} 2.94 at pH 7-8 and 25°C
Volatility v.p. 1.6×10^{-6} mmHg at 25°C
Solubility Water: 142 mg l^{-1} at 25°C. Organic solvents: alcohols, aromatic hydrocarbons, esters, ketones

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 2.4 mg l^{-1}, LC_{50} rainbow trout 4.2 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* sp. 11 mg l^{-1} (1).

Environmental fate

Degradation studies
No degradation under anaerobic conditions (1).
In soil, decomposition is through highly polar triazole compounds with further degradation by ring splitting (2).

Abiotic removal
Aqueous solutions degraded on exposure to light, $t_{1/2}$ 222 days in sterile water; 0.8 days in sensitised sterile water; 25 days in pond water; soil $t_{1/2}$ 66 days in silt loam (1).

Mammalian & avian toxicity

Acute data
LD_{50} bobwhite quail 510 mg kg^{-1} (1).
LD_{50} grey partridge 1635 mg kg^{-1} (1).
LD_{50} oral ♂ rats 1600 mg kg^{-1} for ♀ rats 2290 mg kg^{-1} (1).
LD_{50} oral mouse 1.36->4.42 g kg^{-1} (3).
LD_{50} oral rat 1.6-2.7 g kg^{-1} (3).
LD_{50} dermal rabbit >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
Oral (90 day) rats, dog no effect at 100 mg kg^{-1} diet (1).
Oral (13 wk) rat 0, 6.2, 18.8 or 192 mg kg^{-1} body weight day^{-1} in ♂ and 0, 6.9, 19.6 or 225 mg kg^{-1} body weight day^{-1} in ♀. Histomorphological changes in the liver, kidney and adrenal glands were observed (3).
Oral (12 month) 12 ♂ beagle dogs 0, 0.3, 3.1, 14.3 or 54.2 mg kg^{-1} body weight day^{-1}, ♀ beagle dogs 0, 0.4, 3.8, 15.7 or 58.2 mg kg^{-1} body weight day^{-1}, respectively. There was increased hepatocellular hypertrophy, increased liver weights and increased serum alkaline phosphatase levels in the liver (3).

Carcinogenicity and chronic effects

Oral mice (2 yr) up to 500 ppm, no oncogenic activity noted (3).
Oral rats (1 yr) 800 ppm, no evidence of carcinogenic activity (3).

Teratogenicity and reproductive effects

Oral 25 CRI:CD(5D)BR rats up to 1000 ppm, it decreased number of ♀ delivering litters, increased number of stillborn pups. In the F_1 ♂ diffuse atrophy of the testes, decreased spermatozoa and/or necrotic spermatocytes of the epididymis and atrophy of the prostate were observed (3).
Oral ♀ rats 464 or 700 mg kg^{-1} resulted in mortality (25 and 100%, respectively), decreased body weights, scant faeces, chromodactyorrheoa, red exudate around mouth, rough and urine stained hair coat and salivation (3).

Metabolism and toxicokinetics

Oral gavage ♂/♀ CH:CD1 mouse 2, 20 or 200 mg ^{14}C-myclobutanil kg^{-1} body weight. After 96 hr ~81% excreted in urine and faeces. Comparable amounts were found in urine (41-57%) and faeces (31-52%). Elimination was biphasic with $t_{1/2}$ of 0.6 and 6 to 30.1 hr, respectively (3).
Oral Sprague-Dawley ♂/♀ rats 150 mg ^{14}C-compound kg^{-1} body weight. Eliminated via urine (48% ♂, 37% ♀) and faeces (51% ♂, 63% ♀) (3).
In mice it is extensively metabolised to more polar compounds. The major polar metabolites in rats are the lactone, ketone, alcohol, carboxylate, dialcohol and sulfate conjugates (3).

Irritancy

Eye rabbit (dose, duration unspecified) 91.9% purity caused corneal and conjunctival effects suggestive of moderate to severe irritating potential. Dermal (4 hr) rabbit 0.5 ml was practically non-irritating (3).

Genotoxicity

Bacillus subtilis DNA repair test, negative (3).
Salmonella typhimurium TA98, TA100, TA1535 and TA1537 with or without metabolic activation, negative (3).
In vitro rat hepatocytes, did not induce unscheduled DNA synthesis (3).
In vitro Chinese hamster ovary cells with or without metabolic activation negative (3).

Other effects

Any other adverse effects

Mixed function oxidase activity, of liver as estimated by *N*-demethylation of benzphetamine was significantly increased in ♂ (2.1-3.3 fold at ≥1000 ppm) and ♀ (1.7-2.2 fold at 3000 ppm). There was no increase in peroxisomal [^{14}C]palmitoyl-CoA oxidase activity indicative of peroxisomal proliferation (3).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class III (5).

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4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

M361 myrcene

$$CH_2=CHC(=CH_2)CH_2CH_2CH=C(CH_3)_2$$

$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 123-35-3

Synonyms 7-methyl-3-methylene-1,6-octadiene; β-myrcene

EINECS No. 204-622-5 **RTECS No.** RG 5365000

Uses Intermediate in the manufacture of perfume chemicals.

Occurrence In oil of bay, verbena, hop and other plants.

Physical properties

M. Pt. 167°C **B. Pt.** 120°C **Flash point** 37°C **Specific gravity** 0.789

Solubility Organic solvents: chloroform, diethyl ether, glacial acetic acid

Ecotoxicity

Invertebrate toxicity

LD_{50} (24 hr) ♀ *Musca domestica* 360 μg insect^{-1} (1).

LD_{50} (24 hr) ♂ *Blattella germanica* >1580 μg insect^{-1} (1).

LC_{50} (24 hr) *Sitophilus oryzae* and *Blattella germanica* >100 ppm (1).

Embryotoxic effect in *Blattella germanica* Ooethecae at 0, 198, 395 and 790 μg mean % of Ooethecae producing offspring 90, 80, 63.3, 46.7%, respectively (1).

Environmental fate

Nitrification inhibition

At 25°C it did not significantly affect nitrification in soil (2).

Inhibits activity of ammonium monooxygenase (3).

Inhibition of net mineralisation at low additions progressing to net immobilisation with high additions, apparent inhibition of nitrification was observed (4).

Degradation studies

Aspergillus niger 45% of original substrate was present on the 1st day to 2% by day-7. Main products after 120 hr were: 2-methyl-6-methylen-7-octene-2,3-diol, 6-methyl-2-vinyl-5-heptene-1,2-diol and 7-methyl-3-methylen-6-octene-1,2-diol (5).

Recovery of 30 μl added to soil was 5.28% after 24 days (4).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

CASE prediction of the carcinogenicity in rodents gave a negative result (6).

Metabolism and toxicokinetics

Oral rats, metabolites found in urine were 10-hydroxylinalool, 7-methyl-3-methylenoct-6-ene-1,2-diol, 1-(hydroxymethyl)-4-isopropenylcyclohexanol, 10-carboxylinalool and 2-hydroxy-7-methyl-3-methylenoct-6-enoic acid. Rat liver microsomes *in vitro* studies conversion into 10-hydroxylinalool in the presence of NADPH and oxygen (7).

Rats (4 day) no significant effect on the hepatic drug-metabolising enzymes (8).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (8).

Genotoxicity

In vitro human lymphocytes with or without metabolic activation, induced neither chromosomal aberrations nor sister chromatid exchanges (9).
In vitro V-79 cells with or without metabolic activation did not cause increased mutation frequencies at the *hprt* locus (9).

Other effects

Any other adverse effects
Naturally occurring terpenoids induce cytochrome P_{450} (species unspecified) (10).

Other comments

Not found in nature (11).

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M362 myristic acid

$$CH_3(CH_2)_{12}CO_2H$$

$C_{14}H_{28}O_2$ **Mol. Wt.** 228.38 **CAS Registry No.** 544-63-8

Synonyms tetradecanoic acid; *n*-tetradecanoic acid; 1-tridecanecarboxylic acid; Univol U 316S; *neo*-fat 14

EINECS No. 208-875-2 **RTECS No.** QH 4375000

Occurrence Occurs in the fats of the Myristicaceae; comprises 20% of the fatty acids in palm seed oil.

Physical properties

M. Pt. 58.5°C **B. Pt.** 250.5°C at 100 mmHg **Flash point** 110°C **Specific gravity** 0.8622 at 54°C with respect to water at 4°C **Partition coefficient** log P_{ow} 6.1
Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol, methanol

Ecotoxicity

Fish toxicity
Lethal dose goldfish 8 mg l^{-1} (1).

Environmental fate

Anaerobic effects

At 5 g COD m^{-3} day^{-1} it inhibited *Methanothrix* sp. bacteria (2).

Degradation studies

BOD_5: 2% ThOD (3).

COD: 30% ThOD (3).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 43 mg kg^{-1} (4).

Irritancy

Dermal human (3 day) 75 mg caused moderate irritation (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 and TA1537 with or without metabolic activation, negative (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 Communities recommended level 3.0 (6th and 7th amendments) (8).

Other comments

It is a non-irritant and is safe in present practice of use and concentration in cosmetics (9).

It is present in most species of marine brown and red algae (10).

After a chemical leak into groundwater in the municipality of Les Franqueses del Valleas, Catalonia, Spain, the levels of myristic acid in well water during a 7-month period ranged from 0.6-19.8 μg l^{-1} (11).

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M363 myristyl aldehyde

$$CH_3(CH_2)_{12}CHO$$

$C_{14}H_{28}O$ **Mol. Wt.** 212.38 **CAS Registry No.** 124-25-4

Synonyms tetradecanal; myristic aldehyde; 1-tetradecyl aldehyde; myristaldehyde

EINECS No. 204-692-7 **RTECS No.** XB 7900000

Occurrence Found in several essential oils.

Physical properties

M. Pt. 30°C **B. Pt.** 166°C **Flash point** 110°C

Solubility Organic solvents: acetone, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >5 g kg^{-1} (1).

LD_{50} dermal rabbit >10 g kg^{-1} (1).

Irritancy

500 mg applied to rabbit skin caused moderate irritation (2).

References

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M364 myristyltrimethylammonium bromide

$$CH_3(CH_2)_{13}N^+(CH_3)_3Br^-$$

$C_{17}H_{38}NBr$ **Mol. Wt.** 336.40 **CAS Registry No.** 1119-97-7

Synonyms *N,N,N*-trimethyl-1-tetradecanaminium bromide; trimethyltetradecyl ammonium bromide; Morpan T; Mytab; Quaternium 13

EINECS No. 214-291-9 **RTECS No.** BS 5776000

Uses Disinfectant. Deodorant. Laboratory reagent. Cationic detergent.

Physical properties

M. Pt. 245-250°C

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse, rat 12, 15 mg kg^{-1}, respectively (1).

Irritancy

Classified as strongly irritant in the Draize eye irritation test in rabbits (2).

Other effects

Any other adverse effects

In vitro V79 Chinese hamster cells LC_{50} with and without metabolic activation 26.29 and 4.08 mg l^{-1}, respectively (2).

Growth inhibition test IC_{50} (50% reduction in cell protein) 4.51 mg l^{-1} (2).

IC_{50} in cultures of rat sublingual mucosa and mouse embryo fibroblasts were 5.7 and 0.46 mg l^{-1}, respectively (3).

Legislation

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

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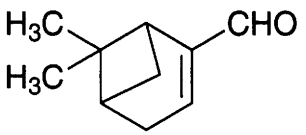
M365 myrtenal



$C_{10}H_{14}O$ **Mol. Wt.** 150.22 **CAS Registry No.** 564-94-3

Synonyms 6,6-dimethyl-bicyclo[3.1.1]hept-2-ene-2-carboxaldehyde; 6,6-dimethyl-2-norpinene-2-carboxaldehyde

EINECS No. 209-274-8 **RTECS No.** DT 5180000

Physical properties

B. Pt. 220-221°C **Flash point** 78°C **Specific gravity** 0.987

Occupational exposure

SE-LEVL 25 ppm (150 mg m^{-3}) **SE-STEL** 50 ppm (300 mg m^{-3})

Environmental fate

Degradation studies

Euglena gracilis Z. reduced unsaturated terpene aldehyde to the corresponding alcohol (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2300 mg kg^{-1} (2).

LD_{50} intravenous mouse 170 mg kg^{-1} (2).

LD_{50} dermal rabbit >5 g kg^{-1} (2).

Legislation

Included in Schedule 4 (Release Into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

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N1 nabam

$$NaS(C{=}S)NHCH_2CH_2NH(C{=}S)SNa$$

$C_4H_6N_2Na_2S_4$ **Mol. Wt.** 256.35 **CAS Registry No.** 142-59-6

Synonyms disodium 1,2-ethanediylbis(carbamodithioic acid); disodium carbamodithioic acid; disodium ethylene-1,2-bisdithiocarbamate; disodium ethylenebis(dithiocarbamate); Dithane D-14

EINECS No. 205-547-0 **RTECS No.** FA 6825000

Uses Fungicide/bactericide/algicide used in aquatic non-food industrial, indoor non-food, terrestrial non-food and indoor food use sites.

Physical properties

M. Pt. decomposes on heating, without melting

Solubility Water: *c.* 200 g l^{-1} at 25°C. Organic solvents: insoluble in common organic solvents

Occupational exposure

UN No. 2771

Supply classification harmful

Risk phrases Harmful if swallowed – Irritating to the respiratory system – May cause sensitisation by skin contact (R22, R37, R43)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container dry – Avoid contact with skin and eyes – If swallowed seek medical advice immediately and show this container or label (S2, S8, S24/25, S46)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) guppy 5.8 mg l^{-1} (1).

Invertebrate toxicity

40 or 100 µg l^{-1} has deleterious effects on survival of developing *Xenopus laevis* embryos. Embryos at high dosage (3 wk) developed severe malformation of the enveloping tissue layers of the notochord with a significant reduction or absence of the collagen fibres of the outer connective tissue cells (2).

Disodium ethylene bis(dithiocarbamate) was not toxic to *Colpidium campylum* at 0.1 mg l^{-1} (3).

LC_{50} *Mercenaria mercenaria* egg (48 hr) <500 ppb, larvae (12 day) 1750 ppb (4).

LC_{50} *Cassostrea virginea* egg (48 hr) <500 ppb (4).

EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 102 mg l^{-1} Microtox test (5).

EC_{50} (48 hr) *Daphnia magna* 0.44 mg l^{-1} (2).

EC_{50} (96 hr) *Chlorella pyrenoidosa* 2.4 mg l^{-1} (2).

Practically non-toxic to bees (6).

Environmental fate

Nitrification inhibition

Maximum inhibitory concentration (3 hr) *Nitrosomonas, Nitrobacter* spp. 32 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 395, 580 mg kg^{-1}, respectively (7,8).

LD_{50} intraperitoneal rat 500 mg kg^{-1} (9).

Sub-acute and sub-chronic data

Intraperitoneal rabbits (30 wk) 330 mg kg^{-1} 6 × wk^{-1} showed degenerate neurons at 18 wk, extensive vacuoles at 24 wk and degenerate nerve fibres at 30 wk (10).

Oral rat (28 day) 0, 50, 100 or 200 mg l^{-1} day^{-1}. Body weight gain decreased but did not significantly affect urinary sodium, potassium was also unchanged. Ethylenethiourea was excreted in urine (11).

Oral rat (28 day) 0-200 mg l^{-1} in drinking water showed no induced morphological alterations in thyroids, but induced ultrastructural changes, namely an increased number of myelin bodies, dilation of the endoplasmic reticulum and increased vacuolisation in the epithelial cells of thyroid follicles (12).

Oral rat (9 day) 500 mg kg^{-1} to weaning rats in diet caused thyroid hyperplasia and weight decrease of the thyroid gland (13).

Oral rat (10 day) 1000-2500 mg kg^{-1} in diet suffered goitrogenic effects (14).

Carcinogenicity and chronic effects

Oral mice (78 wk) 21.5 mg kg^{-1} via gavage from day-7 to weaning, then 73 mg kg^{-1} in diet caused no significant increase in tumours (15).

Teratogenicity and reproductive effects

Subcutaneous mice (6-14 day gestation) 194 mg kg^{-1} day^{-1} caused unspecified teratogenic effects, 418 mg kg^{-1} day^{-1} caused unspecified reproductive effects (16).

Irritancy

19% Solution for unspecified time caused no irritation to rabbits' eyes (17).

Sensitisation

In a study of 25 subjects using patch test with 19% nabam solution, two showed mild erythema and itching, and 13 reacted to the retest with mild to severe erythema and vasiculation, indicating sensitisation (17).

Genotoxicity

No genotoxicity information was available to the study which reported a significant elevation in chromosome damage activity in urine collected during the spraying period of the fruit growing season (18).

Other effects

Other adverse effects (human)

Irritating to skin, mucous membranes and, in high concentration, narcotic (19).

Any other adverse effects

Thiocarbamates are rapidly distributed in the mammalian system and affect a variety of enzymes, phosphatase, phosphotransferase and dopamine β-hydroxylase activity (20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (21).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (22).

WHO Toxicity Class II (23).

EPA Toxicity Class II (formulation) (24).

Other comments

Disodium ethylenebis(dithiodicarbamate) is reviewed as a hazardous material (25).
The environmental effects of dithiocarbamate pesticides including nabam are reviewed (2).

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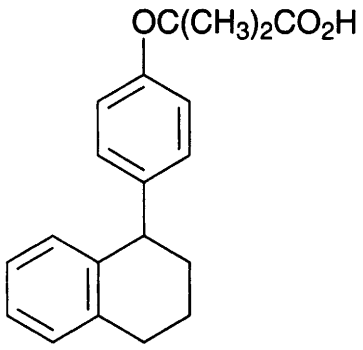
N2 nafenopin



$C_{20}H_{22}O_3$ **Mol. Wt.** 310.39 **CAS Registry No.** 3771-19-5

Synonyms 2-methyl-2-[4-(1,2,3,4-tetrahydro-1-naphthalenyl)phenoxy]propanoic acid; 2-methyl-2-[*p*-(1,2,3,4-tetrahydro-1-naphthyl)phenoxy]-propanoic acid; CH 13-437; CIBA 13437 Su; melipan; Su 13437; TPIA

RTECS No. UF 6125000

Uses Studied for use in treating hypercholesterolaemia or hypertriglyceridaemia at 400-600 mg day^{-1} for 2-6 wk (1).

Physical properties

M. Pt. 127-128°C

Mammalian & avian toxicity

Sub-acute and sub-chronic data

♂, ♀ Rats and mice fed with 0.01-0.25% (w/w) nafenopin showed marked increases in liver weights (2-3).
Rats and beagle dogs orally administered 1-2 mg kg^{-1} day^{-1} for 7 days showed reduced serum cholesterol and triglyceride levels (4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (5).
All ♂ and ♀ wild type (Cs^a strain) mice administered 0.1% (w/w) for 1 yr followed by 0.05% died by wk-56; no liver tumours were detected. ~50% of ♂ and ♀ acatalasemic (Cs^b strain with unstable catalase gene) mice subjected to the same regime died by wk-56. At 18-20 months, 9/9 ♂ and 12/12 ♀ mice developed multiple hepatocellular carcinomas, 5 of which metastasised to the lungs. No tumours developed in controls by wk-20 (6).
12/15 ♂ Fischer 344 rats administered 0.1% (w/w) in diet for 25 months developed tumours (11 hepatocellular carcinomas, 1 pancreatic acinar-cell carcinomas and 2 pancreatic acinar-cell adenomas). None of the controls developed pancreatic or liver tumours. 10/15 treated rats developed Leydig-cell tumours of the testis compared with 6/10 controls (7,8).
Promoted liver tumours in ♂Wistar rats after initiation with diethylnitrosamine (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (10).

Other effects

Any other adverse effects

A single oral or intraperitoneal dose of 200 mg kg^{-1} to rats stimulated hepatic ornithine decarboxylase activity (11).

Nafenopin suppresses, both *in vivo* and *in vitro*, hepatocyte apoptosis in mice and rats induced by transforming growth factor β1 or the DNA damaging drugs etoposide or hydroxyurea. The authors suggest that nafenopin suppresses hepatocyte apoptosis in each case by impinging on a core apoptotic mechanism (12).
Induced proliferation of peroxisomes in liver parenchymal cells of rats and mice (13,14).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

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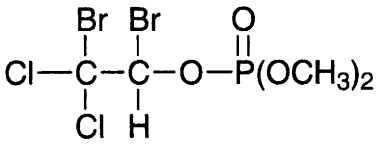
N3 naled



$C_4H_7Br_2Cl_2O_4P$ **Mol. Wt.** 380.78 **CAS Registry No.** 300-76-5

Synonyms phosphoric acid, 1,2-dibromo-2,2-dichloroethyl dimethyl ester; dimethyl 1,2-dibromo-2,2-dichloroethyl phosphate; Alvora; Bromex; Oibrom; Fosbrom; bromchlophos; BRP; Dibrom; Dibromphos

EINECS No. 206-098-3 **RTECS No.** TB 9450000

Uses Insecticide. Acaricide. Wood preservative.

Physical properties

M. Pt. 26.5-27.5°C **B. Pt.** 110°C at 0.5 mmHg **Specific gravity** 1.96 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.20 (1) **Volatility** v.p. 0.002 mmHg at 20°C
Solubility Organic solvents: benzene, carbon tetrachloride, ethanol, mineral oils, petroleum ether, toluene

Occupational exposure

DE-MAK 3 mg m^{-3} (inhalable fraction of aerosol)
FR-VME 3 mg m^{-3}
UK-LTEL 3 mg m^{-3} **UK-STEL** 6 mg m^{-3}
US-TWA 3 mg m^{-3}

UN No. 3018
Supply classification harmful
Risk phrases Harmful in contact with skin and if swallowed – Irritating to eyes and skin (R21/22, R36/38)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) mosquito fish 3.50 ppm (2).
LC_{50} (96 hr) bluegill sunfish, rainbow trout 0.18-0.13 mg l^{-1} (3).
LC_{50} (24 hr) crucian carp, goldfish 2-4 mg l^{-1} (4,5).

Invertebrate toxicity
LC_{50} (96 hr) *Simocephalus serrulatus* 1.1μg l^{-1} (6).
LC_{50} (96 hr) *Daphnia pulex* 350 μg l^{-1} (6).
LC_{50} (24 hr) crab 0.33 mg l^{-1} (4).
EC_{50} (48 hr) *Daphnia magna* 0.36 μg 1^{-1} (1).
LC_{50} (96 hr) *Gammarus lacustris* 110 μg l^{-1} (7).

Bioaccumulation
In 7-day static bioassay did not accumulate in whole body tissue of killifish and was not detected in any fish tissue samples (<0.02 ppm) (8).
Inhibited growth of *Stigeoclonium pachydermum* at >20μg ml^{-1}. Bioconcentration by *Stigeoclonium pachydermum* appeared by absorption of naled to the cell wall (9).

Environmental fate

Abiotic removal
Completely hydrolysed in water within 24 hr (10).
Hydrolysis yields $(MeO)_2P(O)OH$ and $BrCl_2CCHO$ and $(MeO)(HO)P(O)OCHBrCBrCl_2$ and $(MeO)(HO)_2P(O)$ (11).

Mammalian & avian toxicity

Acute data
LD_{50} oral duck 52 mg kg^{-1} (12).
LD_{50} oral rat, mouse 250, 330 mg kg^{-1}, respectively (13,14).
LC_{50} inhalation rat 7700 μg kg^{-1} (duration unspecified) (15).
Inhalation (6 hr) mouse 1500 mg m^{-3} caused no adverse effects (5).
LC_{50} inhalation mouse 156 mg kg^{-1} (duration unspecified) (15).
LD_{50} intraperitoneal rat 35 mg kg^{-1} (15).
LD_{50} dermal rat, rabbit 800, 1100 mg kg^{-1}, respectively (16,17).

Sub-acute and sub-chronic data
LC_{50} (5 day) oral bobwhite quail, Japanese quail, ring-necked pheasant, mallard duck 1300-2725 mg kg^{-1} diet (18).
Oral rat (90 day) 12.5, 25, 50 mg day^{-1}. Decreased body weight and food consumption observed in ♂ rats; ♀ rats had increased food consumption, but body weight was unaffected. Glutathione levels were decreased markedly in kidneys and liver of both sexes (19).

Carcinogenicity and chronic effects
In 2-yr feeding trials, rats receiving 100 mg kg^{-1} in diet showed no ill-effects (5).

Irritancy
500 mg instilled into rabbit eye (24 hr) caused severe irritation (20).
Dermal human (21 day intermittently) 42 mg caused irritation (16).

Genotoxicity

Salmonella typhimurium TA100, TA1535, T.KJ6321 with and without metabolic activation positive; TA98, TA1536, TA1537, TA1538 with and without metabolic activation equivocal (21).
Bacillus subtilis TKJ5211, TKJ6321 with and without metabolic activation positive (21).
Escherichia coli WP2 *her*, with and without metabolic activation negative (22).

Other effects

Other adverse effects (human)
Cholinesterase inhibitor (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (23).
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 3.0 (6th and 7th amendments) (25).
WHO Toxicity Class II (26).
EPA Toxicity Class I (5).
EEC maximum residue level for fruit and vegetables 0.2 ppm (5).

Other comments

Not toxic to bees (5).

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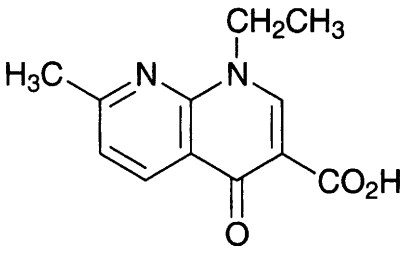
26. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

N4 nalidixic acid



$C_{12}H_{12}N_2O_3$ **Mol. Wt.** 232.24 **CAS Registry No.** 389-08-2

Synonyms 1-ethyl-1,4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3-carboxylic acid; Nacid; nalidixinic acid; Nalix; Negram; Urisal; Wintomylon

EINECS No. 206-864-7 **RTECS No.** QN 2885000

Uses Antibacterial. Used to treat bacterial infections of urinary tract.

Physical properties

M. Pt. 229-230°C

Solubility Water: 0.1 mg ml^{-1} at 23°C. Organic solvents: chloroform, diethyl ether, ethanol, methanol, toluene

Ecotoxicity

Bioaccumulation

Concentrations of nalidixic acid in rainbow trout tissue after administration of 20 mg kg^{-1} for 5 days peaked after 24 hr in liver, kidney, muscle and serum at 5.04-11.89 μg g^{-1} and fell below 0.02 μg g^{-1} after 16 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 572, 1160 mg kg^{-1}, respectively (2,3).

LD_{50} subcutaneous mouse, rat 500, 1584 mg^{-1}, respectively (2,4).

LD_{50} intraperitoneal rat, mouse 319, 871 mg kg^{-1}, respectively (4).

LD_{50} intravenous rat, mouse 88, 101 mg kg^{-1}, respectively (4).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via gavage. Clear evidence of carcinogenicity in ♂ and ♀ rat, equivocal evidence from carcinogenicity (marginal increase in neoplasms which may be chemically related) in ♂ mice but no evidence for carcinogenicity in ♀ mice (5).

♂, ♀ F344/N rats and $B6C3F_1$ mice administered 1000-16,000 ppm for 13 wk showed reduced body weights in rats and mice receiving 8000, 16,000 ppm and reduced food consumption and degradation of the germinal epithelium in the seminiferous tubules of the testis, in rats receiving 16000 ppm. Reduced body weights and feed consumption was also seen in rats and mice administered 0, 2000, 4000 ppm for 2 yr in feed. Dosed ♂ rats showed increased incidence of preputial gland neoplasms and decreased incidence of pituitary gland neoplasms. Dosed ♀ rats showed increased incidence of clitoral gland neoplasms and decreased incidence of leukaemia and mammary gland neoplasms. Subcutaneous tissue fibrosarcomas were marginally increased in dosed ♂ mice (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (7).

Weakly induced new proteins in cultured *Drosophila* cells (8).

Other effects

Other adverse effects (human)

Causes photosensitivity reactions in humans with erythema and bullous eruptions, allergic rashes, urticaria and pruritis (9).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (10).

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N5 naphtha

CAS Registry No. 8030-30-6

Synonyms Amso H-SB; Benzin B70; 160° Benzol; hi-flash naphtha; light ligroin; petroleum naphtha; Super VMP

EINECS No. 232-443-2 **RTECS No.** DE 3030000

Uses Solvent for oils, detergents, fuel, waxes, in paints and in photography

Physical properties

M. Pt. depends on formulation **B. Pt.** 35-80°C **Flash point** ~40°C **Specific gravity** 0.625-0.660

Volatility v.p. depends on formulation ; v.den. depends on formulation

Solubility Organic solvents: miscible with benzene, carbon disulfide, carbon, chloroform, diethyl ether, ethanol

Occupational exposure

US-TWA 400 ppm (1590 mg m^{-3})

UN No. 1255; 1256; 2553

Supply classification toxic

Risk phrases May cause cancer – Harmful: may cause lung damage if swallowed (R45, R65)

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

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow, bluegill sunfish 2, 21 mg l^{-1}, respectively (1).

Invertebrate toxicity

LC_{50} *Daphnia magna* 0.4-2 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LC_{Lo} (5 min) inhalation human 3 pph (2).
LC_{Lo} (6 hr) inhalation rat 1600 ppm (3).
LD_{Lo} intravenous man 27 mg kg^{-1} (4).
LD_{Lo} intraperitoneal man 2500 mg kg^{-1} (5).

Legislation

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

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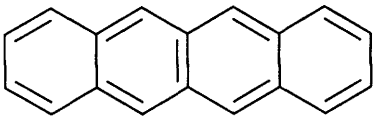
N6 naphthacene



$C_{18}H_{12}$ **Mol. Wt.** 228.29 **CAS Registry No.** 92-24-0

Synonyms benz[*b*]anthracene; 2,3-benzanthracene; chrysogen; rubene; tetracene

EINECS No. 202-138-9 **RTECS No.** QI 7605000

Occurrence Occurs in coal tar.

Physical properties

M. Pt. 341°C (open capillary tube), 357°C (copper block) **Specific gravity** 1.35 **Partition coefficient** log P_{ow} 5.90

Ecotoxicity

Fish toxicity

Exhibited marginal (<20% in 96 hr) photo-induced toxicity to juvenile sunfish at 1.9 μg l^{-1} (1).

Invertebrate toxicity

LC_{50} (0.68 day) *Daphnia magna* 0.6 μg l^{-1} (2).

Environmental fate

Abiotic removal

Photochemically oxidised when irradiated by high-pressure Hg-quartz lamps. More effective on solid carrier than in water (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537, TA1538 with and without metabolic activation positive, TA1535 with metabolic activation negative (4).

Induced unscheduled DNA synthesis in *in vitro* primary rat hepatocyte cultures (5).

Legislation

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

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

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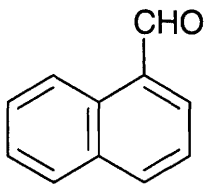
N7 1-naphthaldehyde



$C_{11}H_8O$ **Mol. Wt.** 156.18 **CAS Registry No.** 66-77-3

Synonyms 1-naphthalenecarboxaldehyde; 1-formylnaphthalene; α-naphthaldehyde; α-naphthylaldehyde; 1-naphthylaldehyde; α-naphthylcarboxaldehyde; α-naphthal

EINECS No. 200-633-4 **RTECS No.** QJ 0190000

Physical properties

M. Pt. 1-2°C **B. Pt.** 160-161°C at 15 mmHg **Flash point** >110°C **Specific gravity** 1.150

Ecotoxicity

Invertebrate toxicity

LC_{50} (1 day) *Aedes aegypti, Aedes taeniorhynchus, Culex quinquefasciatus* >10.0 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} mouse (route unspecified) 1100 mg kg^{-1} (2).

LD_{Lo} subcutaneous dog 330 mg kg^{-1} (3).

Legislation

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

Other comments

Lachrymatory.

References

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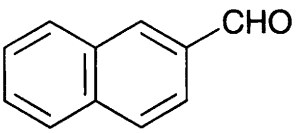
N8 2-naphthaldehyde



$C_{11}H_8O$ **Mol. Wt.** 156.18 **CAS Registry No.** 66-99-9

Synonyms 2-naphthalenecarboxaldehyde; β-formylnaphthalene; 2-formylnaphthalene; β-naphthaldehyde; β-naphthylaldehyde; β-naphthylcarboxaldehyde

EINECS No. 200-640-2 **RTECS No.** QJ 0190010

Physical properties

M. Pt. 59-62°C

Mammalian & avian toxicity

Acute data

LD_{50} mouse (route unspecified) 1500 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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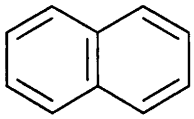
N9 naphthalene



$C_{10}H_8$ **Mol. Wt.** 128.17 **CAS Registry No.** 91-20-3

Synonyms albocarbon; dezodorator; moth flakes; naphthaline; tar camphor; white tar

EINECS No. 202-049-5 **RTECS No.** QJ 0525000

Uses Used in manufacture of dyes, synthetic resins, celluloid, lamp-black, smokeless powder, hydronaphthalenes. Moth repellant and insecticide. Topical antiseptic, anthelmintic.

Occurrence Most abundant single constituent of coal tar/dry coal tar contains about 1% naphthalene.

Physical properties

M. Pt. 80.2°C **B. Pt.** 217.9°C **Flash point** 79°C (open cup) **Specific gravity** 1.162 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 3.30 **Volatility** v.p. 0.177 mmHg at 30°C

Solubility Water: 30 mg l^{-1}. Organic solvents: benzene, chloroform, carbon tetrachloride, diethyl ether, ethanol, methanol, toluene

Occupational exposure

FR-VME 10 ppm (50 mg m^{-3})
UK-LTEL 10 ppm (53 mg m^{-3}) **UK-STEL** 15 ppm (80 mg m^{-3})
US-TWA 10 ppm (52 mg m^{-3}) **US-STEL** 15 ppm (79 mg m^{-3})

UN No. 1334 (crude or refined); 2304 (molten) **HAZCHEM Code** 2Z (crude or refined) **HAZCHEM Code** 2X (molten)

Conveyance classification flammable solid

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) pink salmon, larval rainbow trout, fathead minnow 1.2-6.4 mg l^{-1} (1,2,3).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 0.929 ppm Microtox test (4).

EC_{50} (48 hr) *Daphnia pulex* 4.66 mg l^{-1} (2).

LC_{50} (48 hr) *Daphnia magna* 8.6 mg l^{-1} (5).

50% reduction in cell numbers of *Chlorella vulgaris* compared with controls after 1 day incubation with 33 ppm at 20°C (6).

Marine edible crabs *Scylla serrata* suffered decreased haemolymph free-sugar level and glycogen content of muscle, hepatopancreas, and ovary of different ovarian stages following exposure to naphthalene. The authors conclude that naphthalene affects the vitellogenesis of *Scylla serrata* (7).

Bioaccumulation

Coho salmon exposed to 0.02 ppm at 10°C for 5 wk had 0.24 ppm in muscle tissue dry weight (bioconcentration factor 12) (8).

Oysters exposed in oil-treated enclosure for 2, 8 day had accumulation factors of 6000 and 4000, respectively (9).

Detected in Atlantic cod exposed to 0.1-3.4 ppm crude oils for 24 hr (10).

Environmental fate

Anaerobic effects

50 mg l^{-1} did not inhibit anaerobic digestion on a laboratory scale (11).

Degradation studies

BOD^{250}_{35} 1.92 mg l^{-1} O_2 in seawater/inoculum: enrichment cultures of hydrocarbon oxidising bacteria (12).
Microbiological degradation to CO_2 in seawater at 12°C in the dark after 24 hr incubation with 50 µg l^{-1}, degradation rate 0.10 µg l^{-1} day^{-1} – turnover time 500 days. After addition of aqueous extract of fuel oil 2: degradation rate 1.0-5.0 µg l^{-1} day^{-1} turnover time 10-22 days (13).
Pseudomonas fluorescens, Pseudomonas paucimobilis, Pseudomonas vesicularis and *Alcaligenes denitrificans* completely degraded naphthalene in soil samples. Maximum degradation rate 4.8 mg naphthalene ml^{-1} day^{-1} (14).

Abiotic removal

Naphthalene is rapidly and effeciently converted into CO_2 in the presence of TiO_2 under simulated solar light, but the presence of amphiphiles and organic components from soil is inhibitory (15).

Adsorption and retention

In estuarine waters at 30 µg l^{-1}, 0.7% absorbed on particles after 3 hr (16).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 490, 533 mg kg^{-1}, respectively (17,18).
LD_{50} oral guinea pig 1200 mg kg^{-1} (19).
LD_{Lo} oral dog, cat 400, 1000 mg kg^{-1}, respectively (20).
LD_{50} intraperitoneal mouse 150 mg kg^{-1} (21).
LD_{50} subcutaneous mouse 969 mg kg^{-1} (22).

Carcinogenicity and chronic effects

National Toxicology Program testing in progress in mice by inhalation. No evidence for carcinogenicity in ♂ mice, some evidence for carcinogenicity (increased incidence of chemically related neoplasms, malignant, benign or combined) in ♀ mouse (23).

Teratogenicity and reproductive effects

Pregnant ♀ CD-1 mice dosed orally with 300 mg kg^{-1} day^{-1} on day 6-13 of gestation were allowed to deliver. Of 50 mice treated 10 died (0/50 in control groups) and 26/28 litters were viable (40/40 in control group) (24).

Irritancy

495 mg dermal rabbit caused mild irritation (25).
100 mg instilled into rabbit eye caused mild irritation (26).

Other effects

Other adverse effects (human)

Ingestion of naphthalene can cause headaches, nausea, vomiting, diarrhoea, profuse perspiration, dysuria, haematuria, acute haemolytic anaemia, coma and convulsions. Doses as low as 2 g have been fatal to a small child (27).

Any other adverse effects

Perfusion of mouse lung with 1.28 mg naphthalene resulted in swelling and vacuolation of Clara cells followed by reduction of these cells amongst epithelial cells in the terminal airway by 33%. Concentration-dependent decreases in GSH were observed (28).
Damage to Clara cells and lung damage in the bronchiolar region was observed in ♂ mice 24 hr after intraperitoneal administration of 200 mg kg^{-1}. No lung damage was detected after administration of 100 mg kg^{-1} (29).
Induced cataracts in rat lenses (30).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (31).
Included in Schedule 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (32).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th ammendment) (33).

Other comments

Reviews on human health effects, experimental toxicity, environmental effects, ecotoxicity, exposure levels, epidemiology and workplace experience listed (34).

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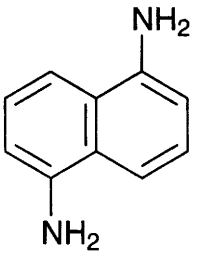
N10 1,5-naphthalenediamine



$C_{10}H_{10}N_2$ **Mol. Wt.** 158.20 **CAS Registry No.** 2243-62-1

Synonyms 1,5-diaminonaphthalene; 1,5-naphthylenediamine

EINECS No. 218-817-8 **RTECS No.** QJ 3400000

Uses Intermediate for 1,5-naphthalene diisocyanate and dye manufacture.

Physical properties

M. Pt. 185-187°C

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

Supply classification harmful

Supply classification dangerous for the environment

Risk phrases Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R40, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S36/37, S60, S61)

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 36.2 ppm Microtox test (1).

EC_{50} (60 hr) *Tetrahymena pyriformis* 45 mg l^{-1} (2).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

In 8-wk feeding trials, ♂, ♀ Fischer 344 rats and B6C3F_1 mice received up to 3.0% in diet. Mean body weight gain was depressed and some treated with 3.0% died. In chronic studies (duration unspecified) with up to 0.1% in rats, 0.2% in mice, no compound-related lesions were observed (3).

Carcinogenicity and chronic effects

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

50 ♂, 50♀ B6C3F_1 mice fed 1000 or 2000 mg kg^{-1} in diet for 103 wk were observed at wk 105-106. There was no significant association between dose and overall mortality. Significant dose-related increases were seen in C-cell carcinomas of the thyroid gland in ♀, neoplasms of the thyroid gland in carcinogenicity ♂, ♀ hepatocellular carcinomas in ♀ and alveolar/bronchiolar adenomas and carcinomas in ♀, compared with controls (3).

Groups of 50 ♂, 50 ♀ Fischer 344 rats fed 500 or 1000 mg kg^{-1} in diet for 103 wk were observed at wk 106-107. No significant association between dose and mortality was seen but a significant dose-related increase in incidence of adenomas and carcinomas of the clitoral gland was observed compared with controls (3).

The National Toxicology Program investigated 1,5-naphthalenediamine in rats and mice. Designated non-carcinogenic in ♂ rat, carcinogenic in ♀ rat and ♂, ♀ mouse (5).

Genotoxicity

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

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Reviews on human health effects, experimental toxicity and workplace experience listed (8).

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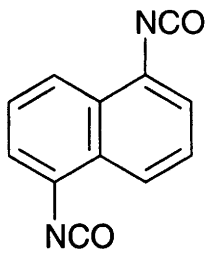
N11 naphthalene 1,5-diisocyanate



$C_{12}H_6N_2O_2$ **Mol. Wt.** 210.19 **CAS Registry No.** 3173-72-6

Synonyms isocyanic acid, 1,5-naphthylene ester; 1,5-diisocyanatonaphthalene

EINECS No. 221-641-4 **RTECS No.** NQ 9600000

Uses In production of polyurethane elastomers.

Occurrence Detected in workplace atmosphere at unspecified levels in polyurethane rubber and shoe manufacturing industry (1).

Physical properties

M. Pt. 130-132°C

Occupational exposure

DE-MAK 0.01 ppm (0.087 mg m^{-3})
FR-VME 0.01 ppm (0.095 mg m^{-3}) **FR-VLE** 0.02 ppm (0.19 mg m^{-3})
SE-LEVL 0.005 ppm (0.04 mg m^{-3}) **SE-CEIL** 0.01 ppm (0.09 mg m^{-3})
UK-LTEL MEL 0.02 mg m^{-3} (as NCO) **UK-STEL** MEL 0.07 mg m^{-3} (as NCO)
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

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (1).

Other effects

Other adverse effects (human)
Workers producing polyurethane rubber exposed to 1,5-naphthalene diisocyanate experienced acute damage to the respiratory tract (pharyngitis and bronchitis) and conjunctivitis (2,3).
Incidence of bronchitis was associated with levels of 1,5-naphthalene diisocyanate in air of <0.17 mg m^{-3} (4).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Other comments

Reviews on human health effects, experimental toxicity, physico-chemical properties, epidemiology, workplace experience and ecotoxicology listed (6).

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N12 naphthenic acid

CAS Registry No. 1338-24-5

Synonyms Acidol; NS130; NS160; SP230; Sunaptic B

EINECS No. 215-662-8 **RTECS No.** QK 8750000

Physical properties

B. Pt. 131-243°C **Flash point** 148.8°C (open cup) **Specific gravity** 0.982 at 20°C with respect to water at 4°C
Solubility Organic solvents: oil

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3000 mg kg^{-1} (1).

LD_{50} intraperitoneal rat 640 mg kg^{-1} (1).

Irritancy

Moderate irritation of eye and skin in rabbits and of respiratory tract of unspecified species after inhalation (dose unspecified) (2).

Other effects

Any other adverse effects

Changes in the liver and stomach (unspecified) seen in mice after repeated oral doses (dose and duration unspecified) (2).

Single and repeated oral administration to rats (dose and duration unspecified) affected central nervous system (2).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

Other comments

Reviews on human health effects and experimental toxicity listed (4).

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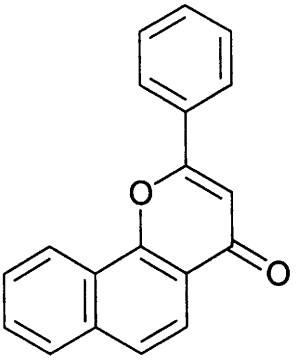
N13 α-naphthoflavone



$C_{19}H_{12}O_2$ **Mol. Wt.** 272.30 **CAS Registry No.** 604-59-1

Synonyms 7,8-benzoflavone; ANF; 2-phenyl-4*H*-naphtho[1,2-*b*]pyran-4-one

EINECS No. 210-071-1 **RTECS No.** QL 6250000

Physical properties

M. Pt. 156-159°C

Ecotoxicity

Fish toxicity

Biochemical effects reported in rainbow trout at 0.63 mmol (6 days) (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Induced hepatocellular carcinomas at 0.4% in the diet to ♂ Syrian hamsters exposed to diethylstilbestrol or 17α-ethinylestradiol (implanted subcutaneously every 3 months as 20 and 30 mg pellets, respectively). Studies of the effects of these treatments on hamster hepatic microsomal preparations, isolated hepatocytes and hamster bile *in vivo* suggest that the metabolic activation of α-naphthoflavone, rather than that of the oestrogens, plays an important role in carcinogenic effect seen in this animal liver tumour model (2).

Genotoxicity

Induced sister chromatid exchanges and chromosome aberrations in Chinese hamster ovary cells when coincubated with 2,3,7,8- tetrachlorodibenzo-*p*-dioxin-induced microsomes, but not with phenobarbital-induced or control microsomes (3).

Induced sister chromatid exchanges in cultured human lymphocytes (4).

Other comments

Effect on diethylstilbestrol metabolism and liver carcinogenesis reviewed (5).

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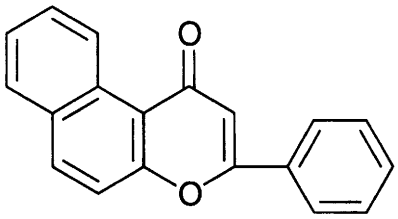
N14 β-naphthoflavone



$C_{19}H_{12}O_2$ **Mol. Wt.** 272.30 **CAS Registry No.** 6051-87-2

Synonyms 5,6-benzoflavone; 3-phenyl-1*H*-naphtho[2,1-*b*]pyran-1-one

EINECS No. 227-958-4 **RTECS No.** QL 6200000

Uses As a positive control in biochemical studies of cytochrome P_{448} enzyme induction.

Physical properties

M. Pt. 164-166°C

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Modest thymic atrophy occurred in mice after four daily doses of 80 mg kg^{-1} (route unspecified) (1).

Carcinogenicity and chronic effects

No primary reports on carcinogenicity are available, however its enzyme inducing properties on tumorigenesis of other chemicals have been examined, and hence it has been used as a control in these studies (2).

Administered intraperitoneally to mice at 150 mg kg^{-1}, once weekly for 12-14 wk it had no tumorigenic effect (3).

In another study a high level of forestomach papillomas occurred in combined control groups of mice fed β-naphthoflavone and other control vehicles (dose and duration unspecified), but the pooled control data did not allow comparison of β-naphthoflavone with other controls (4).

No hepatic tumours were reported in castrated ♂ hamsters fed 0.2% for up to 10 months as a control in studies of synthetic oestrogens (5).

It has protective effects on the pulmonary carcinogenicity of benzo[*a*]pyrene in mice and on tumorigenicity of 3-methylcholanthrene in mice, and on nephrotoxicity of cephaloridine in rats (2).

β-naphthoflavone-treated microsomes decreased activation of cyclophosphamide and aflatoxin B_1 to mutagenic products, but it increased activation of 2,4-diaminoanisole, quinoline, benzo[*a*]pyrene and 2-aminoanthracene to mutagenic products (2).

Teratogenicity and reproductive effects

15 mg kg^{-1} day^{-1} intraperitoneally for 8 days mid-pregnancy caused marked foetotoxicity and reduced foetal growth in rats (6,7).

β-naphthoflavone was not teratogenic in mice (dose, duration and route unspecified), but when co-administered with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin teratogenicity and foetolethalility were significantly increased. This could be due to the perturbation of their interaction with cytochrome P_{448} induction, or that cytochrome P_{448} induction by 2,3,7,8- tetrachlorodibenzo-*p*-dioxin resulted in formation of a more reactive metabolite of β-naphthoflavone (2,8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537, TA1538 with and without metabolic activation negative (9).

Other effects

Any other adverse effects

Strong renal carbonic anhydrase inhibitor and mild hepatotoxin according to NMR studies in the rat (10).

Other comments

Synthetic analogue of a large series of naturally occurring flavonoids which are widely distributed in vascular plants.

Mutagenicity and carcinogenicity reviewed (2).

Potent cytochrome P_{448} inducer (2).

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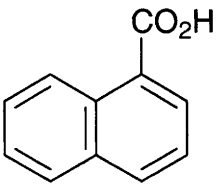
N15 1-naphthoic acid



$C_{11}H_8O_2$ **Mol. Wt.** 172.18 **CAS Registry No.** 86-55-5

Synonyms 1-naphthalenecarboxylic acid; 1-carboxynaphthalene; naphthalene-α-carboxylic acid; α-naphthoic acid; α-naphthylcarboxylic acid

EINECS No. 201-681-9 **RTECS No.** QL 0960000

Physical properties

M. Pt. 160.5-162°C **B. Pt.** 300°C

Solubility Water: slightly soluble in hot water. Organic solvents: diethyl ether, hot ethanol

Environmental fate

Degradation studies

Confirmed to be biodegradable (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2370 mg kg^{-1} (2).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. *The list of existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* Chemicals Inspection and Testing Institute, Japan.
2. *NTIS Report PB85-143766* Natl. Tech. Inf. Ser., Springfield, VA, USA.
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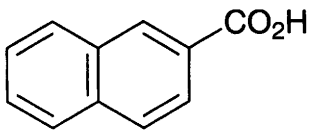
N16 2-naphthoic acid



$C_{11}H_8O_2$ **Mol. Wt.** 172.18 **CAS Registry No.** 93-09-4

Synonyms 2-carboxynaphthalene; isonaphthoic acid; 2-maythic acid; β-naphthoic acid; 2-naphthalenecarboxylic acid

EINECS No. 202-217-8 **RTECS No.** QL 1050000

Physical properties

M. Pt. 184-185°C **B. Pt.** >300°C

Solubility Water: slightly soluble in hot water. Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies

Confirmed to be biodegradable (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 4500-4700 mg kg^{-1} (2).

LD_{Lo} intraperitoneal mouse 500 mg kg^{-1} (3).

Legislation

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

Reported in EPA TSCA Inventory.

References

1. *The list of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* Chemicals Inspection and Testing Institute, Japan.
2. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR.
3. *Summary Tables of Biol. Tests* 1952, **4**, 379.
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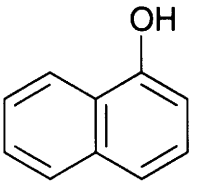
N17 1-naphthol



$C_{10}H_8O$ **Mol. Wt.** 144.17 **CAS Registry No.** 90-15-3

Synonyms α-hydroxynaphthalene; 1-hydroxynaphthalene; 1-naphthalenol; α-naphthol

EINECS No. 201-969-4 **RTECS No.** QL 2800000

Uses Manufacture of dyes and synthetic perfumes.

Physical properties

M. Pt. 96°C **B. Pt.** 278-290°C **Specific gravity** 1.0954 at 98.7°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.84 **Volatility** v.p. 1 mmHg at 94°C
Solubility Water: slightly soluble. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful in contact with skin and if swallowed – Irritating to respiratory system and skin – Risk of serious damage to eyes (R21/22, R37/38, 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 – Wear suitable gloves and eye/face protection (S2, S22, S26, S37/39)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) carp 2.6-3.13 mg kg^{-1} (1).
Log LC_{50} (96 hr) fathead minnow –1.49 (2).

Invertebrate toxicity
EC_{50} (72 hr) *Dunaliella bioculata* 14 mg l^{-1} (3).
EC_{50} (5 min) *Photobacterium phosphoreum* 3.71-5.61 ppm Microtox test (4).

Environmental fate

Degradation studies
Degrades to carbon dioxide in estuarine water; turnover time 41 days (5).
Biodegradable (6).

Inhibited gas production in tests of anaerobic degradation by incubating diluted sludge at 35°C for >60 days (7).
Degradation by immobilised bacteria was 100 mg l^{-1} in batch culture, and efficiency increased significantly in continuous culture (8).
Mineralisation was negligible in moist or flooded soils in continuous flow-through system over 28 days (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral cat, mouse 134, 275 mg kg^{-1}, respectively (10).
LD_{50} dermal rabbit 880 mg kg^{-1} (11).
Mice dosed orally with 0.5-2 g kg^{-1} suffered histopathological lesions of the kidney and stomach (12).

Teratogenicity and reproductive effects
Teratogenic and reproductive effects reported in mice after subcutaneous administration of 90 mg kg^{-1} (total dose) on days 6-14 of pregnancy (13).

Metabolism and toxicokinetics
Metabolised to its sulfate and glucuronide conjugates in isolated perfused rat kidney; clearance was 5.36-6.24 ml min^{-1} $kidney^{-1}$ (14).

Irritancy
550 mg (duration unspecified) caused moderate skin irritation, and 1 mg caused severe eye irritation in rabbits (15).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (16).
Bacillus subtilis H17/M45, HLL3g/HJ-15 agar incorporation test or spot test negative (17).
Escherichia coli AB1157/JC5547 spot test positive, AB1157/JC5547 agar incorporation test negative; AB1157/JC2921, AB1157/JC2926, AB1157/JC5519 spot test or agar incorporation test negative (17).

Other effects

Any other adverse effects
Intraperitoneal injection of 56-562 mg kg^{-1} to mice demonstrated a cataractogenic potency between that of naphthalene and naphthoquinones (18).
Toxicity may be mediated by naphthoquinone formation (19).

References

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6. *The List of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* 1987, Chemicals Inspection & Testing Inst., Japan.
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11. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
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14. Redegeld, F. A. et al *J. Pharmacol. Exp. Ther.* 1988, **244**(1), 263-267.
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18. Wells, P. G. et al *Toxicol. Appl. Pharmacol.* 1989, **99**(3), 466-473.
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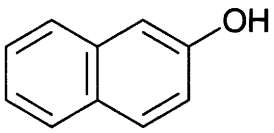
N18 2-naphthol



$C_{10}H_8O$ **Mol. Wt.** 144.17 **CAS Registry No.** 135-19-3

Synonyms isonaphthol; β-naftol; C.I. 37500; naphth-2-ol; 2-naphthalenol; naphthol B; β-naphthyl alcohol; β-naphthyl hydroxide; 2-hydroxynaphthalene

EINECS No. 205-182-7 **RTECS No.** QL 2975000

Uses Formerly used as an anthelmintic. Manufacture of dyes, pigments and antioxidants for rubber, fats, oils; synthesis of fungicides, pharmaceuticals and perfumes.

Physical properties

M. Pt. 121-123°C **B. Pt.** 285-286°C **Flash point** 152.8°C **Specific gravity** 1.22 **Partition coefficient** log P_{ow} 2.7 **Volatility** v.p. 10 mmHg at 145.5°C ; v.den. 4.97

Solubility Water: 740 mg l^{-1} at 25°C. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

Supply classification harmful, dangerous for the environment

Risk phrases Harmful by inhalation and if swallowed – Very toxic to aquatic organisms (R20/22, R50)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S24/25, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 3.5 mg l^{-1} (1).

LC_{50} (27 day) rainbow trout 0.12 mg l^{-1} (1).

Invertebrate toxicity

LC_{50} (48 hr) *Daphnia magna* 3.5 mg l^{-1} (1).

EC_{50} (4 hr) *Selenastrum capricornutum* 19 mg l^{-1}(1).

EC_{50} (5-30 min) *Photobacterium phosphoreum* 0.275 ppm Microtox test (2).

♂ and ♀ American lobsters (*Homerus americanus*) were injected intrapericardially with 0.25 g kg^{-1} 2-naphthol. The total body clearance for ♀s was 26.4 ±6.5 ml hr^{-1} kg^{-1}, and for ♂s was 11.1 ±5.9 ml hr^{-1} kg^{-1}. 2-Naphthol was converted into 2-naphthyl-β-D-glucoside (major metabolite) and 2-naphthyl sulfate (minor metabolite) (3).

Environmental fate

Degradation studies

Biodegradable (4).

Gas production was inhibited by 2-naphthol in tests of anaerobic degradation potential by incubating diluted sludge at 35°C for >60 days (5).

Activated sludge test (initial concentration 43 mg l^{-1}, acclimation 1 day, % removal COD 20, TOC 8) did not indicate degradability, but results of respiration meter tests (initial concentration 100 mg l^{-1}, % removal COD 96, TOC 97) did indicate that it is biodegradable (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1960 mg kg^{-1} (7).

LD_{Lo} subcutaneous guinea pig, rabbit 2670-3000 mg kg^{-1} (8,9).

Intraperitoneal injection of 50 mg kg^{-1} caused lung damage in mice 24 hr after administration (10).

Metabolism and toxicokinetics

Absorption from a paste containing 20% with sulfur and soft soap was 5-41% of amount applied to 10 patients (11).

After intraperitoneal injection of 50 mg kg^{-1} to mice, tissue concentration of 2-naphthol reached maximum levels 1-2 hr later and then rapidly decreased. Pulmonary reduced glutathione level was considerably depleted, suggesting formation of reactive metabolites such as epoxides (10).

Irritancy

500 mg caused mild skin irritation and 100 mg caused moderate eye irritation in rabbits (duration unspecified) (12).

Genotoxicity

Salmonella typhimurium TA100, TA98, TA1535, TA1537, TA1538 with and without metabolic activation negative (13).

Bacillus subtilis H17/M45, HLL3g/HJ-15 agar incorporation test or spot test negative (13).

Escherichia coli agar incorporation test positive, spot test negative (13).

Other effects

Other adverse effects (human)

Overdose causes abdominal cramp, nausea, vomiting, diarrhoea, haemolysis, lens opacities, oliguria, and convulsions. Nephritis has followed absorption from intact skin. It should not be used for patients with glucose-6-phosphate dehydrogenase deficiency, nor during pregnancy (12).

Other comments

Hazards reviewed (14).

References

1. Millemann, R. E. et al *Trans. Am. Fish. Soc.* 1984, **113**, 74-85.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
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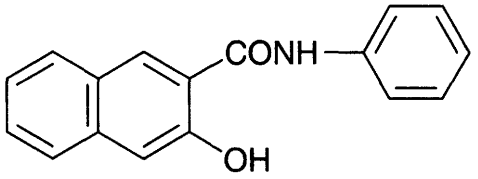
N19 Naphthol AS



$C_{17}H_{13}NO_2$ **Mol. Wt.** 263.30 **CAS Registry No.** 92-77-3

Synonyms 3-hydroxy-*N*-phenyl-2-naphthalenecarboxamide; 2-hydroxy-3-naphthoanilide; Acna Naphthol; Azotol A; Cibanaphthol RF; C.I. 37505; Naphthol AS-A; nitrazol I-AS

EINECS No. 202-188-1

Uses In dyes, pigments and printing inks.

Physical properties

M. Pt. 247-250°C

Mammalian & avian toxicity

Acute data

LD_{50} oral F344 rat >5 g kg^{-1} (1).

Sub-acute and sub-chronic data

Oral (92 day) F344 rat 0.56, 1.67 and 5.0% diet caused suppression of body weight at largest dose in both sexes. Serum levels of creatine kinase and aspartate aminotransferase activities decreased at 0.56% and triglycerides decreased at >1.67%. No significant change was observed in organ weights and haematological and histological examinations (1).

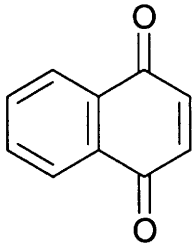
Carcinogenicity and chronic effects

Division of Toxicology, National Institute of Hygienic Services, Tokyo tested oral Fischer 344 rat (2 yr) 0.1, 5.0% (results not yet available) (2).

References

1. Takada, K. et al *Eisei Shikensho Hokoku* 1986, **104**, 51-58 (Japan.) (*Chem. Abstr.* **106**, 190521y).
2. *Directory of Agents being tested for Carcinogenicity* 1992, No.15, WHO/IARC, Lyon, France

N20 1,4-naphthoquinone



$C_{10}H_6O_2$ **Mol. Wt.** 158.16 **CAS Registry No.** 130-15-4

Synonyms 1,4-dihydro-1,4-diketonaphthalene; 1,4-naphthalenedione; α-naphthoquinone

EINECS No. 204-977-6 **RTECS No.** QL 7175000

Occurrence Substituted 1,4-naphthoquinones such as phthiocol and vitamin K, occur in nature.

Physical properties

M. Pt. 125-126°C **Specific gravity** 1.422

Solubility Water: slightly soluble. Organic solvents: benzene, chloroform, carbon disulfide, diethyl ether

Ecotoxicity

Invertebrate toxicity

EC_{50} (74 hr) *Dunaliella bioculata* 0.011 mg l^{-1} (1).

Environmental fate

Degradation studies

Pseudomonas putida J1 and J2, enriched from soil with juglone, are capable of totally degrading 1,4-naphthoquinone (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig 190, 400 mg kg^{-1}, respectively (3).

LD_{Lo} oral mouse 80 mg kg^{-1} (4).

LD_{50} subcutaneous rat 202 mg kg^{-1} (5).

LD_{50} intraperitoneal mouse 5.50 mg kg^{-1} (6).

Carcinogenicity and chronic effects

11/77 mice surviving to 200 days developed papillomas after skin painting with 0.1 or 0.25% 1,4-naphthoquinone in benzene. 2/46 mice painted with quinone plus 1,4-naphthoquinone developed lung cancer (7).

Teratogenicity and reproductive effects

Subcutaneous injection of 10 mg day^{-1} for 14 days had no effect on oestrous cycle in rats, but ovarian weight was reduced (8).

Genotoxicity

Did not induce gene mutations in V79 cells (9).

Other effects

Any other adverse effects

Intraperitoneal injection of 5-250 mg kg^{-1} initiated cataracts in mice in a dose-dependent manner (10).

Legislation

Land disposal prohibited by US Federal Resource Conservation and Recovery Act (11).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

References

1. Helddal, M. et al *Environ. Pollut., Ser. A* 1984, **35(2)**, 119-132.
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9. Ludewig, G. et al *Environ. Health Perspect.* 1989, **82**, 223-228.
10. Wells, P. G. et al *Toxicol. Appl. Pharmacol.* 1989, **99(3)**, 466-473.
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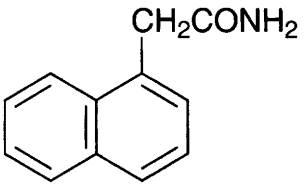
N21 1-naphthylacetamide



$C_{12}H_{11}NO$ **Mol. Wt.** 185.23 **CAS Registry No.** 86-86-2

Synonyms 2-(1-naphthyl)acetamide; 1-naphthaleneacetamide; *N*-acetyl-1-naphthylamine; NAAm

EINECS No. 201-704-2 **RTECS No.** QJ 0590000

Uses Plant growth regulator.

Physical properties

M. Pt. 184°C **Flash point** non-flammable **Volatility** v.p. $<7.5 \times 10^{-8}$ mmHg

Solubility Water: 39 mg kg^{-1} at 40°C. Organic solvents: acetone, ethanol, isopropanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat ~6400 mg kg^{-1} (1).

LD_{50} dermal rabbit >5000 mg kg^{-1} (1).

Irritancy
Not irritating to eyes or skin (species and dose unspecified) (1).

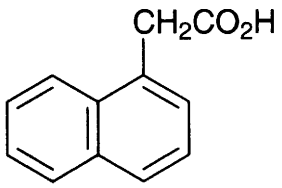
Legislation

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).
EPA Toxicity Class III (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. 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

N22 1-naphthylacetic acid



$C_{12}H_{10}O_2$ **Mol. Wt.** 186.21 **CAS Registry No.** 86-87-3

Synonyms 1-naphthaleneacetic acid; α-naphthylacetic acid; 2-(1-naphthyl)acetic acid; Biokor; Fruitofix; Nafusaku; Planofix

EINECS No. 201-705-8 **RTECS No.** QJ 0876000

Uses Plant growth regulator. Choleretic.

Physical properties

M. Pt. 134.5-135.5°C
Solubility Water: 0.38 g l^{-1} at 17°C. Organic solvents: acetone, chloroform, diethyl ether, ethanol, xylene

Ecotoxicity

Bioaccumulation
Confirmed to be non-accumulative or poorly accumulative (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 743, 1000 mg kg^{-1}, respectively (2,3).
LD_{50} dermal rabbit >5000 mg kg^{-1} (acid) (4).
LD_{50} intraperitoneal rat, mouse 100, 609 mg kg^{-1}, respectively (5,6).

Sub-acute and sub-chronic data

8-day dietary LC_{50} mallard duck, bobwhite quail >10,000 mg kg^{-1} (4).

Groups of 10 ♂, 10 ♀ Wistar rats fed 0, 200, 1000, 5000 ppm in diet for 90 days showed no significant effects in renal concentration test, urinalysis, renal histochemistry or histology of a range of organs. At the 5000 ppm level growth and food intake was reduced in ♂ and relative weights of thyroid, testes, brain and liver were increased. Possible liver damage occurred at 5000 ppm (7).

Irritancy

100 mg instilled into rabbit eye (72 hr) caused severe irritation (5).

Legislation

Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) Statutory Instrument No.472, 1991 (8).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (9).

WHO Toxicity Class Table 5 (10).

EPA Toxicity Class III (formulation) (11).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

Not toxic to bees (4).

Nodulation, nitrogen fixation and yield of *Trifolium alexandrinum* were enhanced with treatment of 4.66-9.31 mg l^{-1} naphthylacetic acid (13).

References

1. *The list of existing substances tested on biodegradability by microorganisms or bioaccumulation in fish body* 1987, Chemical Inspection and Testing Institute, Japan.
2. Perkow, W. *Wirksubstanzen der Pflanzenschutz- und Schaedlingsbekaempfungsmittel* 1971/76, Verlag Paul Parey, Berlin, Germany.
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5. *Pestic. Toxic Chem. News* 1980, **9**, 10.
6. *Toho Igakkai Zasshi* 1968, **15**, 443.
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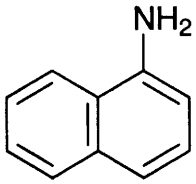
N23 1-naphthylamine



$C_{10}H_9N$ **Mol. Wt.** 143.19 **CAS Registry No.** 134-32-7

Synonyms 1-naphthalenamine; 1-aminonaphthalene; α-naphthylamine; naphthalidine

EINECS No. 205-138-7 **RTECS No.** QD 7300000

Uses In dyestuff manufacture, toning prints made with cerium salts.

Physical properties

M. Pt. 50°C **B. Pt.** 301°C **Flash point** (base) 157°C **Specific gravity** 1.13 **Partition coefficient** log P_{ow} 2.25
Volatility v.p. 1 mmHg at 104.3°C ; v.den. 4.93
Solubility Water: soluble in 590 parts. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2077 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification harmful
Supply classification dangerous for the environment
Risk phrases Harmful if swallowed – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R51/53)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S24, S61)

Ecotoxicity

Bioaccumulation
Confirmed to be non-accumulative or low accumulative (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 779 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 96 mg kg^{-1} (3).
LD_{Lo} subcutaneous rabbit 300 mg kg^{-1} (4).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).
Excess incidence of bladder cancer reported in workers exposed to 1-naphthylamine alone for >5 yr, but at the time commercial 1-naphthylamine may have been contaminated with 4-10% 2-naphthylamine (an IARC group 1 carcinogen). In other cohort studies excess bladder cancer incidence reported in workers exposed to 1-naphthylamine and other substances (5).
Not carcinogenic after oral administration to dogs or hamsters; results in mice were inconclusive. Lung adenoma bioassay in mice negative. Inconclusive results after subcutaneous injection of newborn mice (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 without metabolic activation negative; TA1535, TA1537 with metabolic activation negative; TA100, TA98, TA1538 with metabolic activation positive (6).

Unlike other isomers of aminoquinolines and their *N*-acetyl derivatives, 1-naphthylamine is less mutagenic to *Salmonella typhimurium* than 2-naphthylamine (7).
Salmonella typhimurium TA1535/pSK1002 *umu* test negative (8).
Escherichia coli K12 with and without metabolic activation negative (6).
Did not induce sex-linked recessives in *Drosophila melanogaster* (6).
Did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro* (9).
Increased incidence of chromosomal aberrations in cultured rat and hamster cells, but results for sister chromatid exchanges, mutation and DNA damage in cultured rodent cells was inconclusive (6).
Mouse lymphoma L5178Y cell forward mutation assay positive (6).
Did not induce micronuclei in bone marrow cells of mice treated *in vivo* (6).

Legislation

Reportable quantity regulated in USA by the Federal Comprehensive Environmental Response, Compensation and Liability Act (10).
Land disposed prohibited under US Federal Resource Convervation and Recovery Act (11).
Listed as a carcinogen by OSHA (12).

Other comments

Carcinogenicity, biological and chemical properties relative to 2-naphthylamine reviewed (13).

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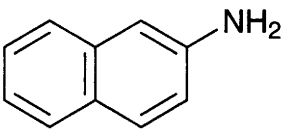
N24 2-naphthylamine



$C_{10}H_9N$ **Mol. Wt.** 143.19 **CAS Registry No.** 91-59-8

Synonyms 2-aminonaphthalene; 2-naphthalenamine; β-naphthylamine

EINECS No. 202-080-4 **RTECS No.** QM 2100000

Uses In dye manufacture.

Physical properties

M. Pt. 111-113°C **B. Pt.** 306°C **Flash point** 157°C **Specific gravity** 1.061 at 98°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.4 **Volatility** v.p. 1 mmHg at 108°C ; v.den. 4.95
Solubility Water: soluble in hot water. Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 0.001 ppm (0.005 mg m^{-3})

UN No. 1650 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer – Harmful if swallowed – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R22, R51/53)
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) – Avoid release to the environment. Refer to special instructions/safety data sheet – Restricted to professional users (S53, S45, S61)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 727 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (3).
Case studies and epidemiological studies in the 1950s and 1960s found occupational exposure was associated with bladder cancer (3,4).
Induced bladder tumours in hamsters, dogs and non-human primates, and liver tumours in mice, after oral administration. A low incidence of bladder carcinomas was reported in rats after oral administration (3).
Positive results were reported in the lung-adenoma bioassay in mice by intraperitoneal injections (3); the tumour incidence was low, and in another similar study using a more strenuous level of significance ($p \leq 0.01$) negative results were reported (5).
4/18 ♀ rats histologically examined after oral administration of 300 mg kg^{-1} 1 × wk^{-1} for 57 wk had bladder cancers. This supports the possibility that production of the active carcinogenic metabolite in rats is influenced by a non-enzymatic, pH-dependent, urinary mechanism (6).
Weak carcinogen, producing 1 hepatoma, in rats after oral administration of 30 mg kg^{-1} day^{-1} for 1 yr. Survival in ♀ rats was much lower than for ♂ rats (7).

Metabolism and toxicokinetics
The corresponding *N*-arylformamide and *N*-arylacetamide were identified in urine of rabbits after oral administration of 2-naphthylamine (8).
Metabolites identified in rats, rabbits, dogs or guinea pigs include 2-amino-1-naphthol in all four species, 6-amino-2-naphthol in rats and rabbits, *N*-acetyl-*S*-(2-aminonaphth-1-yl)-L-cysteine in rats and dogs (9).
Studies of *in vitro* metabolic N-oxidation in dog bladder found N-oxidation occurred mostly in the liver and the bladder played, at most, a minor role in the formation of the presumed proximate urinary carcinogens (9).

Irritancy
Mild skin irritant and may cause contact dermatitis (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1538 with metabolic activation positive (10,11).
Salmonella typhimurium TA100 without metabolic activation positive (12).
Escherichia coli WP2 with metabolic activation negative (13).
Saccharomyces cerevisiae gene conversion with and without metabolic activation positive (14).

Sex-linked recessive mutations in *Drosophila melanogaster* equivocal (15).
Induced unscheduled DNA synthesis in human hepatocytes (16) and fibroblasts *in vitro*, and chromosomal aberrations and sister chromatid exchanges in Chinese hamster cells *in vitro* with metabolic activation. Induced DNA strand breaks in animals cells *in vitro*, and unscheduled DNA synthesis in primary rat hepatocytes *in vitro* (17).
Mouse bone marrow micronucleus test negative (18).
Mutagenic in the mouse spot test and induced DNA strand breaks in hepatocytes of rats treated *in vitro* (17).
Mice and rats treated *in vivo* had increased incidences of sister chromatid exchanges (19).
May undergo PGS-catalysed metabolic activation to products causing DNA damage in human fibroblasts (20).

Legislation

Land disposal prohibited under US Federal Resource Conservation and Recovery Act (21).
An EC Directive on the protection of the health and safety of workers from the risk related to chemical agents at work has been adopted. It prohibits the production, manufacture or use at work of 2-naphthylamine and its salts. Member states must implement the Directive by 5 May 2001 (22).

Other comments

Toxicity and hazards reviewed (23).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (24).

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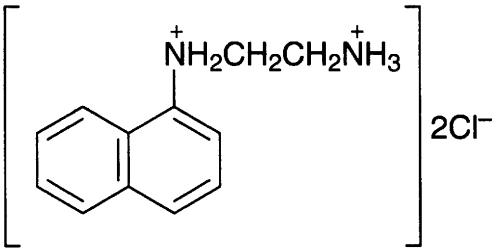
N25 *N*-(1-naphthyl)ethylenediamine dihydrochloride



$C_{12}H_{16}N_2Cl_2$ **Mol. Wt.** 259.18 **CAS Registry No.** 1465-25-4

Synonyms *N*-1-naphthalenyl-1,2-ethanediamine dihydrochloride; NCI-C03281

EINECS No. 215-981-2 **RTECS No.** KV 5330000

Uses Determination of sulfanilamide in body fluids; also in determination of potassium, nitrites and sulfates.

Physical properties

M. Pt. 188-190°C

Solubility Water: readily soluble in hot water, slightly soluble in cold. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

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

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via feed. No evidence of carcinogenicity in rats or mice (2).

References

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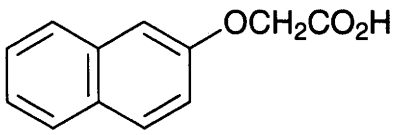
N26 (2-naphthyloxy)acetic acid



$C_{12}H_{10}O_3$ **Mol. Wt.** 202.21 **CAS Registry No.** 120-23-0

Synonyms 2-naphthalenyloxyacetic acid; 2-naphthoxyacetic acid; β-naphthoxyacetic acid

EINECS No. 204-380-0 **RTECS No.** AI 9659000

Uses Plant growth regulator.

Physical properties

M. Pt. 156°C

Solubility Water: sparingly soluble. Organic solvents: acetic acid, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1000 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 III (4).

Other comments

Non-toxic to bees (1).

References

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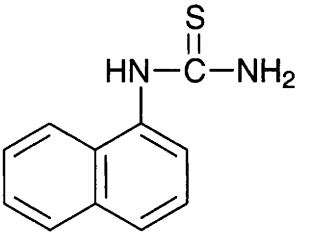
N27 1-naphthylthiourea



$C_{11}H_{10}N_2S$ **Mol. Wt.** 202.28 **CAS Registry No.** 86-88-4

Synonyms ANTU; 1-(1-naphthyl)-2-thiourea; α-naphthothiourea; *N*-(1-naphthyl)thiourea; α-naphthylthiocarbamide

EINECS No. 201-706-3 **RTECS No.** YT 9275000

Uses Formerly used as a rodenticide.

Physical properties

M. Pt. 198°C **Volatility** v.p. <7.5 mmHg at 20°C

Solubility Water: 0.06 g 100 ml^{-1} at 25°C. Organic solvents: acetone, triethylene glycol

Occupational exposure

DE-MAK 0.3 mg m^{-3} (inhalable fraction of aerosol)

FR-VME 0.3 mg m^{-3}

US-TWA 0.3 mg m^{-3}

UN No. 1651 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Very toxic if swallowed – Possible risk of irreversible effects (R28, R40)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the eyes – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S25, S36/37, S45)

Ecotoxicity

Bioaccumulation
Calculated bioconcentration of 17 indicates bioconcentration in fish is unlikely (1).

Environmental fate

Abiotic removal
Trophospheric $t_{1/2}$ 6 hr from photochemically produced hydroxyl radicals (2).

Adsorption and retention
Estimated soil adsorption coefficient 130 (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral dog, rat 0.38, 6 mg kg^{-1}, respectively (3,4).
LD_{50} intraperitoneal rat 2470 μg kg^{-1} (5).
LD_{50} intraperitoneal mouse, dog 10, 16 mg kg^{-1}, respectively (6,7).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (8).
Cases of bladder tumours reported in rat catchers exposed to 1-naphthylthiourea which contained up to 0.2% 2-naphthylamine (a human carcinogen) (9).
Although no increased tumour incidence was reported in rats given 50-800 mg kg^{-1} for 2 yr orally or mice given 2.15 mg kg^{-1} intragastrically, IARC considered the studies inadequate for evaluation (8).

Metabolism and toxicokinetics
Rapidly absorbed from the gut, especially in the presence of fat. Differences between oral and parenteral LD_{50} suggest gut absorption may be incomplete in some species. Its lung toxicity appears to require activation by mixed-function oxidases at the thiocarbonyl moiety (8).
Metabolised by hepatic microsomes to α-naphthylurea and H_2S (10).

Irritancy
A case of eczema has been attributed to occupational exposure (6).

Genotoxicity

Salmonella typhimurium TA1537, TA1538, TA98 with metabolic activation positive, without metabolic activation negative (9).
Salmonella typhimurium TA1535 with and without metabolic activation negative (9).
Did not induce unscheduled DNA synthesis in primary rat hepatocytes *in vitro* (11).
Induced a transformed phenotype in Syrian hamster ovary cells *in vitro* (8).

Other effects

Other adverse effects (human)
Non-fatal poisoning from accidental or suicidal ingestion of a mixture of 1-naphthylthiourea and chloralose has been reported. Symptoms resemble chloralose toxicity, including coma, motor agitation and respiratory difficulty. Ingestion of 15 g 1-naphthylthiourea with alcoholic beverage caused vomiting 75 min later, dyspnoea and cyanosis (8).

Any other adverse effects

Causes massive pleural effusion and pulmonary oedema in experimental animals (12-14).

The perfusion of isolated rat lung with 10 mg l^{-1} 1-naphthylthiourea for 90 min increased the lung weight and perfusion pressure and decreased 5-hydroxytryptamine metabolic rate in the lung. It was demonstrated that 1-naphthylthiourea toxicity to lung does not require extrapulmonary metabolism and pulmonary activation by cytochrome P_{450} (15).

Oral albino rats 10 mg kg^{-1}, after 20 hr 40% was excreted in urine and <1% in faeces. Maximum 1-naphthylthiourea content reached in rat pleural effusion, lung, skeletal muscles and pancreas 4 hr after oral administration of 10 mg kg^{-1} (16).

Legislation

Designated as hazardous waste by the US EPA since 1980; disposal must comply with Federal hazardous waste management programme regulations (8).

Land disposal prohibited under US Federal Resource Conservation and Recovery Act (17).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (18).

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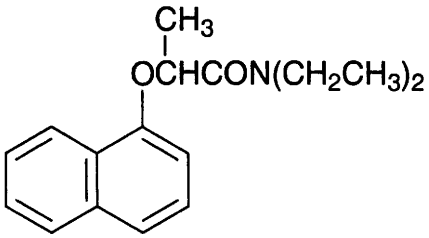
N28 napropamide



$C_{17}H_{21}NO_2$ **Mol. Wt.** 271.36 **CAS Registry No.** 15299-99-7

Synonyms *N,N*-diethyl-2-(1-naphthyloxy)propionamide; *N,N*-diethyl-2-(1-naphthalenyloxy)propanamide; 2-(α-naphthoxy)-*N,N*-diethylpropionamide; Devrinol

EINECS No. 239-333-3 **RTECS No.** UE 3600000

Uses Selective systemic herbicide.

Physical properties

M. Pt. 74.8-75.5°C **Partition coefficient** log P_{ow} 3.362 **Volatility** v.p. 3.75×10^{-6} mmHg at 25°C
Solubility Water: 73 mg l^{-1} at 20°C. Organic solvents: acetone, ethanol, hexane, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) goldfish, rainbow trout, bluegill sunfish >10, 16.6, 30 mg l^{-1}, respectively (1).

Invertebrate toxicity
LD_{50} 0.121 mg bee^{-1} (2).

Environmental fate

Degradation studies
Microbial degradation in soil is slow, $t_{1/2}$ 8-12 wk. Degradation products are: 2-(α-naphthoxy)-*N*-ethylpropionamide, 2-(α-naphthoxy)propionamide, 1-naphthol and 1,4-naphthoquinone (3).

Abiotic removal
Decomposed by sunlight; stable to hydrolysis between pH 4 and 10 (1).

Adsorption and retention
Sorption by montmorillonite clays decreased when dissolved in humic acid derived from peat (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >500 mg kg^{-1} (1).
LD_{50} dermal guinea pig, rabbit >2000, >4640 mg kg^{-1}, respectively (1).

Sub-acute and sub-chronic data
In 13-wk feeding trials rats receiving 50 mg kg^{-1} day^{-1} showed no ill-effects; 100 mg kg^{-1} day^{-1} caused weight loss, reduced haemoglobin level and raised serum alkaline phosphatase activity (1).

Metabolism and toxicokinetics
98.6% of oral dose to mammals is excreted (species and dose unspecified) within 96 hr (1).

Irritancy
Not irritating to eyes or skin (species and dose 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).
EC maximum residue limit for pome fruit is 0.1 ppm (1).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (7).
WHO Toxicity Class Table 5 (8).
EPA Toxicity Class III (formulation) (2).
ADI 0.1 mg kg^{-1} (2).

Other comments

Unstated stereochemistry.
Metabolic pathways reviewed (9).

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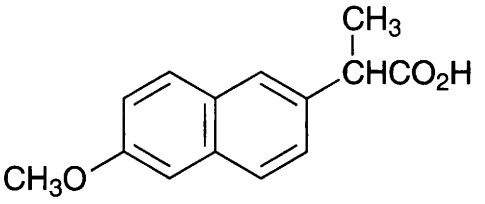
N29 naproxen



$C_{14}H_{14}O_3$ **Mol. Wt.** 230.26 **CAS Registry No.** 22204-53-1

Synonyms (+)-2-(6-methoxy-2-naphthyl)propionic acid; *d*-2-(6-methoxy-2-naphthyl)propionic acid; MNPA

EINECS No. 244-838-7 **RTECS No.** UF 5275000

Uses Non-steroidal anti-inflammatory drug.

Physical properties

M. Pt. 157-158°C
Solubility Water: insoluble. Organic solvents: chloroform, diethyl ether, ethanol, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 534, 1234 mg kg^{-1}, respectively (1).
LD_{50} intravenous mouse, rat 435, 575 mg kg^{-1}, respectively (1).

Metabolism and toxicokinetics

Readily absorbed from the human gut; peak plasma concentrations are reached in 2-4 hr, increasing proportionally with dose up to 500 mg day^{-1}; at higher doses increased clearance is due to saturation of plasma proteins. At therapeutic levels, >99% is bound to plasma proteins. Plasma $t_{1/2}$ 13 hr. 95% is excreted in urine as naproxen and 6-*O*-desmethylnaproxen and their conjugates. It crosses the placenta and is excreted in breast milk (2).

Other effects

Other adverse effects (human)

Adverse effects include haemolytic anaemia, aplastic anaemia, agranulocytosis, corneal opacities, erythema, skin eruptions, jaundice, kidney failure and necrosis, and renal nephritis. Gastro-intestinal effects are more frequently reported. Hypersensitivity (rhinorrhoea, dyspnoea and wheezing) has been reported in aspirin-sensitive patients (2).

Other comments

Pharmacology (1,3-5), mode of action (6), metabolism (7) and clinical studies (8,9) reviewed. Bioavailability reviewed (10).

References

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3. Brogen, R. N. et al *Drugs* 1979, **18**, 241-277.
4. Todd, P. A. et al *Drugs* 1990, **40**(1), 91-137.
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7. Runkel et al *J. Pharm. Sci.* 1972, **61**, 703.
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9. Runkel et al *Chem. Pharm. Bull.* 1972, **20**, 1457.
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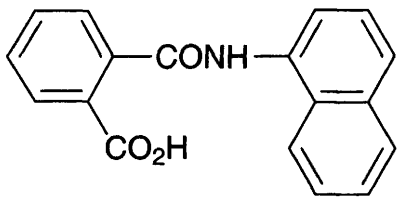
N30 naptalam



$C_{18}H_{13}NO_3$ **Mol. Wt.** 291.31 **CAS Registry No.** 132-66-1

Synonyms *N*-1-naphthylphthalamic acid; 2-[(1-naphthalenylamino)carbonyl]benzoic acid; α-naphthylphthalamic acid

RTECS No. TH 7350000

Uses Pre-emergence, selective herbicide. Analytical reagent for thorium and zirconium.

Physical properties

M. Pt. 185°C **Specific gravity** 1.36 at 20°C **Partition coefficient** log P_{ow} 0.104 at pH 5 **Volatility** v.p. <0.99 mmHg at 20°C
Solubility Water: 200 mg l^{-1} at 20°C. Organic solvents: dimethylformamide, dimethyl sulfoxide

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 76, 354 mg l^{-1}, respectively (1).

Environmental fate

Degradation studies
Residual activity 3-8 wk, depending on soil type and moisture content. Completely decomposes in soil in 6-8 wk by microbial degradation (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 8200 mg kg^{-1} (1).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (8 day) mallard duck, bobwhite quail >10000 mg kg^{-1} diet (1).
In 90-day feeding trials rats and dogs fed 1000 mg sodium salt kg^{-1} showed no ill-effects (1).

Irritancy
Eye irritant (species and dose unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class Table 5 (5).
EPA Toxicity Class I (formulation) (6).
ADI 0.05 mg kg^{-1} (6).

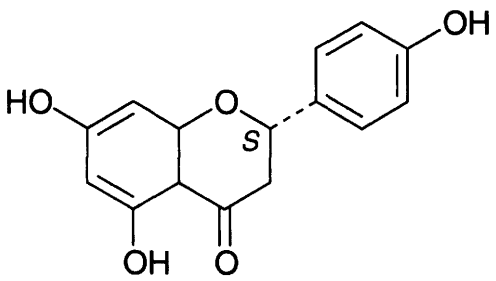
Other comments

Non-toxic to bees (1).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Smith, A. E. et al *J. Agric. Food Chem.* 1957, **5**, 748.
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. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
6. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK

N31 naringenin



$C_{15}H_{12}O_5$ **Mol. Wt.** 272.26 **CAS Registry No.** 480-41-1

Synonyms 2,3-dihydro-5,7-dihydroxy-2-(4-hydroxyphenyl)-4*H*-1-benzopyran-4-one; 4',5,7-trihydroxyflavanone; (–)-(2*S*)-naringenin; (–)-naringenin; (2*S*)-naringenin; naringenine; naringetol; salipurol; salipurpol

EINECS No. 207-550-2

Occurrence Polyphenolic plant flavonoid.

Physical properties

M. Pt. 251 °C (needles from dilute alcohol)
Solubility Water: practically insoluble. Organic solvents: benzene, ethanol, ether

Environmental fate

Degradation studies
Four strains of *Clostridium* capable of cleaving the C-ring of naringenin between C-3 and C-4 have been isolated from human faecal flora (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (2).

Other effects

Any other adverse effects
Naringenin induced a concentration-dependent peroxidation of nuclear membrane lipids concurrent with DNA strand breaks in isolated rat liver nuclei under aerobic conditions. Polyphenolic flavonoids such as naringenin are generally considered as anti-oxidants and anticarcinogens. The authors suggest that polyphenolic flavonoids may play a dual role in mutagenesis and carcinogenesis (3).
Naringenin binds to rat α-fetoprotein with Kd *c.* 5×10^{-7}. The authors suggest that this is sufficiently high that naringenin may modulate estradiol and estrone binding to rat α-fetoprotein *in vivo* when present at dietary levels (4).

Other comments

Naringenin can have both oestrogenic and anti-oestrogenic activity (5).
Naringenin suppresses mutagenesis in *Salmonella typhimurium* TA100 NR induced by the direct-acting carcinogen *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine (MMNG). It appears to act by preventing the passage of the carcinogen into bacterial cells or by altering some cellular processes (6).
Naringenin (300 μg plate^{-1}) showed antimutagenic activity (> 70% inhibition rate) against the mutagen aflotoxin B1 (1 μg plate^{-1}) in *Salmonella typhimurium* TA100 with metabolic activation. It showed little antimutagenic activity towards MNNG (0.5 μg plate^{-1}) at 300 μg plate^{-1} (7).

In vitro and *in vivo* studies showed that a number of flavonoid aglycones inhibited the hyaluronidase activity of five different venoms dose-dependently but that naringenin, catechin and flavonoid glycosides had no effect (8).
The two-stage carcinogenesis by 7,12-dimethylbenz[*a*]anthracene and 12-*O*-tetradecanoylphorbol-13-acetate in mice was inhibited by flavonol glycosides, but not by the flavonone naringenin (9).
Naringenin inhibited the hydroxylation of benzo[*a*]pyrene by human liver microsomes (10).
Naringenin inhibited the oxidation of the dihydropyridines nifedipine and felodipine in human liver microsomal preparations. The same human liver cytochrome P450 (IIIA4) appears to be a major catalyst in both nifedipine oxidation and aflatoxin B1 activation. Several flavones inhibited the *in vitro* activation of aflatoxin B1 in system employing umuC gene activation due to DNA damage in *Salmonella typhimurium* Ta1535/pSK1002, with naringenin being as effective as any. The high concentration of derivatives of naringenin in certain citrus fruits may be of relevance to cancer chemoprevention involving those carcinogens that are activated by cytochrome P450IIIA4 (11).
*Phyto*chemical mimicry of reproductive hormones and modulation of herbivore fertility by phytoestrogens reviewed (12).

References

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2. Brown, J. P. et al *Mutat. Res.* 1979, **66**, 223-240.
3. Sahu, S. C. et al *Food Chem. Toxicol.* 1997, **35**(5), 443-447.
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6. Francis, A. R. et al *Carcinogenesis* 1989, **10**(10), 1953-1955.
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9. Yasukawa, K. et al *Chem. Pharm. Bull.* 1990, **38**(3), 774-776.
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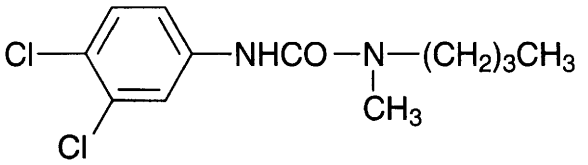
11. Guengerich, F. P. et al *Carcinogenesis (London)* 1990, **11**(12), 2275-2279.
12. Hughes, C. R., Jr. *Environ. Health Perspect.* 1988, **78**, 171-175

N32 neburon



$C_{12}H_{16}Cl_2N_2O$ **Mol. Wt.** 275.18 **CAS Registry No.** 555-37-3

Synonyms 1-butyl-3-(3,4-dichlorophenyl)-1-methylurea; *N*-butyl-*N'*-(3,4-dichlorophenyl)-*N*-methyl urea; 3-(3,4-dichlorophenyl)-1-methyl-1-*n*-butylurea; Granurex; Kloben

EINECS No. 209-096-0 **RTECS No.** YS 3810000

Uses Selective pre-emergence herbicide.

Physical properties

M. Pt. 102-103°C
Solubility Water: 5 mg l^{-1} at 25°C

Ecotoxicity

Fish toxicity

90% mortality of four unspecified fish species at 0.6-0.9 mg l^{-1} for 96 hr (1).

Invertebrate toxicity

EC_{50} (10 day) *Chlorococcum* sp., *Dunaliella terticulata* 0.02 mg l^{-1} (2).

Environmental fate

Degradation studies

Residual activity in soil 3-4 months. Degradation involves dealkylation of the terminal nitrogen, ring hydroxylation, degradation to dichlorohydroxyaniline, presumably followed by ring opening (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat>11000 mg kg^{-1} (1).

LD_{50} intravenous mouse 180 mg kg^{-1} (3).

Irritancy

15% suspension in dimethyl phthalate is a mild skin irritant in guinea pigs (duration unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

WHO Toxicity Class Table 5 (6).

Other comments

Low toxicity to bees.

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Walsh, G. E. *Hyacinth Control J.* 1972, **10**, 45-48.
3. US Army Armament Research and Development Command NX 03862, Aberdeen Proving Ground, MD, USA.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 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

N33 neodymium

Nd

Nd **Mol. Wt.** 144.24 **CAS Registry No.** 7440-00-8

EINECS No. 231-109-3 **RTECS No.** QO 8575000

Occurrence 12-24 ppm of Earth's crust; found in cerium cores; cerite, monazite sand and gadolinite.

Physical properties

M. Pt. ~1024°C **B. Pt.** 3127°C **Specific gravity** 7.003

Mammalian & avian toxicity

Acute data

TD_{Lo} intracerebral human 17 μg kg^{-1} (1).

References

1. *J. Clin. Invest.* 1942, **21**, 447

N34 neomycin

CAS Registry No. 1404-04-2

Synonyms Myacyne; Mycrifradin; Nivemycin

EINECS No. 215-766-3 **RTECS No.** QP 3850000

Uses Aminoglycoside antibiotic, active agent many strains of Gram-negative bacteria.

Occurrence Produced by *Streptomyces fradine.*

Ecotoxicity

Invertebrate toxicity

1% of coliform bacteria isolated from sludge samples from a wastewater treatment plant were resistant to neomycin (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2750, 2880 mg kg^{-1}, respectively (2,3).

LD_{50} intraperitoneal mouse 116 mg kg^{-1} (3).

LD_{50} intravenous mouse 35 mg kg^{-1} (4).

LD_{50} subcutaneous rat 200 mg kg^{-1} (5).

Metabolism and toxicokinetics

Poorly absorbed from the human gut; 97% of oral doses are excreted unchanged in faeces. 3 g by mouth produces a peak plasma concentration of up to 4 μg ml^{-1}. Mucosal damage or inflamation may increase absorption. It is rapidly excreted by the kidneys after absorption; $t_{1/2}$ 2-3 hr (6).

Irritancy

Neomycin sulfate was classified as a mild skin irritant in human studies with a 20% test concentration (duration unspecified); based on this and guinea pig maximisation test and mouse ear swelling test data a potency index of 2.66 (moderate skin irritant) has been estimated (7).

Neomycin was one of the commonest allergens in a cutting fluid patch-test series in humans (8).

Genotoxicity

Escherichia coli DNA cell-binding assay in presence of lysozyme or liver extract positive (9).

Other effects

Other adverse effects (human)

Nephrotoxicity and ototoxicity preclude parenteral administration. Large oral doses cause nausea, vomiting and diarrhoea; prolonged oral administration can cause a severe malabsorption syndrome and supra-infection. It has a neuromuscular blocking action and respiratory depression and arrest following intraperitoneal instillation have been fatal. Hypersensitivity is common and cross-sensitisation to other aminoglycoside antibiotics may occur (6).

References

1. Radtke, T. M. et al *J. Environ. Health* 1989, **52**(2), 102-105.
2. *Toxicol. Appl. Pharmacol.* 1971, **18**, 185.
3. Korzyoski, T. et al (Eds.) *Antibiotics: Origin, Nature and Properties* 1978, Am. Soc. Microbiol., Washington, DC, USA.
4. *Arzneim.-Forsch.* 1963, **13**, 391.
5. *Arzneim.-Forsch.* 1962, **12**, 597.
6. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
7. Gad, S. C. *J. Appl. Toxicol.* 1988, **8**(5), 361-368.
8. Grattan, C. E. H. et al *Contact Dermatitis* 1989, **20**, 372-376.
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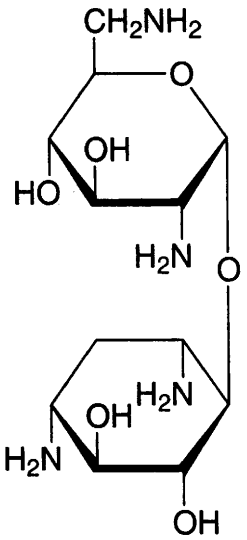
N35 neomycin A



$C_{12}H_{26}N_4O_6$ **Mol. Wt.** 322.36 **CAS Registry No.** 3947-65-7

Synonyms Neamine; Nebramycin; Negamicin; 2-deoxy-4-O-(2,6-diamino-2,6-dideoxy-α-D-gluco-pyranosyl)-D-streptamine

RTECS No. QP 3860000

Occurrence Component of the antibiotic complex neomycin; formed by the hydrolysis of neomycins B and C.

Physical properties

M. Pt. 225-226°C (decomp.)

Mammalian & avian toxicity

Acute data

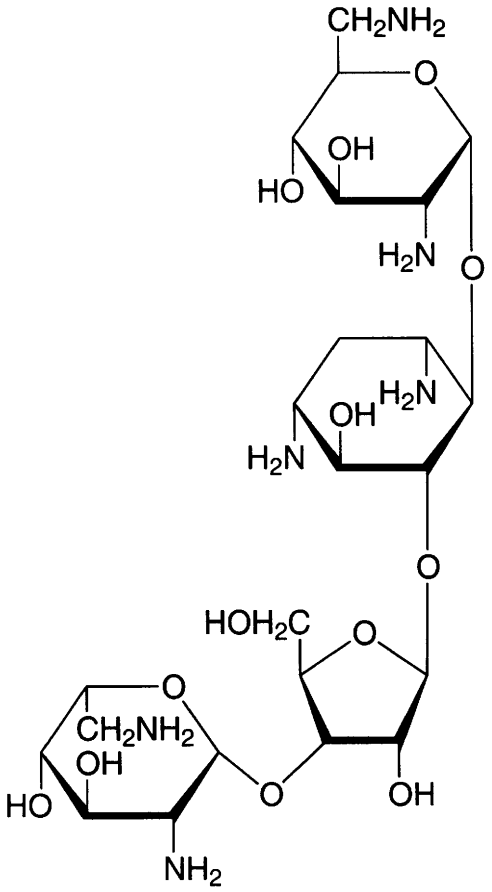
LD_{50} intravenous mouse 125-320 mg kg^{-1} (1,2).

LD_{50} subcutaneous mouse 1250 mg kg^{-1} (2).

References

1. *J. Antibiot.* 1974, **27**, 677.
2. Korzyoski, T. et al (Eds.) *Antibiotics: Origin, Nature and Properties* 1978, Am. Soc. Microbiol., Washington, DC, USA

N36 neomycin B



$C_{23}H_{46}N_6O_{13}$ **Mol. Wt.** 614.65 **CAS Registry No.** 119-04-0

Synonyms *O*-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl-(1→4)-*O*-[*O*-2,6-diamino-2,6-dideoxy-β-L-idopyranosyl-(1→3)-β-D-ribofuranosyl]-(1→5)]-2-deoxy-D-streptamine; Framyetin; Actilin

EINECS No. 204-292-2 **RTECS No.** QP 4025000

Uses Antibacterial.

Mammalian & avian toxicity

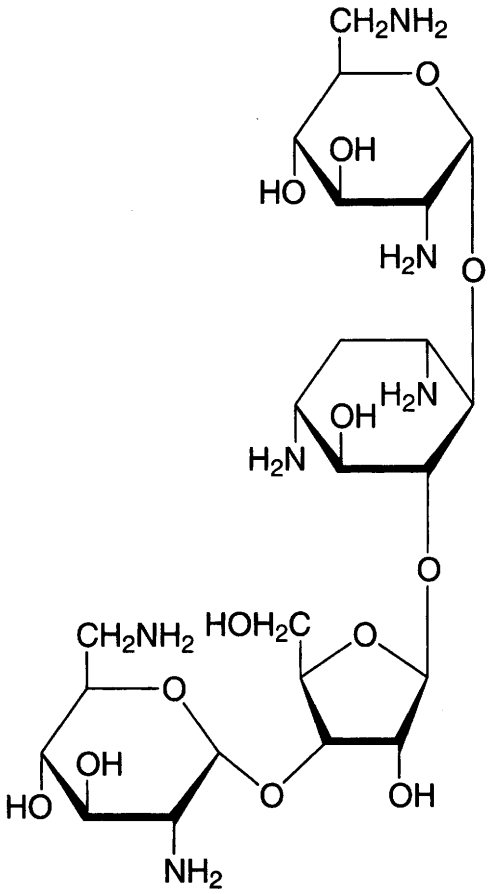
Acute data

LD_{50} intravenous mouse 24-64 mg kg^{-1} (1,2).
LD_{50} intraperitoneal mouse 250 mg kg^{-1} (3).
LD_{50} subcutaneous mouse 220 mg kg^{-1} (4).

References

1. *J. Antibiot.* 1974, **27**, 677.
2. *Ann. Pharm. Franc.* 1953, **11**, 44.
3. Korzyoski, T. et al (Eds.) *Antibiotics: Origins, Nature and Properties* 1978, Am. Soc. Microbiol., Washington, DC, USA.
4. *Handbook of Toxicology* 1959, W. B. Saunders, Philadelphia, PA, USA

N37 neomycin C



$C_{23}H_{46}N_6O_{13}$ **Mol. Wt.** 614.65 **CAS Registry No.** 66-86-4

RTECS No. QP 4200000

Uses Antibacterial.

Mammalian & avian toxicity

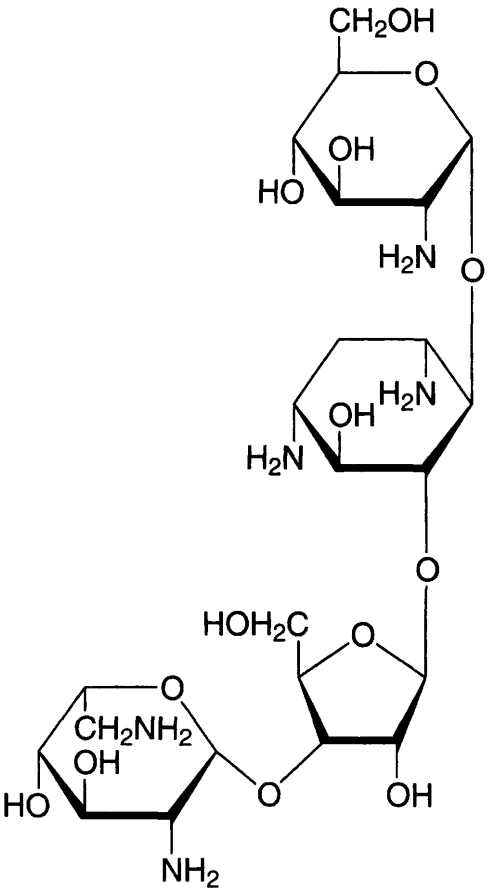
Acute data

LD_{50} intraperitoneal mouse 116 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 290 mg kg^{-1} (2).
LD_{50} intravenous mouse 44 mg kg^{-1} (3).

References

1. *CRC Handbook of Antibiotic Compounds* 1980, CRC Press, Boca Raton, FL, USA.
2. *Handbook of Toxicology* 1959, W. B. Saunders, Philadelphia, PA, USA.
3. *J. Antibiot.* 1974, **27**, 677

N38 neomycin E



$C_{23}H_{45}N_5O_{14}$ **Mol. Wt.** 615.64 **CAS Registry No.** 7542-37-2

Synonyms aminosidin; antibiotic SF 767B; *O*-2-amino-2-deoxy-α-D-glucopyranosyl-(1→4)-*O*-[*O*-2,6-diamino-2,6-dideoxy- β-L-idopyranosyl-(1→3)-β-D-ribofuranosyl-(1→5)]-2-deoxy-D-steptamine; Crestomycin; Estomycin; hydroxymycin; Pargonyl

EINECS No. 231-423-0 **RTECS No.** WK 2315000

Physical properties

Solubility Water: soluble. Organic solvents: methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 2275, 21620 mg kg^{-1}, respectively (1,2).

LD_{50} subcutaneous mouse, rat 423, 1010 mg kg^{-1}, respectively (3,4).

LD_{50} intravenous mouse, rat 90, 156 mg kg^{-1}, respectively (1,3).

References

1. Korzyoski, T. et al (Eds.) *Antibiotics: Origin, Nature and Properties* 1978, Am. Soc. Microbiol., Washington, DC, USA.
2. *Chemotherapy* 1968, **16**, 124.
3. *Antibiot. Chemother. (Washington, D. C.)* 1959, **9**, 730.
4. *Antibiot. Chemother. (Washington, D. C.)* 1962, **12**, 243

N39 neopentane

$$C(CH_3)_4$$

C_5H_{12} **Mol. Wt.** 72.15 **CAS Registry No.** 463-82-1

Synonyms tetramethylmethane; *tert*-pentane; 2,2-dimethylpropane; 1,1,1-trimethylethane

EINECS No. 207-343-7 **RTECS No.** TY 1190000

Occurrence In petroleum naphtha.

Physical properties

M. Pt. –19.8°C **B. Pt.** 9.5°C **Flash point** –7°C **Partition coefficient** log P_{ow} 3.11

Occupational exposure

DE-MAK 1000 ppm (3000 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. 2044 **HAZCHEM Code** 2WE **Conveyance classification** flammable gas

Supply classification extremely flammable

Risk phrases Extremely flammable (R12)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Mammalian & avian toxicity

Acute data

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

Legislation

Log P_{ow} exceeds the European Union recommended limit of 3.0 (2).

Other comments

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

References

1. *Hind. Antibiot. Bull.* 1968, **10**, 206.
2. *1967 Directive on Classification, Packaging and Labelling of Dangerous Substances 67/548/EEC; 7th Amendment EEC Directive 91/32/EEC* 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

N40 neopentyl glycol

$$(H_3C)_2C(CH_2OH)_2$$

$C_5H_{12}O_2$ **Mol. Wt.** 104.15 **CAS Registry No.** 126-30-7

Synonyms 2,2-dimethyl-1,3-propanediol; dimethylolpropene; hydroxypiralyl alcohol; neopentanediol; neopentylene glycol

EINECS No. 204-781-0 **RTECS No.** TY 5775000

Uses Catalyst. Cross-linking agent. Fire-proofing agent.

Physical properties

M. Pt. 127°C **B. Pt.** 208°C **Flash point** 107°C

Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies

Confirmed nonbiodegradable (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 3200 mg kg^{-1} (2).

References

1. *Ministry of International Trade and Industry (MITI)* 1984, Japan.
2. Kodak Company Report, 21 May, 1971

N41 neopentyl glycol diacrylate

$$(H_2C{=}CHCO_2CH_2)_2C(CH_3)_2$$

$C_{11}H_{16}O_4$ **Mol. Wt.** 212.25 **CAS Registry No.** 2223-82-7

Synonyms 2-propenoic acid, 2,2-dimethyl-1,3-propanediyl ester; acrylic acid, 2,2-dimethyltrimethylene ester; 2,2-dimethyltrimethylene diacrylate; neopentanediol diacrylate; NK Ester A-NPG

EINECS No. 218-741-5 **RTECS No.** AS 8925000

Uses Used in photo-curing materials including those for industrial and dental use.

Physical properties

Flash point >110°C **Specific gravity** 1.031

Occupational exposure

Supply classification toxic

Risk phrases Toxic in contact with skin – Irritating to eyes and skin – May cause sensitisation by skin contact (R24, R36/38, R43)

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 eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S39, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6730 mg kg^{-1} (1).

LD_{50} dermal rabbit 400 mg kg^{-1} (2).

Irritancy

Dermal rabbit 500 mg, open, caused severe irritation (1).

Sensitisation

Apparently conflicting guinea pig sensitisation data on diacrylates and dimethacrylates are analysed in terms of the relative alkylation index model. Analysis shows overload effect, in that some of the diacrylates have failed to show sensitisation when tested at high induction doses, but are revealed as strong sensitisers when tested at lower induction doses (3).

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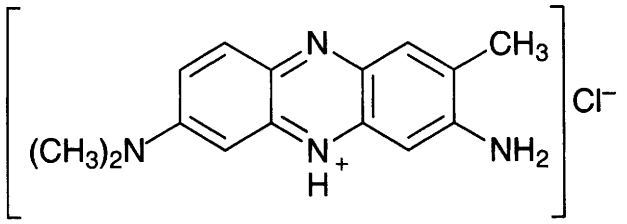
N42 Neutral Red



$C_{15}H_{17}ClN_4$ **Mol. Wt.** 288.78 **CAS Registry No.** 553-24-2

Synonyms C.I. Basic Red 5; N^8,N^8,3-trimethyl-2,8-phenazinediamine monohydrochloride; C.I. 50040

EINECS No. 209-035-8 **RTECS No.** SG 1400000

Uses As an indicator, and biological stain for Golgi apparatus in cells.

Physical properties

M. Pt. 290°C (decomp.)

Ecotoxicity

Invertebrate toxicity

LC_{50} (duration unspecified) *Cyprinus carpio, Daphnia carinata, Indoplanorbis exustus,* larvae of *Sympetrum frequens* and tadpoles of *Bufo bufo japonicus* and *Rana brevipoda porosa* 1.5->40 ppm (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Photocarcinogen when applied (dose and duration unspecified) to mouse skin followed by long UV and visible light (2).

Teratogenicity and reproductive effects

Malformations including ectopic abdominal viscera, stunting, lower body curvature and dorsal displacement of limbs reported in chick embryos after application of Neutral Red during day-2 of incubation (3).

Genotoxicity

Salmonella typhimurium (strains unspecified) with and without metabolic activation positive (4-6).

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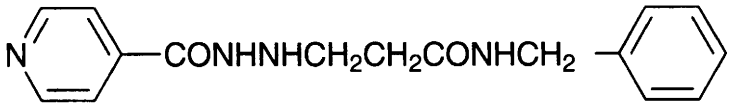
N43 nialamide



$C_{16}H_{18}N_4O_2$ **Mol. Wt.** 298.34 **CAS Registry No.** 51-12-7

Synonyms *N'*-[(2-benzylcarbamoyl)ethyl]isonicotinoylhydrazide; *N*-benzyl-β-(isonicotinoyl-hydrazino)propionamide; 4-pyridinecarboxylic acid, 2-[3-oxo-3-[(phenylmethyl)amino]propyl]hydrazide; Surgex

EINECS No. 200-079-3 **RTECS No.** NS 1225000

Uses Irreversible inhibitor of monoamine oxidase types A and B, used as an antidepressant.

Physical properties

M. Pt. 152-153°C

Solubility Water: sparingly soluble

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 590 mg kg^{-1} (1).

LD_{50} intravenous mouse 120 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse, rat 200, 760 mg kg^{-1}, respectively (2,3).

Teratogenicity and reproductive effects

Reproductive effects reported in mice following subcutaneous administration of a total dose of 24 mg kg^{-1} on days 1-6 of pregnancy (4).

Genotoxicity

Salmonella typhimurium TA1535 with metabolic activation positive; TA1537, TA1538 without metabolic activation negative (5).

Other comments

Reacts with oxygen to form hydrogen peroxide, which inactivates DNA (6).

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N44 nickel

Ni

Ni **Mol. Wt.** 58.69 **CAS Registry No.** 7440-02-0

Synonyms

EINECS No. 231-111-4 **RTECS No.** QR 5950000

Uses Manufacture of Raney nickel catalysts, Monel metal, stainless steel and nickel-chrome resistance wire. Nickel-plating. Catalyst for oil (and other organic substances) hydrogenation.

Occurrence Occurs free in meteorites. Abundance in earth's crust: 0.018%. Found in many ores as sulfides, arsenides, antimonides, oxides or silicates occurring mainly as the ores pentlandite and garnierite. May enter surface water (naturally) from three sources, as particulate matter in rain water, through dissolution of primary bedrock minerals and from secondary soil phases.

Physical properties

M. Pt. 1547-1555°C **B. Pt.** 2837°C (calc.) **Specific gravity** 8.90 at 25°C **Volatility** v.p. 1 mmHg at 1810°C

Occupational exposure

FR-VME 1 mg m^{-3}
JP-OEL 1 mg m^{-3}
SE-LEVL 0.5 mg m^{-3}
UK-LTEL MEL 0.5 mg m^{-3}
US-TWA 1.5 mg m^{-3}
Supply classification harmful
Risk phrases Possible risk of irreversible effects – May cause sensitisation by skin contact (R40, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing (S2, S22, S36)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) banded killifish, striped bass, pumpkin seed, white perch, American eel, carp 6.2-46.2 mg l^{-1} (salt unspecified) (1,2).

Rainbow trout exposed to nickel (salt unspecified) had a reduction in glucidic stores which is consistent with direct metal interactions with membranes and enzyme thiolic groups of cells of the pancreas (3).

Life-cycle study fathead minnow (pH 7.8, 18°C, 210 mg $CaCO_3$ hardness) ≤0.38 mg l^{-1} (salt unspecified) did not adversly effect reproduction, survival or growth, but 0.78 mg l^{-1} (salt unspecified) significantly effected the number and hatchability of eggs, although growth survival of the 1st generation was not effected (4).

LC_{50} (74 hr) carp eggs, larvae 6.1, 8.4 mg l^{-1} (salt unspecified), respectively. 3 mg l^{-1} caused increased in the numbers of abnormal larvae and embryos which failed to hatch (5).

LC_{50} (from fertilisation to 4 days after hatching) channelcatfish, goldfish 0.71, 2.78 mg l^{-1} (salt unspecified), respectively) (6).

Invertebrate toxicity

Growth inhibition of filamentous fungi *Achyla* sp. 5 mg l^{-1} (salt unspecified) *Aspergillus niger*, *Gliocladium* sp. 1000 mg l^{-1} (salt unspecified) (7).

Growth inhibition actinomycetes and eubacteria (non-marine and marine) 5-30 mg l^{-1} (salt unspecified) and yeasts 1-40 mg l^{-1} (salt unspecified) (8).

Growth inhibition blue-green algae 1-5 mg l^{-1} (salt unspecified), *Chlorella* sp. lethal concentrations 10-30 mg l^{-1} (salt unspecified) (9).

Growth inhibition *Pediastrum tetras, Ankistrodesmus falcatus, Scenedesmus quadricauda, Scenedesmus dimorphus* 0.1 mg l^{-1}. No effect on *Anabaena cylindrica* at 0.6 mg l^{-1} (salt unspecified) (10).
EC_{50} growth inhibition (7 day) 24°C, pH 6.3-6.9 0.9925 mg l^{-1} (salt unspecified) (11).
Lemna minor (3 wk) 0.05 mg l^{-1} (salt unspecified) stimulate growth; >0.1 mg l^{-1} (salt unspecified) inhibited growth (12).
LC_{50} (48 hr) midge larvae 1st instar, 2nd instar 79.5 mg l^{-1} 169 mg l^{-1} (salt unspecified), respectively (13).
Midge larvae (30 day) from egg to pupation 0-25 mg l^{-1} (salt unspecified) had little effect on percentage hatch but larval growth was significantly reduced at 2.5 mg l^{-1} (salt unspecified). Threshold concentration for effect on growth (calc.) 1.1 mg l^{-1} (13).
LC_{50} (64 hr) *Daphnia magna* 0.32 mg l^{-1} (salt unspecified) at 25°C (14).
LC_{50} (96 hr) *Juga plicifera, Physa gyrina* 0.237, 0.239 mg l^{-1} (salt unspecified), respectively (15).
EC_{50} (48 hr) immobilisation *Daphnia magna* 7.59 ppm (salt unspecified) (16).

Toxicity to other species

Four-year-old Scots pine (*Pinus sylvestris* L.) saplings did not survive in quartz sand treated with > 150 ppm Ni (as nickel sulfate). A copper sulfate/nickel sulfate combination was lethal at 15 ppm Cu + 15 ppm Ni (17).

Bioaccumulation

Terrestrial plants contain 0.05-5 mg kg^{-1} dry weight nickel (18).
Certain plants mostly of the genus *Ailyssum* growing on serpentine soils can accumulate nickel at concentrations >1000 mg kg^{-1} (19).
Algae in contaminated aquatic environments have been found to accumulate levels as high as 150.9 mg kg^{-1} dry weights (20).
The calculated bioconcentration factors for *Euglena gracilis, Elodea densa* and *Lemna minor* are 200-2000 (21-23).
Rainbow trout (180 day) in 1 mg l^{-1} (salt unspecified) in the water, showed little capacity for accumulation (24).
Coots resting and feeding by a pond that was used for fly ash disposal, no accumulation in coots' livers over 2 yr (25).
Brown trout exposed to water containing 0.1 or 10 μg l^{-1} $^{63}Ni^{2+}$ for 1 or 3 wk. After 1 wk exposure whole fish nickel concentrations were 3 × higher than the water concentrations and after 3 wk exposure they were 7-8 × higher than the water concentrations (26).
Earthworms from four locations had body nickel concentrations of 2.9-17.9 ppm (27).
Catfish exposed to sublethal nickel (salt unspecified) concentrations had nickel accumulated in kidney >gill >liver >intestine for 30 days after treatment. There was a dose-related effect observed with concentration and exposure time (28).

Environmental fate

Nitrification inhibition

Nickel (form unspecified) inhibits nitrification by denitrifying bacteria more than copper and zinc (29).
Threshold concentration for the inhibition of nitrification/denitrification by activated sludge 10 mg l^{-1} (form unspecified) (30).
100% inhibition of nitrification by activated sludge 5.0 mg l^{-1} (form unspecified) (31).
Threshold concentration for growth reduction of *Nitrosomonas* sp. 0.250 mg l^{-1} (32).

Degradation studies

The toxic effects of nickel (as Ni^{2+}) on activated sludge treatment efficiency were studied; ≤10 mg l^{-1} did not adversely effect treatment efficiency, whereas 25 mg l^{-1} severely upset the system (33).

Adsorption and retention

In brown forest and peat muck soils, nickel exhibited high mobility within the soil profile. Nickel accumulated in the top organic layer, concentration increased with depth in the subsequent mineral layer (34).
Most nickel compounds are relatively soluble at pH <6.5. At pHs >6.7 nickel is generally in the form of insoluble nickel hydroxides. Therefore acid rain has the effect of mobilising nickel in the soil and elevating levels in ground water (35).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 5 mg kg^{-1} guinea pig 5 mg kg^{-1} (form unspecified), respectively (36,37).
LD_{Lo} oral rabbit, rat 7.5, 12.5 mg kg^{-1} (form unspecified), respectively (38).
Intraperitoneal ♂ rat 3 or 6 mg kg^{-1} (form unspecified) kidney effects included a decrease in Bowmann's space, dilated tubules, loss of brush border, flattened epithelia and some regenerative activity (39).
LD_{Lo} intraperitoneal rabbit 7 mg kg^{-1} (form unspecified) (38).
LD_{Lo} intravenous dog, mouse 10, 50 mg kg^{-1} (form unspecified), respectively (40,41).
LD_{Lo} intratracheal rat 12 mg kg^{-1} (form unspecified) (42).

Sub-acute and sub-chronic data

Sprague-Dawley rats were administered nickel fumes or powdered nickel oxides (Ni_2O_3 and NiO) dispersed in saline at single doses up to 14.3 mg kg^{-1}, and repeated installations of 5.9 mg kg^{-1} of fumes. The Ni_2O_3 produced the most retarded body wt. gain and the severest changes in the lungs, followed by nickel fumes. The NiO powder produced no histopathological effects. Repeated administration of nickel fumes produced persistent oedema and proteinosis in the alveoli. The authors conclude that the acute lung toxicity observed on exposure to nickel fumes is mediated by the 3% Ni_2O_3 component and by the ultrafine particle size (43). Inhalation (≤20 month) hamster nickel-enriched fly ash 17 or 70 μg m^{-3}. Lung weights and volumes were significantly increased at 70 μg m^{-3} and dose-dependent anthracosis, interstitial reaction and bronchiolisation were also observed (44).
Inhalation (4 wk) rabbit 0.5-2.0 mg m^{-3} phagocytic activity of alveolar macrophages was increased (45,46).

Carcinogenicity and chronic effects

Nickel and nickel compounds, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (47).
Inhalation (21 month) mouse, rat, guinea pig 15 mg m^{-3} nickel powder (particles ≤4 μm) 6 hr day^{-1} 4-5 day wk^{-1}. All mice and most rats had died by 15 months and most guinea pigs by 18 months. Mice developed 2 (experimental group 20) lymphosarcomas. Rats and guinea pigs lungs showed abnormal multicentric adenomatoid formation affecting the alveolar structures and atypical proliferations of the epithelial lining of the terminal bronchioli. 1 guinea pig had an anaplastic intra-alveolar carcinoma. In all studies no control groups were used (48).
Inhalation (18 month) rat, hamster (dose unspecified) nickel powder no tumours observed (49).
Intramuscular (12 month), rat, hamster 5 mg nickel powder in 0.2 ml trioctanoin, 5 injections at monthly intervals. 38/50 rats developed fibrosarcomas within 11 months of treatment and 2/50 hamsters (50).
Intravenous (2 yr) mouse 0.005% suspension twice, rabbit 1% suspension at a rate of 0.5 ml kg^{-1} wkly for 6 wk, no tumours observed. Rat 0.5% suspension at a rate of 0.5 ml kg^{-1}. 7/25 animals developed tumours close to the site of injection within 7-8 months after the 1st injection (51).
Intrapleural (18 month) rat 5 monthly injections of 5 mg. 2/10 animals developed pleural mesotheliomas, there was none in the controls (52).
Intraperitoneal rat 46/48 developed sarcomas, mesotheliomas and carcinomas (53).
Subdermal implantation rat, within 104 wk 5/10 had developed sarcomas around the pellet, no tumours were observed in the control group (54).

Teratogenicity and reproductive effects

Nickel wire inserted into the uterine horn of rats on day-3 of pregnancy cause a decrease in the number of implantations and an increase in the number of resorption sites (55).
Three generations of rats exposed to 5 mg l^{-1} in drinking water (salt unspecified) showed no effects to fertility (56).
♀ Rats (7 month) ^{63}Ni at 5×10^{-1} to 5×10^{-4} mg kg^{-1} before and during pregnancy caused dose-dependent embryotoxic effects (57).

Metabolism and toxicokinetics

In vivo Syrian golden hamsters exposed to a highly respirable aerosol containing nickel-enriched fly ash (9% nickel content) 220 mg m^{-3} (single 6-hr exposure) or 190 mg m^{-3} (60 days 6 hr day^{-1}). 95% of the total deposited amount was found in deep lung 1 month after exposure indicating very slow clearance. A similar slow clearance was observed in the sub-acute exposure group (58).

In mice exposed (4 hr) to nickel-containing welding fume aerosols, no lung clearance of deposited nickel or absorption into the blood stream had occurred by 24 hr (59).
Poorly absorbed from diets in dogs. Nickel intake was equivalent to output in urine and faeces; faeces contained 90% of the administered dose (60).
Oral ♂ humans 251-309 mg nickel, 89% eliminated in faeces (61).
Will cross the human placenta (46).

Sensitisation

Hypersensitivity to nickel contact is an increasing problem, nickel is found in sources such as jewellery, coins, fasteners and cooking utensils (62,18).
Nickel and its water-soluble salts are potent skin sensitisers. After the initial sensitisation, even tiny amounts of nickel or its water-soluble salts, applied dermally or by ingestion, will cause an eczematous response within 12 hr which is fully developed by 48-72 hr, and then subsides (46).
Nickel allergy is a cell-mediated immune response. Most cases of nickel allergy can be related to skin contact with nickel-containing metallic items. Epidemiological studies have shown a sensitisation frequency of 20% in young females and 10% in the elderly. 2-4% of males are sensitised. The biologically significant parameter is not the nickel concentration in the alloy or coating but the amount released to the skin during exposure to human sweat. A threshold of 0.5 μ cm^{-2} wk^{-1} has been established, where only a minor number of nickel-sensitive people will react (63).

Genotoxicity

MEL 0.5 mg m^{-3} (organic compounds) *In vitro* human peripheral blood lymphocytes sister chromatid exchanges weakly positive, chromosomal aberrations negative (46,64).

Other effects

Other adverse effects (human)

Patients undergoing dialysis developed nickel poisoning when nickel leached from a nickel-plated water heater tank. The symptoms occurred during and after dialysis, the plasma nickel concentrations were ~3 mg l^{-1}. The symptoms included nausea (37/37 patients), vomiting (31/37 patients), weakness (29/37 patients), headache, (22/37 patients) and palpitation (2/37 patients) recovery occurred within 3-13 hr after stopping dialysis (65).
Nickel refinery workers who had worked for ≥5 yr in process areas where lung and nasal cancer were the highest also suffered a significantly elevated mortality from non-malignant respiratory disease (20 deaths, expected 11.1) (66).
Workers in a Welsh nickel refinery had increased incidences of nasal and lung cancer compared with the general population. Of those workers employed before 1925, lung cancer rates were 5-10 × the national average and nasal cavity cancers were 100-900 × higher. Workers employed after 1925 did not have increased cancer rates (67).

Any other adverse effects

Toxicity testing in modified Chinese hamster ovary cells showed LC_{50} values of 45-60 μg Ni ml^{-1} for water soluble salts (68).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nickel 50 μg l^{-1} (69).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (70).

Other comments

Soils and volcanoes are the major sources of airborne nickel, 40-50% of natural sources, whilst from man-made sources combustion of oil and incineration of waste contribute 70% and nickel mining and refining 17%.
In vitro incubation with water, rat serum and renal cytosol for 72 hr at 37°C, nickel dissolved more rapidly in cytosol and serum than in water (71).
Suggested differences in the carcinogenic potential of various nickel compounds may be due to their capacity to form nickel ions within target cells. Nickel ions may initiate carcinogenesis by causing DNA damage (72).

Metabolism in animals and humans reviewed (73).
Incidences of nickel allergy in the population reviewed (74).
Hazards and current legislation in France reviewed (75).
Human health effects caused by occupational exposure reviewed (76-79).
Nickel-DNA interactions reviewed (80).
Toxicity reviewed (81).
Carcinogenicity including cellular and molecular mechanisms and epidemiology reviewed (82-85).
Animal carcinogenicity reviewed (86,87).
Soluble in dilute nitric acid.

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N45 nickel ammonium sulfate

$$(NH_4)_2Ni(SO_4)_2$$

$H_8N_2NiO_8S_2$ **Mol. Wt.** 286.89 **CAS Registry No.** 15699-18-0

Synonyms sulfuric acid, ammonium nickel(2+) salt (2:2:1); ammonium nickel sulfate

EINECS No. 239-793-5 **RTECS No.** WS 6050000

Uses Electroplating metals.

Physical properties

Specific gravity 1.923
Solubility Water: 6.10 wt % at 20°C

Occupational exposure

SE-LEVL 0.1 mg m^{-3} (as Ni)
UK-LTEL MEL 0.1 mg m^{-3} (as Ni)
US-TWA 0.1 mg m^{-3} (as Ni)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 400 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Nickel and nickel compounds, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (2).
Intramuscular implantation (18 month) rat 7 mg formed into a pellet with sheep fat. No tumours were observed at the implantation site (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nickel maximum admissible concentration 50 μg l^{-1}, sulfates; maximum admissible concentration 250 mg l^{-1}, guide level 25 mg l^{-1} (4).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

Other comments

Toxicity, environmental effects, metabolism of nickel compounds reviewed (6).

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N46 nickel chloride

$NiCl_2$

Cl_2Ni **Mol. Wt.** 129.60 **CAS Registry No.** 7718-54-9

Synonyms nickel(II) chloride; nickel chloride ($NiCl_2$); nickel dichloride; nickelous chloride

EINECS No. 231-743-0 **RTECS No.** QR 6475000

Uses Anhydrous salt as an absorbent for ammonia in gas masks. Nickel-plating cast zinc, manufacture of sympathetic ink.

Physical properties

M. Pt. 1001°C **B. Pt.** 987°C (sublimes) **Specific gravity** 3.55

Solubility Water: 642 g l^{-1} at 20°C. Organic solvents: ethanol, ethylene glycol

Occupational exposure

SE-LEVL 0.1 mg m^{-3} (as Ni)

UK-LTEL MEL 0.1 mg m^{-3} (as Ni)

US-TWA 0.1 mg m^{-3} (as Ni)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow, bluegill sunfish 4.9-5.3 mg l^{-1} in soft water (20 mg $CaCO_3$ l^{-1}) or 43.5-39.6 mg l^{-1} in hard water (300 mg $CaCO_3$ l^{-1}) (1).

LC_{50} (48 hr) rainbow trout 20, 80 mg l^{-1} in soft, hard water, respectively (1).

LC_{50} (96 hr) tidewater silver side larvae, adult spot fish 30, 70 mg l^{-1}, respectively (2).

Invertebrate toxicity

Sea urchin embryos 0.59-5.9 mg $nickel^{-1}$ able to gastrulate but failed to develop dorsoventral symmetry, 59-590 mg nickel l^{-1} gastrulation was inhibited (3).

LC_{50} (2 day) *Daphnia magna* 7.3 mg kg^{-1} (4).

EC_{50} (2 day) mobility *Daphnia magna* 7.59 mg l^{-1} (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 105 mg kg^{-1} (6).

Intratracheal rat 9.5, 95.2, 952 μg kg^{-1}. 24 hr after dosing no adverse effects were noted. By day-7 after dosing multifocal alveolitis and some type II hyperplasia were observed. In medium-high dose groups increased numbers of neutrophils and macrophages were recorded in lung lavage fluid (7).

LD_{50} intravenous dog 40-80 mg kg^{-1} (8).

Intraperitoneal rabbit, 2.6 mg kg^{-1} caused a reduction in the maximum kidney tubular transport rate for aspartate (9).

Intraperitoneal rat (12, 24 mg kg^{-1}), mice (5, 10, 15 mg kg^{-1}) resulted in hypothermia that lasted for >1 hr (10-12).

LD_{50} intraperitoneal pregnant rat, ♀ rat 38, 29 mg kg^{-1}, respectively (13,14).

LD_{50} intramuscular ♀ rat, pregnant rat 71, 98 mg kg^{-1}, respectively (15).

LD_{50} intramuscular rabbit 27 mg kg^{-1} (16).

Sub-acute and sub-chronic data

Oral rat (2-4 wk) 0.5-5.0 mg kg^{-1} day^{-1}, inhalation 0.05-0.5 mg m^{-3} significantly decreased iodine uptake by the thyroid, the effect was more pronounced in the inhalation study (17).

Carcinogenicity and chronic effects

Nickel and nickel compounds, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (18).

Intramuscular implantation (18 month) black rat (7 mg formed into pellets with sheep fat), no tumours were observed (19).

Teratogenicity and reproductive effects

Intramuscular Fischer 344 rat single injection on day-8 of gestation 12 or 16 mg kg^{-1}. Mean number of live pups dam^{-1} significantly reduced, reduced body weight of foetuses on day-20 of gestation and in pups 4-8 wk after birth (20).

Intramuscular Fischer 344 rat on days 6-10 of gestation 1.5 or 2.0 mg kg^{-1}. 2.0 mg cause significant intra-uterine mortality but no reduction in body weight of live pups (15).

Intraperitoneal CD-1 mice 1.2-6.9 mg kg^{-1} single injection between days 7-11 of gestation caused a dose-related increase in foetal deaths and malformations (20).

In vitro mouse embryos at 2-, 4-, and 8-cell stages cultured in nickel chloride hexahydrate at 1.3-130.0 mg l^{-1}. 1.3 mg l^{-1} adversely effected development of 2-cell stage embryos, 39 mg l^{-1} was needed to effect 8-cell stage embryos (21).

Intraperitoneal mice, days 1-6 of gestation, 20 mg kg^{-1} nickel chloride hexahydrate 20 mg kg^{-1} single injection. Implantation frequency (on day-19) of ♀ treated on day-1 of gestation was significantly decreased. ♀ treated on days 1, 3 or 5 of gestation had a significant reduction in litter size. The frequency of foetal abnormalities was higher in foetuses of treated females than controls (22).

Chicken eggs injected on day 0, 1, 2 or 3 of gestation, 0.02 or 0.7 mg egg^{-1}. Examination on day-8 of gestation showed malformations such as exencephaly, everted viscera, short twisted necks or limbs, microphthalmia, haemorrhage and reduced body size. Treatment on day-2 caused the most malformations (23).

Metabolism and toxicokinetics

Nickel absorption depends on the solubility of the nickel compound. Soluble salts dissociate readily in the aqueous environment of biological membranes and so the nickel ions are easily transported, insoluble compounds are poorly absorbed (13).

Inhalation (2 hr) mouse 644 μg m^{-3} clearance of 70% of the deposited fraction was found in the lung 4 days after exposure (24).

In rats administered radiolabelled nickel chloride intratracheally, most of the dose was found in the kidney (53%) and the lung (30%) with small amounts being found in the liver, pancreas, spleen, heart and testes (25).

Dermal guinea pig after 24 hr 0.05%, 0.51% of applied dose was found in the plasma and urine, respectively (26).

Will cross the placenta of pregnant mice, maximum nickel concentrations were measured in the maternal blood and placenta 2 hr after intraperitoneal injection of 0.1 ml and by 8 hr in the foetal tissue (27).

In lactating ♀ rats receiving 1.3, 6.5 or 13 mg kg^{-1} subcutaneously, dose-dependent increases in nickel in milk were observed by 4 hr (28).

Irritancy

Dermal human threshold concentration for irritancy 1% with occlusion and 10% without occlusion (29).

Sensitisation

Intracutaneous single injection guinea pig ear 100-200 μg sensitisation developed within 4-10 day reaching a peak by day-20 (30).

Nickel and its water-soluble salts are potent skin sensitisers. After the initial sensitisation exposure, even tiny amounts of nickel or its water-soluble salts, applied dermally or by ingestion, will cause eczematous response within 12 hr which is fully developed by 48-72 hr and then subsides (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (31).

Escherichia coli WP2, WP67, CM871 with and without metabolic activation DNA-repair test negative (31).

Bacillus subtilis H17, M45 without metabolic activation negative (32).

Saccharomyces cerevisiae D7 without metabolic activation positive (33).

In vitro Chinese hamster ovary cells DNA strand breaks positive (34).
In vitro mouse FM3A mammary carcinoma cells, Chinese hamster ovary cells, human peripheral blood lymphocytes chromosomal aberrations sister chromatid exchanges positive (13,35-38).
In vitro Chinese hamster ovary cells, chromosomal aberrations positive (39,40).
In vivo mice reduced sperm counts, sperm mobilities, induced sperm chromosomal aberrations, damaged testes ultrastructure, caused sperm head abnormalities and induced micronuclei in the polychromatic erythrocytes (41,42).
Mice intraperitoneal injection 6-24 mg kg^{-1} induced bone marrow chromosomal aberrations (43).

Other effects

Other adverse effects (human)
Of 32 workers who accidentally drank water contaminated with nickel sulfate and nickel chloride (1.63 g nickel l^{-1}), 20/32 developed symptoms including nausea, headache, vomiting, giddiness, diarrhoea and cough. The symptoms persisted typically for a few hr but in 7 cases they lasted for 1-2 days (44).
Workers involved in electrolysis who were exposed mainly to nickel chloride and nickel sulfate had elevated levels of chromosomal aberrations; sister chromatid exchanges were not observed (cell type unspecified) (45).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nickel: maximum admissible concentration 50 μg l^{-1}, chlorides guide level 25 mg l^{-1} (46).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (47).

Other comments

Biological effects reviewed (48).

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N47 nickel hydroxide

$Ni(OH)_2$

H_2NiO_2 **Mol. Wt.** 92.70 **CAS Registry No.** 12054-48-7

Synonyms nickel hydroxide ($Ni(OH)_2$); nickel dihydroxide; nickel(II) hydroxide; nickelous hydroxide; green nickel oxide

EINECS No. 235-008-5 **RTECS No.** QR 7040000

Uses As an electrode material for secondary cells.

Physical properties

M. Pt. 200°C (decomp.) **Specific gravity** 4.15
Solubility Water: 0.0127 g l^{-1} at 20°C

Occupational exposure

FR-VME 1 mg m^{-3} (as Ni)
SE-LEVL 0.1 mg m^{-3} (as Ni)
UK-LTEL MEL 0.5 mg m^{-3} (as Ni)
US-TWA 1 mg m^{-3} (as Ni)
Supply classification harmful
Risk phrases Harmful by inhalation and if swallowed – Possible risk of irreversible effects – May cause sensitisation by skin contact (R20/22, R40, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing (S2, S22, S36)

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Nickel and nickel compounds, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (1).

Implantation rat (dose, duration unspecified) 19/40 developed tumours at the implantation site (2).

Intramuscular Wistar rat sarcomas induced by crystalline form but not amorphous form (3).

Metabolism and toxicokinetics

Nickel absorption depends on the solubility of the nickel compound. Soluble salts dissociate readily in the aqueous environment of biological membranes and so the nickel ions are easily transported, insoluble compounds are poorly absorbed (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nickel: maximum admissible concentration 50 $\mu g\ l^{-1}$ (5).

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

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N48 nickel nitrate

$$Ni(NO_3)_2$$

NiN_2O_6 **Mol. Wt.** 182.70 **CAS Registry No.** 13138-45-9

Synonyms

EINECS No. 236-068-5 **RTECS No.** QR 7200000

Uses Nickel-plating and nickel-cadmium batteries.

Physical properties

M. Pt. 56.7°C **B. Pt.** 137°C **Specific gravity** 2.05

Solubility Water: 1 in 0.4 parts. Organic solvents: ethanol

Occupational exposure

SE-LEVL 0.1 mg m^{-3} (as Ni)

UK-LTEL MEL 0.1 mg m^{-3} (as Ni)

US-TWA 0.1 mg m^{-3} (as Ni)

UN No. 2725 **HAZCHEM Code** 1Y **Conveyance classification** oxidising substance

Ecotoxicity

Invertebrate toxicity

LC_{50} (calc.) (14 day) earthworm 757 mg kg^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} intravenous mouse 9 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Nickel and nickel compounds, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (3).

Metabolism and toxicokinetics

Nickel absorption depends on the solubility of the nickel compound, soluble salts dissociate readily in the aqueous environment of biological membranes and so the nickel is easily transported, insoluble compounds are poorly absorbed (4).

Sensitisation

Nickel and its water-soluble salts are potent skin sensitisers. After the initial sensitisation exposure, even tiny amounts of nickel or its water-soluble salts, applied dermally or by ingestion, will cause an eczematous response within 12 hr which is fully developed by 48-72 hr and then subsides (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (5).
Escherichia coli WP2, WP67, CM871, test negative (5).
In vivo mouse BALB/c micronuclei negative (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nickel: maximum admissible concentration 50 μg l^{-1}, nitrates: maximum admissible concentration 50 mg l^{-1}, guide level 25 mg l^{-1} (7).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

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N49 nickel subsulfide

Ni_3S_2

Ni_3S_2 **Mol. Wt.** 240.20 **CAS Registry No.** 12035-72-2

Synonyms nickel sulfide (Ni_3S_2); trinickel subsulfide

EINECS No. 234-829-6 **RTECS No.** QR 9800000

Occurrence May be formed during the production of nickel from sulfide ores.
As the mineral heazlewoodite.

Physical properties

M. Pt. 790°C **Specific gravity** 5.82

Occupational exposure

FR-VME 1 mg m^{-3} (as Ni)
SE-LEVL 0.01 mg m^{-3} (as Ni)
UK-LTEL MEL 0.5 mg m^{-3} (as Ni)
US-TWA 0.1 mg m^{-3} (as Ni)
Supply classification toxic
Risk phrases May cause cancer by inhalation – May cause sensitisation by skin contact (R49, R43)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Toxicity to other species
Newt lens regeneration was inhibited by intraocular injection of nickel subsulfide and the phagocytic activity of macrophages involved in depigmentation in the early stages of regeneration was greatly reduced (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} intraperitoneal guinea pig 102 μg kg^{-1} (2).
Intratracheal rat 3.2, 32, 320 μg kg^{-1} no effects observed 24 hr after dosing. 7 days after dosing multifocal alveolitis with some type II hyperplasia was seen and in the highest dose group an increased number of neutrophils and macrophages were observed in the lung lavage fluid (3).

Sub-acute and sub-chronic data
Inhalation (78 wk) rat (dose unspecified) lung changes included abscesses and metaplastic changes (4).
Inhalation rat, mice 0.6-10 mg m^{-3}. Lesions were observed in the respiratory tract with extensive lesions in lungs, including necrotising pneumonia. 5-10 mg m^{-3} rat dose groups developed emphysema and 5 mg m^{-3} mice developed fibrosis. All dose groups except 0.6 mg m^{-3} mice showed degeneration of the respiratory epithelium and atrophy of the olfactory epithelium. Clinical symptoms included reduced body weight gain, dehydration, emaciation and laboured respiration (5,6).
Intratracheal mice (≤ 4 wk). The particle size of nickel subsulfide has a significant effect on the LD_{50} for single exposure, fine particles 1.8 μm 4 mg kg^{-1}, larger particles 13.3 μm 50 mg kg^{-1}. Repeated exposure once a wk for 4 wk changed the LD_{50} for fine, large particles to 1, 2 mg kg^{-1}, respectively, indicating that repeated exposure to large particles enhanced lethality (7).

Carcinogenicity and chronic effects
Nickel and nickel compounds, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (8).

Inhalation (108 wk) Fischer 344 rats 1 mg m^{-3} 6 hr day^{-1} 5 days wk^{-1} for 78 wk followed by 30 wk observation. A significantly higher incidence of pulmonary hyperplastic and neoplastic lesions originating from the bronchial and bronchoalveolar segments was observed in exposed rats. 14% of treated animals developed lung tumours (benign and malignant) compared with 1% of the controls. The malignant neoplasms included adenocarcinomas, squamous-cell carcinomas and fibrosarcomas (9).
(104 wk) ♂ Fischer 344 rats were administered two intramuscular simultaneous bilaterial injections, 10 mg injection $site^{-1}$ in penicillin G procaine. 100% of treated rats developed sarcomas in at least one injection site while 40% developed sarcomas at both injection sites; all treated rats had died by 47 wk after injection. No control animals developed sarcomas and all survived to the end of the experimental period. 81% of the primary sarcomas were classified as rhabdomyosarcomas and distant metastases were found in 57% of the treated animals (10).
Subcutaneous or intramuscular (18 month) Fischer 344 rat, single injections of 3.3 or 10 mg suspended in aqueous penicillin G procaine. Half of each group was administered 2 × wkly injections of saline for 52 wk. The incidences of sarcomas, mainly rhabdomyosarcomas, for all groups and routes were 85-97%. No tumours were found in the controls (11,12).
Intramuscular (2 yr) ♀ Fischer 344 rats, single injection 0.63-5 mg suspended in penicillin G procaine. Dose-response relationship was observed for local sarcoma induction (13,14).
Implantation into right gluteal region (256 day) Fischer 344 rat compressed solid discs ~250 mg. The implants were removed after 2, 4, 8, 16, 32, 64, 128 or 256 days. Palpable local tumours developed in groups that had had implants for 64, 128, 256 days, 4, 7, 10 (out of 15), respectively (15).
Implantation into rat thigh muscle of millipore diffusion chambers which contained 10 mg nickel subsulfide resulted in the induction of 9/17 rhabdomyosarcomas and 3/17 fibrosarcomas. This indicates that direct contact between cell and nickel subsulfide is not necessary for carcinogenesis (16).
Intratracheal (29 month) mice 0.024-1.1 mg kg^{-1} wkly for 4 wk followed by 27 months observation, no neoplastic or non-neoplastic lesions observed in the lungs (17).
Intratracheal (duration unspecified) rat 0.063, 0.125 or 0.15 mg wkly for 15 wk. Adenocarcinomas and squamous cell carcinomas were induced at all doses and mixed tumours were observed at the two highest dose levels (18).

Teratogenicity and reproductive effects
Intramuscular (day 6-10 of gestation) rat 80 mg kg^{-1} reduced the number of live pups dam^{-1}, did not cause any skeletal or visceral abnormalities (19).

Metabolism and toxicokinetics
In vivo species unspecified, radiolabelled-nickel subsulfide persisted at the site of injection for several months, eventually it could be surrounded by neoplastic tissue. It was not detected in muscle or tumour tissue (20).
In vivo rats administered radiolabelled-nickel subsulfide, after 20 wk 19% remained at the injection site with <0.1% localised to distant organs (21).
Intramuscular, rat radiolabelled-nickel subsulfide, $t_{1/2}$ 24 days for elimination in urine and faeces (22).
Intratracheal mice radiolabelled-nickel subsulfide, 4 hr after administration 85% of the dose remained in the lungs and declined to 10% by 35 days (23).

Genotoxicity

In vitro Chinese hamster ovary without metabolic activation, DNA strand breaks positive (24).
In vitro human peripheral blood lymphocytes sister chromatid exchanges weakly positive (25).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nickel: maximum admissible concentration 50 $\mu g\ l^{-1}$ (26).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (27).

Other comments

Soluble in nitric acid.

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N50 nickel sulfate

$NiSO_4$

NiO_4S **Mol. Wt.** 154.75 **CAS Registry No.** 7786-81-4

Synonyms sulfuric acid, nickel(2+) salt (1:1); nickel monosulfate; nickel(II) sulfate; nickelous sulfate

EINECS No. 232-104-9 **RTECS No.** QR 9350000

Uses In nickel-plating. As mordant in dyeing and printing fabrics. Blackening zinc and brass. Jewellery manufacture.

Occurrence Occurs as the minor mineral morenosite.

Physical properties

M. Pt. 840°C **Specific gravity** 3.86

Solubility Water: 27.3-27.7 wt% at 20°C. Organic solvents: methanol

Occupational exposure

FR-VME 0.1 mg m^{-3} (as Ni)

SE-LEVL 0.1 mg m^{-3} (as Ni)

UK-LTEL MEL 0.1 mg m^{-3} (as Ni)

US-TWA 0.1 mg m^{-3} (as Ni)
Supply classification harmful
Risk phrases Harmful if swallowed – Possible risk of irreversible effects – May cause sensitisation by inhalation and skin contact (R22, R40, R42/43)
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} (duration unspecified) rainbow trout 0.36 mg l^{-1} (1).
LC_{50} (14 day) coho salmon 11.2 mg l^{-1} (2).
LC_{50} (1 day) giant gourami 96 mg l^{-1} (3).

Invertebrate toxicity
Daphnia magna three generations 5-10 μg nickel l^{-1} caused extermination of the population (4).
LC_{50} (2 day) *Crungonyx pseudogracilis*, sowbug 252-435 mg l^{-1} (5).

Environmental fate

Nitrification inhibition
75% inhibition of ammonia oxidation by activated sludge 1050 mg l^{-1} (6).

Mammalian & avian toxicity

Acute data
LD_{Lo} subcutaneous cat, rabbit, dog 24, 33, 38 mg kg^{-1}, respectively (7).
LD_{Lo} intravenous rabbit, dog, mouse 33, 38, 76.4 mg kg^{-1}, respectively (7,8).
Intratracheal rat 10.5, 105.2, 1052 μg kg^{-1} no adverse-effects observed 24 hr after dosing. 7 days after dosing multifocal alveolitis with some type II hyperplasia was observed and in medium-high dose groups increased numbers of neutrophils and macrophages in lung lavage fluid. Increased levels of enzymes, total protein and sialic acid were also seen (9).
LD_{50} intraperitoneal mouse, rat 55 mg kg^{-1} 500 mg kg^{-1}, respectively (10,11).

Sub-acute and sub-chronic data
Inhalation (12 day) rat, mice 3.5-6.0 mg m^{-3}. Surviving animals at 3.5 mg m^{-3} had lesions in the nose, lung, bronchial and mediastinal lymph nodes (12,13).
Dermal (15 or 30 day) ♂ rat 40, 60 or 100 mg kg^{-1} no symptoms of toxicity observed. Examination of the livers of rats killed at 15 days (60 and 100 mg kg^{-1}) showed microscopic changes consisting of swollen hepatocytes and feathery degeneration. At 30 days liver changes were more marked with focal necrosis, the testes also showed adverse effects (14).

Carcinogenicity and chronic effects
Nickel and nickel compounds, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (15).
Intramuscular (20 month) Wistar rat 5 mg into both thighs no tumours were observed (16).

Teratogenicity and reproductive effects
Single subcutaneous injection ♂ rat 6.19 μg kg^{-1}. After 18 hr examination of the testes and epididymis revealed shrinkage of the tubules and complete degeneration of the spermatozoa (17).
Oral (120 day) ♂ rat 25 mg kg^{-1} day^{-1} infertility was observed (18).
Dermal (30 day) rat 40-100 mg kg^{-1} day^{-1}. At 30 days dose-related tubular damage and spermatozoal degeneration were observed at doses ≥60 mg kg^{-1} day^{-1}. Examination at day-15 showed no adverse effects on the testes (14).

Metabolism and toxicokinetics

Nickel absorption depends on solubility of the nickel compound. Soluble salts dissociate readily in the aqueous environment of biological membranes and so the nickel ions are easily transported, insoluble compounds are poorly absorbed (19).

Intractracheal rat nickel sulfate solution 1 μg, 11.2 μg, 105.7 μg rat^{-1}, after 4 hr 49, 21, 8%, respectively, of the instilled dose was found in the lungs (20).

In humans receiving 12-50 μg kg^{-1} in drinking water or food the amounts absorbed were ≤44% of dose ingested in water and ≤1.1% of the same dose ingested in food (21).

Irritancy

Dermal (30 day) rat 40-100 mg kg^{-1} caused skin atrophy, acanthosis and hyperkeratinisation (14).

Dermal human threshold concentration for irritation 20% on unbroken skin, 0.13% on scarified skin, applied once daily for 3 days (22).

Sensitisation

Nickel and its water-soluble salts are potent skin sensitisers. After sensitisation exposure, even tiny amounts of nickel or its water-soluble salts, applied dermally or by ingestion, will cause an eczematous response within 12 hr which is fully developed by 48-72 hr and then subsides (19).

Dermal mice 0.5% in DMSO applied under occlusion resulted in the induction of lymphocyte proliferative responses in lymph nodes which drained the exposure site (23).

Guinea pigs were inducted intradermally (0.01-3.0%) and topically (0.25-10%) and then challenged with a 1% solution. After 48 hr a linear relationship was seen between intradermal induction dose (not topical) and the response (24).

Dermal (4 wk) guinea pig 1% day^{-1} 4 days per wk. 6.3-80% of the animals developed skin allergy (25).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 without metabolic activation negative (26).

Escherichia coli WP2 without metabolic activation negative (26).

Photobacterium fischeri bioluminescence test negative (27).

Saccharomyces cerevisiae D7 gene conversion equivocal (28).

In vitro Syrian hamster embryo cells, Chinese hamster ovary cells, $P338D_1$ mouse macrophage line human peripheral blood lymphocytes, sister chromatid exchanges positive (29-31).

In vitro Syrian hamster cells and human peripheral blood lymphocytes, unscheduled DNA synthesis and chromosomal aberrations positive (32,29).

In vivo rat bone marrow, chromosomal aberrations negative (33).

Other effects

Other adverse effects (human)

A 2½ yr old girl ate ~15 g nickel sulfate crystals. She became drowsy, had wide unresponsive pupils, high pulse rate and pulmonary bronchi. After 4 hr she died of a cardiac arrest. Analysis of blood urine and liver tissue revealed increased nickel levels of 7.5 and 25 mg kg^{-1} in blood and liver, respectively, and 50 mg l^{-1} in urine (34).

In 32 workers who accidentally drank water contaminated with nickel sulfate and nickel chloride (1.63 g nickel l^{-1}). 20/32 developed symptoms including nausea, headache, vomiting, giddiness, diarrhoea, and cough. Symptoms typically lasted a few hr, but in 7 cases they lasted for 1-2 days (35).

Workers involved in electrolysis who were exposed mainly to nickel chloride and nickel sulfate had elevated levels of chromosomal aberrations; sister chromatid exchanges were not observed (cell type unspecified) (36).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nickel: maximum admissible concentration 50 μg l^{-1}, sulfates maximum admissible concentration 250 mg l^{-1}, guide level 25 mg l^{-1} (37).

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (38).

Other comments

Biological effects reviewed (39).

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N51 nickel tetracarbonyl

$Ni(CO)_4$

C_4NiO_4 **Mol. Wt.** 170.73 **CAS Registry No.** 13463-39-3

Synonyms (*T*-4)-nickel carbonyl ($Ni(CO)_4$); nickel carbonyl; tetracarbonylnickel

EINECS No. 236-669-2 **RTECS No.** QR 6300000

Uses In organic synthesis, catalyst production. In nickel vapour plating.

Physical properties

M. Pt. –19.3°C **B. Pt.** 43°C **Flash point** <4°C **Specific gravity** 1.318 at 17°C **Volatility** v.p. 400 mmHg at 25.8°C ; v.den. 5.9

Solubility Organic solvents: acetone, benzene, carbon tetrachloride, chloroform, ethanol

Occupational exposure

FR-VME 0.05 ppm (0.12 mg m^{-3})
JP-OEL 0.001 ppm (0.007 mg m^{-3})
SE-LEVL 0.001 ppm (0.007 mg m^{-3}) **UK-STEL** 0.1 ppm (0.24 mg m^{-3} (as Ni)
US-TWA 0.05 ppm (0.12 mg m^{-3}) (as Ni)

UN No. 1259 **Conveyance classification** toxic substance, danger of fire (flammable liquid)
Supply classification highly flammable, very toxic
Risk phrases May cause harm to the unborn child – Highly flammable – Very toxic by inhalation – Possible risk of irreversible effects (R61, R11, R26, R40)
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

Unstable in air and decomposes to form nickel carbonate. At 25°C 1 ng m^{-3} has a lifetime of 1 min which increases by 1 min for every mg m^{-3} of carbon dioxide present (1).

Mammalian & avian toxicity

Acute data

LC_{50} (20-30 min) inhalation mouse, cat, rat 0.067-0.24 mg l^{-1} (2,3).
LC_{90} (30 min) inhalation dog 2.5 mg l^{-1} (4).
LD_{50} subcutaneous rat 21 mg kg^{-1} (5).
LD_{50} intraperitoneal rat 13 mg kg^{-1} (5).
LD_{50} intravenous rat 22 mg kg^{-1} (5).

Carcinogenicity and chronic effects

Nickel and nickel compounds, sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (6).

Inhalation (30 month) Wistar rat 0.03 and 0.06 mg l^{-1} thrice wkly for 12 months. All animals were dead by 30 months, of controls only three were alive after 2 yr. In the treated group 4/9 surviving rats at 2 yr developed lung neoplasms including adeno-/squamous-cell carcinoma with (in one case) metastases to the kidney and mediastinum and papillary bronchial adenomas (7,8).

Inhalation (2 yr) ♂ Wistar rat 0.6 mg l^{-1} single 30 min dose. One pulmonary adenocarcinoma with metastases observed in the 35 remaining rats. This type of tumour very rarely occurs spontaneously in Wistar rats (9).

Inhalation (2 yr) ♂ Wistar rats 0.03 mg l^{-1} for 30 min 3 × wkly until death. One rat of the eight rats remaining alive for 2 yr developed pulmonary adenocarcinoma with metastases, none was found in the controls (9).

Intravenous (life time study) Sprague-Dawley rat, 9 mg kg^{-1} at 2-4 wk intervals. Of the rats that survived the injections 16% developed malignant tumours at various sites: liver; kidney; lung; and mammary glands. This was statistically significant, compared with the controls (10).

Teratogenicity and reproductive effects

Intravenous Fischer 344 rat, day-7 gestation 11 mg kg^{-1} caused foetal mortality, reduced body weight of live born and a 15% incidence of foetal malformations, including anophthalmia, microphthalmia, cystic lungs and hydronephrosis (11).

Inhalation hamster day 4 or 5 of gestation 60 mg m^{-3} for 15 min. Decreased foetal viability and increased foetal malformations (12).

Inhalation ♂ rat 2-6 wk before breeding 50 mg m^{-3} for 15 min no effect on fertilisation or reproductive yield. Intravenous injection during the same period 22 mg kg^{-1} reduced the number of live offspring sired during the 5th wk (11).

Metabolism and toxicokinetics

Inhalation rat (3 or 52 wk) 30 or 60 mg m^{-3} for 30 min 3 × a wk. In all studies nickel was found in the respiratory tissues, brain, liver, kidneys, urinary bladder, adrenal glands, renal cortex, heart diaphragm and blood, from where it was mobilised after exposure (within 2 days) (13).

Unchanged nickel tetracarbonyl is present in the blood several hr after inhalation and can pass the pulmonary alveoli without decomposition. The nickel tetracarbonyl in the blood undergoes slow intracellular decomposition to nickel oxides and is then oxidised to Ni^{2+} which can bind to nucleic acids, proteins or albumin in the plasma (species unspecified) (14).

Irritancy

In rabbits caused reddening of the mucosa of the eye (details unspecified) (15).

Other effects

Other adverse effects (human)

Acute toxic effects occur in two stages, intermediate and delayed. First-stage symptoms include frontal headache, vertigo, nausea, vomiting and insomnia. This is followed by a period without symptoms before the onset of pulmonary symptoms, including constrictive chest pains, dry coughing, dyspnoea, cyanosis and tachycardia. These symptoms resemble those of viral pneumonia. Pulmonary haemorrhage and oedema or pneumonitis accompanied derangement of alveolar cells, bronchial epithelium degeneration and the appearance of a fibrinous intra-alveolar exudate were observed in men who had died due to nickel tetracarbonyl exposure (7).

Occupational exposure for long periods to low levels caused an engineer to develop asthma, Lottler's syndrome and eczematous dermatitis of the hands (16).

Neurotoxicity has been recorded in occupationally exposed workers (17).

Occupationally exposed workers have increased incidences of sister chromatid exchanges but not chromosomal aberrations (cell type unspecified) (18).

Any other adverse effects

Effects of acute exposure to the lungs of mammals include intra-alveolar oedema and haemorrhage and pulmonary congestion (7).

Nickel tetracarbonyl is a volatile liquid, the vapours of which easily penetrate the alveolar membrane. It is the only nickel compound to cause acute poisoning when inhaled (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nickel: maximum admissible concentration 50 $\mu g\ l^{-1}$ (19).

Other comments

Hazards, carcinogenicity and toxicology reviewed (20-22).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (23).

Explodes at 60°C.

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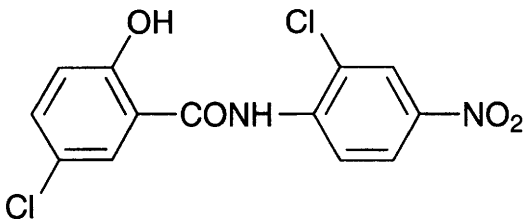
N52 niclosamide



$C_{13}H_8Cl_2N_2O_4$ **Mol. Wt.** 327.12 **CAS Registry No.** 50-65-7

Synonyms 5-chloro-*N*-(2-chloro-4-nitrophenyl)-2-hydroxybenzamide; 2',5-dichloro-4'-nitrosalicylanilide; Bayluscid; Yomesan; Sulqui; Lintex

EINECS No. 200-056-8 **RTECS No.** VN 8400000

Uses Molluscicide used to control schistosomiasis and fascioliasis in humans by killing the fresh-water snails which act as intermediate hosts. Drug used to destroy intestinal tape worms.

Physical properties

M. Pt. 230°C **Partition coefficient** log P_{ow} 1.0 at pH 9.6 (1) **Volatility** v.p. $<7.52 \times 10^{-6}$ mmHg
Solubility Water: 5-8 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) cichlid 0.21 mg l^{-1} (2).

LC_{50} (48 hr) rainbow trout, carp 0.05, 0.235 mg l^{-1}, respectively (1).

Invertebrate toxicity

LC_{50} (24 hr) *Biomphalaria glabrata* (albino), *Biomphalaria pfeitteri* 0.063, 0.049 mg l^{-1}, respectively (2).

LC_{50} (4 hr) *Schistosoma mansoni* cercaria 0.0008 mg l^{-1} (2).

NOEC 21 day *Daphnia magna* reproduction test 0.02 mg l^{-1} (3).

EC_{50} (24 hr) *Daphnia magna* 0.16 mg l^{-1}, EC_0 0.058 (3).

EC_{50} (48 hr) *Scenedesmus subspicatus* >0.96 mg l^{-1} (4).

IC_{50} (toxic end point) mixed population of soil microorganisms 450 mg l^{-1} (2).

Environmental fate

Degradation studies

$t_{1/2}$ in pond sediments 1.1-2.9 day, no appreciable degradation in paddy fields (5).

Abiotic removal

Decomposes under UV irradiation (1)

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >60 mg kg^{-1} (6).

LD_{50} oral mouse 1000 mg kg^{-1} (7).

LD_{Lo} oral rat 10 g kg^{-1} (8).

LD_{50} oral rat >3710 mg kg^{-1} (1).

LC_{50} (1 hr) inhalation rat >20 mg l^{-1} (5).

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

LD_{50} intraperitoneal rat 250 mg kg^{-1} (8).

LD_{50} intravenous mouse 7.5 mg kg^{-1} (9).

Carcinogenicity and chronic effects

NOEL (2 yr) oral rat 8000 mg kg^{-1} diet (5).

NOEL (1 yr) oral dog 100 mg kg^{-1} diet (5).

Metabolism and toxicokinetics

In mammals metabolised to 2',5-dichloro-4'-aminosalicylanilide by reduction of the nitro group to an amino group (1).

In humans it is not significantly absorbed from the gastro-intestinal tract (10).

Genotoxicity

Salmonella typhimurium TA98, TA1538 with metabolic activation positive (highly toxic without metabolic activity), TA1978, UTH8413 with and without metabolic activation negative (11).

Escherichia coli pol A^+/pol A^- with and without metabolic activation negative (12).

In vitro human peripheral lymphocytes without metabolic activation negative with metabolic activation induced dose-related increase in chromosomal aberrations in 3 out of 5 patients (13).

In vivo human peripheral lymphocytes showed an increase in the percentage of chromosomal aberrations (13).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (14).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (15).

WHO Toxicity Class Table 5 (16).
EPA Toxicity Class II (formulation) (5).

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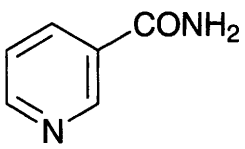
N53 nicotinamide



$C_6H_6N_2O$ **Mol. Wt.** 122.13 **CAS Registry No.** 98-92-0

Synonyms 3-pyridinecarboxamide; nicotinic acid amide; β-pyridinecarboxamide; niacinamide; vitamin PP; Benicot; Nicasir

EINECS No. 202-713-4 **RTECS No.** QS 3675000

Uses Enzyme cofactor vitamin. Nutritional factor in animals and man

Occurrence Plants and animals in conjugated form (in enzyme systems).

Physical properties

M. Pt. 128-131°C **B. Pt.** 150-160°C at 5×10^{-4} mmHg (distills) **Specific gravity** 1.40

Solubility Water: 1000 g l^{-1}. Organic solvents: ethanol, glycerol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2.5 g kg^{-1} (1).

LD_{50} subcutaneous rat, mouse 1.68, 2 g kg^{-1}, respectively (2,3).

LD_{50} intraperitoneal mouse 2.3 g kg^{-1} (4).

LD_{50} intravenous rat 2.2 g kg^{-1} (5).

Teratogenicity and reproductive effects

In vitro pre-implantation mouse embryos grown in culture, embryo development was severly inhibited by concentrations 1000 × normal human blood concentration (normal concentration = 840 μg 100 ml^{-1}). Development was arrested at the two-cell stage (6).

Metabolism and toxicokinetics

[^{13}N]Nicotinamide administered to mice was transported (mainly by diffusion) into the brain and heart where it was trapped or metabolised to hydrophilic compounds. A large amount was also found trapped in the small intestine (7).

In omnivores it is catabolised to N^1-methylnicotinamide, followed by N^1-methyl-2-pyridone-5-carboxamide (60-90% of total urinary excretion). In carnivores N^1-methylnicotinamide is the primary metabolite detected in urine (>90%), whereas herbivores excrete 80-100% of nicotinamide unchanged in urine (8).

Genotoxicity

Salmonella typhimurium TA102 with and without metabolic activation weakly positive, TA97 with and without metabolic activation negative (9).

In vitro Chinese hamster ovary cells without metabolic activation induced sister chromatid exchanges (10).

Other comments

Influence on *in vivo* carcinogenesis reviewed (11).

Pharmacology and human toxicity reviewed (12).

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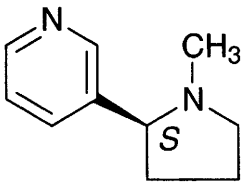
N54 nicotine



$C_{10}H_{14}N_2$ **Mol. Wt.** 162.23 **CAS Registry No.** 54-11-5

Synonyms 3-(1-methyl-2-pyrrolidinyl)pyridine; flux maag; 3-(*N*-methylpyrrolidino)pyridine; nicotin; L-nicotine; XL All Insecticide

EINECS No. 200-193-3 **RTECS No.** QS 5250000

Uses Insecticide for control of aphids, white fly and thrips. In chewing gum or skin patches as an aid to giving up smoking.

Occurrence An alkaloid found in tobacco.

Physical properties

M. Pt. <–80°C **B. Pt.** 123-125°C at 17 mmHg, 247°C at 745 mmHg **Flash point** 95°C (closed cup)
Specific gravity 1.0097 at 20°C with respect to water at 4°C **Volatility** v.p. 1 mmHg at 61.8°C ; v.den. 5.61
Solubility Water: miscible with water below 60°C (with the formation of an hydrate). Organic solvents: chloroform, diethyl ether, ethanol, petroleum ether, kerosene

Occupational exposure

DE-MAK 0.07 ppm (0.47 mg m^{-3})
FR-VME 0.5 mg m^{-3}
UK-LTEL 0.5 mg m^{-3} **UK-STEL** 1.5 mg m^{-3}
US-TWA 0.5 mg m^{-3}

UN No. 1654 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Toxic if swallowed – Very toxic in contact with skin (R25, R27)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing 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 ~4 mg l^{-1} (1).
Trout, bluegill sunfish 5 ppm caused death within 22 and 7 hr, respectively. 5 ppm (24 hr) goldfish no effect was observed (2).
Steel trout, bridge sucker 2 mg l^{-1} caused death within 2 hr of exposure (3).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 0.24 mg l^{-1} (4).
EC_{50} (48 hr) *Daphnia pulex* at 17°C 0.326 mg l^{-1} at 20°C 0.242 mg l^{-1} (5).

Environmental fate

Abiotic removal

Decomposes quickly under the influence of light and air (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral dog 9.2 mg kg^{-1} (7).
LD_{50} oral mouse, rat 3.34, 50 mg kg^{-1}, respectively (8,9).
LD_{50} oral redwing blackbird, starling, coturnix 18, 42, 316 mg kg^{-1}, respectively (10).
LD_{50} dermal rat 140 mg kg^{-1} (11).
LD_{50} dermal rabbit 50 mg kg^{-1} (6).
LD_{50} subcutaneous rat 25 mg kg^{-1} (12).
LD_{Lo} subcutaneous mouse 16 mg kg^{-1} (13).
LD_{50} intraperitoneal mice 0.3 mg kg^{-1} (7).
LD_{50} intraperitoneal mice, rat 9.5, 14.5 mg kg^{-1}, respectively (7,14).
LD_{50} intratracheal rat 19.3 mg kg^{-1} (15).

Teratogenicity and reproductive effects

In vitro rat embryos, nicotine exposure caused growth retardation, impairment of the developement of the nervous system especially the forebrain and the branchial arches. Dose-dependent cellular disruption and necrosis was observed in the neuroepithelium and underlying mesenchyme as well as severe disruption to cell and organelle membranes (16).
Gavage (for gestation period) rat 3 mg kg^{-1} day^{-1} foetal weight was not significantly decreased compared to controls (17).
Fischer 344 and Buffalo rats were exposed to nicotine in a life time study (dose unspecified). Fertility was greatly reduced in both strains, Fischer rats were more tolerant. Both strains of rats became extinct after one generation of foetal and postnatal exposure. The total reproduction period was shortened in both strains. The teratological effects were caused by inflammatory processes indicated by increased numbers of lymphocytes and/or polymorphonuclear leukocytes. Inflammation was not transmitted to new-born rats, but occurred in the neonates during the nursing period or later (18).
In vivo subcutaneous ♂ mice 0.9-2.7 mg kg^{-1} day^{-1} (equivalent to 10-30 cigarettes day^{-1}) for 7-14 days. Decreased the number of spermatogonia and primary spermatocytes and the spermatocytes-spermatids conversion process (19).

Metabolism and toxicokinetics

Nicotine disposition kinetics in humans were tested using the stable isotope-labelled compound 3',3'-dideuteronicotine. Labelled nicotine was detected in the blood 9 hr after a 30 min intravenous infusion, elimination $t_{1/2}$ 203 min. Plasma clearance was 14.6 ml min^{-1} hr^{-1} (20).
The mean level of nicotine in the urine of smokers was 0.78 mg kg^{-1} creatinine, the levels in the blood correlated with the number of cigarettes smoked each day (21).
Can cross the placental barrier and has been found in breast milk (22).
Metabolised mainly in the liver to cotinine and nicotine *N*-oxide. These metabolites and unchanged nicotine are found in urine (22).

Irritancy

Nicotine production workers have been reported to contract dermatosis (23).
Dermal human patch test positive (23).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 with and without metabolic activation negative (24).
Escherichia coli PQ37 with and without metabolic activation SOS chromotest negative (24).
In vivo intraperitoneal rat 0.8 mg kg^{-1} did not increase urinary mutagenicity (test system unspecified) (25).

Other effects

Other adverse effects (human)

It is a rapid acting poison which can be absorbed from the gut, lungs and skin. In fatal cases death is often induced within 1 hr and it is usually caused by respiratory paralysis. Symptoms include nausea, vomiting, bowel and bladder evacuation, twitching and convulsions (26).

Mean lethal dose 30-60 mg (calc.) (27).

Dew on tobacco leaves will dissolve nicotine, exposing tobacco pickers to levels as high as 600 ml day^{-1}. Such exposure can lead to green tobacco sickness, the symptoms of which include vomiting, dizziness, nausea and prostration (28).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (29).

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (30).

WHO Toxicity Class Ib (31).

EPA Toxicity Class I (formulation) (32).

Other comments

Foetal nicotine exposure reviewed (33).

Effects on human metabolism reviewed (34-36).

Pharmacology, cardiovascular physiology, devlopmental neurotoxicity reviewed (37-39).

Human genetic predisposition to smoking and genetic influences on animal responses to nicotine reviewed (40).

Autoignition temperature 244°C.

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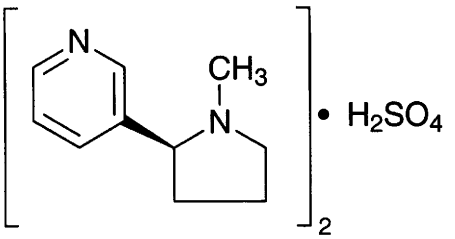
N55 *nicotine sulfate*



$C_{20}H_{32}N_4O_4S$ **Mol. Wt.** 424.56 **CAS Registry No.** 65-30-5

Synonyms (*S*)-3-(1-methyl-2-pyrrolidinyl)pyridine sulfate (2:1); nicotine sulfate (2:1); black leaf

EINECS No. 200-606-7 **RTECS No.** QS 9625000

Occupational exposure

UN No. 1658 **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 – 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

LC_{50} (4 day) bluegill sunfish, rainbow trout, goldfish, fathead minnow 4.3-19.7 mg l^{-1} (1).

Trout, bluegill sunfish, yellow perch 5 ppm caused death within 1, 4, 23 hr, respectively. Goldfish 5 ppm caused sickness within 1 hr, death did not occur within 24 hr (2).

Threespined stickleback, steelhead trout 10 mg l^{-1} caused no adverse effects over 24 hr (3).

Invertebrate toxicity

LC_{50} (4 day) crayfish, snail >38.2 mg l^{-1} (1).

EC_{50} (2 day) *Daphnia magna* 3.25 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral starling, common grackle, house sparrow, house finch, rednecked pheasant >100 mg kg^{-1} (4).
LD_{50} oral brown headed cowgill, white crowned sparrow, redwing blackbird 31.6-75 mg kg^{-1} (4).
LD_{50} oral mouse, rat 16, 55 mg kg^{-1}, respectively (5,6).
LD_{50} dermal rat 285 mg kg^{-1} (7).

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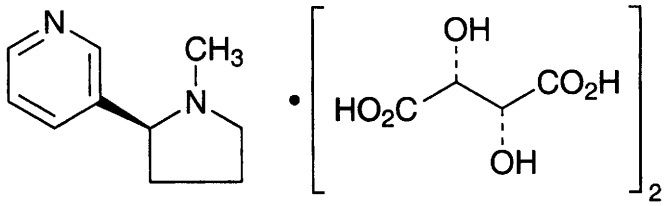
N56 nicotine tartrate



$C_{18}H_{22}N_2O_{12}$ **Mol. Wt.** 458.38 **CAS Registry No.** 65-31-6

Synonyms pyridine, 3-(1-methyl-2-pyrrolidinyl)-, (*S*)-, [*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (2:1); nicotine acid tartrate; nicotine bitartrate; nicotine hydrogen tartrate

EINECS No. 200-607-2 **RTECS No.** QT 0350000

Physical properties

M. Pt. 88-89°C
Solubility Water: very soluble. Organic solvents: ethanol

Occupational exposure

UN No. 1659 **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 – 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)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 65 mg kg^{-1} (1).

LD_{Lo} subcutaneous mouse 59 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 9.1 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 83 mg kg^{-1} (4).
LD_{50} intravenous mouse 300 μg kg^{-1} (1,5).
LD_{50} intravenous rat 600 μg kg^{-1} (1).

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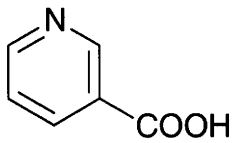
N57 nicotinic acid



$C_6H_5NO_2$ **Mol. Wt.** 123.11 **CAS Registry No.** 59-67-6

Synonyms pyridine-β-carboxylic acid; 3-pyridinecarboxylic acid; niacin; antipellagra vitamin; Niac; Nicocap

EINECS No. 200-441-0

Uses Vitamin (enzyme cofactor). Prevention and treatment of pellagra-like disease in dogs. Vasodilator/lipid reduction drug. Electroplating bath ingredient.

Occurrence Found in all living cells. Appreciable amounts found in liver, yeast, milk, adrenal glands, white meat, alfalfa, legumes, whole cereals, corn.

Physical properties

M. Pt. 236-239°C **Specific gravity** 1.473 **Partition coefficient** log P_{ow} –0.59 at pH 4 and 25°C; –2.34 at pH 7 and 25 °C **Volatility** v.p. <0.75 mmHg at 20°C (calc.)

Solubility Water: 15 g l^{-1} at 20°C. Organic solvents: propylene glycol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) Microtox test 214 mg l^{-1} (1).
EC_{50} (2.5 days, growth) 2.8 g l^{-1} (2).

Environmental fate

Degradation studies

The lignan-degrading fungus *Phanerochaete chrysosporium* accumulated 3-pyridinemethanol in the culture medium when nicotinic acid was added (3).

Resting cells of a bacterial strain (Mena 23/3-3c, with a high degree of 16S rRNA sequence similarity to members of the genera *Ralstonia* and *Burkholderia*) isolated from enrichment cultures with 6-methylnicotinic acid as the sole

source of carbon and energy were able to hydroxylate nicotinic acid at the C2 position but did not further degrade the compound (4).

Mammalian & avian toxicity

Acute data

LD_{50} redwinged blackbird, starling, coturnix >1000 mg kg^{-1} for all three species (5).
LD_{50} oral mouse, rat 3720, 7000 mg kg^{-1}, respectively (6,7).
LD_{50} oral rabbit 4550 mg kg^{-1} (8).
LD_{50} subcutaneous mouse, rat 3500, 5000 mg kg^{-1}, respectively (7,8).
LD_{50} intraperitoneal mouse, rat 358, 730 mg kg^{-1}, respectively (8).
LD_{50} intravenous mouse 5000 mg kg^{-1} (9).
LD_{Lo} intravenous rat 3500 mg kg^{-1} (10).
LD_{Lo} intravenous guinea pig 3500 kg^{-1} (10).

Metabolism and toxicokinetics

Following oral administration to man, readily absorbed from the gastro-intestinal tract and widely distributed throughout the body, including breast milk (11).
Conversion into *N*-methylnicotinamide and the 2- and 4-pyridone derivatives is the main route of metabolism in man. Nicotinuric acid is also formed. Small amounts of unchanged nicotinic acid are excreted in the urine following therapeutic doses (11).

Irritancy

Moderately irritant to the human eye (12).

Other effects

Other adverse effects (human)

Myopathy and hepatotoxicity have been reported in patients receiving therapeutic doses (13,14).
When administered orally or by injection in therapeutic doses may cause effects due to vasodilator action, e.g. flushing, sensation of heat, faintness, pounding in the head (11).

Legislation

No classification or labelling for nicotinic acid are required by the EEC. With respect to transport nicotonic acid is non-dangerous goods (15).

Other comments

Daily human requirement probably 15-20 mg. Converted in the body into NAD and NADP (11).
Degradation pathway of nicotonic acid by *Clostridium barkeri* reviewed (16).
A complete pathway for *Azorhizobium caulinodans* catabolism of nicotinate has been elucidated (17).
Metabolism of nicotinic acid by a *Sarcina* sp. described (18).
Nicotinic acid (0.1-10 mM) reduced oxygen toxicity in a mouse alveolar macrophage model in a dose-dependent fashion. Nicotinic acid has also been shown to reduce oxygen toxicity in bacteria and paraquat toxicity in bacteria and rats (19).
Oral Swiss albino mice administered 0.09375 and 0.0625% nicotine-HCl and 1% nicotinic acid continuously in drinking water from 5-7 wk-old for life appeared not to suffer any carcinogenic effects (20).

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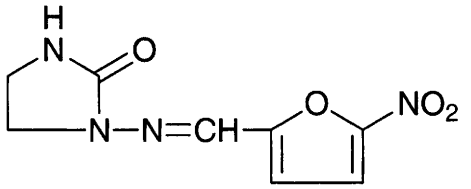
N58 nifuradene



$C_8H_8N_4O_4$ **Mol. Wt.** 224.18 **CAS Registry No.** 555-84-0

Synonyms *N*-(5-nitrofurfurylidene)-1-amino-2-imidazolidinone; 1-[(5-nitrofurfurylidene)amino]-2-imidazolidinone; *N*-[(5-nitro-2-furfurylideneamino)]-2-imidazolidinone; NF-246; Oxafuradene; Renafur

RTECS No. NJ 0875000

Uses Has been used as an antiseptic.

Physical properties

M. Pt. 261.5-263°C (decomp.)
Solubility Water: 88 mg l^{-1}. Organic solvents: dimethylformamide, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 1700 mg kg^{-1} (1).
LD_{50} oral rat 540 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 1000 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).
Oral rat (66 wk) 1500 mg kg^{-1} diet; of 31 rats that survived more than 10 wk, all developed tumours, in total 38, including 2 benign mammary tumours and 29 mammary carcinomas, 5 lymphoblastic lymphomas and 2 tumours at other sites. The first mammary tumour was detected at 30 wk. One benign mammary tumour occurred among 25 controls (4).

Metabolism and toxicokinetics

In rats administered 100 mg kg^{-1} (route unspecified) plasma levels of 4.7 mg l^{-1} were demonstrated after 4 hr. When administered 280 mg kg^{-1} 10% was recovered in the urine and 0.1% in faeces within 48 hr. Milk obtained from dogs and pigs administered 20 mg kg^{-1} contained 19 mg l^{-1} (5).

Urinary metabolites identified in man include the 4-hydroxy derivative and nitrofurantoin (6).

Other comments

Physical properties, use, carcinogenicity and metabolism reviewed (7,8).

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6. Pugh, D. L. et al *J. Med. Chem.* 1972, **15**, 270-272.
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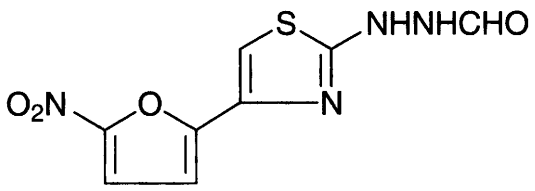
N59 nifurthiazole



$C_8H_6N_4O_4S$ **Mol. Wt.** 254.23 **CAS Registry No.** 3570-75-0

Synonyms 2-(2-formylhydrazino)-4-(5-nitro-2-furyl)thiazole; formic 2-[4-(5-nitrofuryl)-2-thiazolyl] hydrazide; 2-[4-(5-nitro-2-furanyl)-2-thiazolyl] hydrazinecarboxaldehyde; FNT; Refurthiozole

RTECS No. LQ 9275000

Uses Antibacterial agent.

Physical properties

M. Pt. 215.5°C (decomp.)

Solubility Organic solvents: *n*-butanol, dimethylformamide, dimethyl sulfoxide, ethanol, polyethylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1400 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 445 mg kg^{-1} (1).

Carcinogenicity and chronic effects

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

Oral mouse (52 wk) 500 mg kg^{-1} diet for 30 wk followed by control diet for 19 wk. Of 20/30 mice that survived

≥10 wk, 19 developed a total of 24 tumours, including 11 papillomas and 1 carcinoma of the forestomach, 2 pulmonary alveolar-cell carcinomas and 10 lymphocytic leukaemias (leukaemia was present in 2/29 controls) (3).
Oral rat (75 wk) 2000 mg kg^{-1} diet for 2 wk followed by a control diet for 1 wk, then 1000 mg kg^{-1} diet for 43 wk, followed by a control diet up to the wk 75. Of the 51 treated rats, 49 developed a total of 78 tumours including 49 mammary adenocarcinomas, 8 forestomach papillomas, 8 renal tubular adenocarcinomas, 4 transitional-cell carcinomas of the renal pelvis, 3 lymphocytic leukaemias and 6 tumours at other sites. Of 71 controls, 18 developed 19 tumours, including 12 benign and 6 malignant mammary tumours (4).
Oral hamster (70 wk) 1000 mg kg^{-1} diet for 48 wk followed by a control diet for 22 wk. All of the 24 treated animals developed tumours, including 13 forestomach papillomas, 9 urinary bladder transitional-cell carcinomas, 6 adrenal adenomas and 1 renal pelvis transitional-cell carcinoma. One adrenal carcinoma occurred in 24 controls (5).

Metabolism and toxicokinetics

Following oral administration to rats and mice of ^{14}C-labelled nifurthiazole (labelled in the thiazole ring) 95% of ^{14}C was eliminated within 96 hr, principally via the urine. <10% of ^{14}C in the urine was unchanged nifurthiazole. In addition, ^{14}C-nifurthiazole was covalently bound to renal and hepatic cytosol macromolecules (6).

Genotoxicity

CASE structure-activity methodology predicts it to be positive for mutagenicity to *Salmonella typhimurium* (7).

Other comments

Physical properties, use, analysis, carcinogenicity and mammalian toxicity reviewed (8).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).

References

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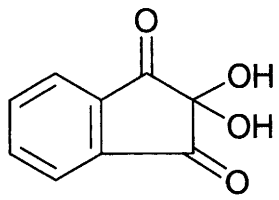
N60 ninhydrin



$C_9H_6O_4$ **Mol. Wt.** 178.14 **CAS Registry No.** 485-47-2

Synonyms 2,2-dihydroxy-1*H*-indene-1,3(2*H*)-dione; 2,2-dihydroxy-1,3-indandione; ningidrin; triketohydrindene hydrate

EINECS No. 207-618-1 **RTECS No.** NK 5425000

Uses Reagent used to detect free amino and carboxyl groups in proteins and peptides, yielding a blue colour.

Physical properties

M. Pt. 240°C (decomp.)
Solubility Organic solvents: ethanol

Environmental fate

Nitrification inhibition
Nitrosomonas sp. inhibition of ammonia oxidation 100 mg l^{-1} 30% inhibition, 10 mg l^{-1} 31% inhibition (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 250 mg kg^{-1} (2).
LD_{50} intraperitoneal mice 78 mg kg^{-1} (3).

References

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N61 niobium

Nb

Nb **Mol. Wt.** 92.91 **CAS Registry No.** 7440-03-1
Synonyms columbium
EINECS No. 231-113-5 **RTECS No.** QT 9900000

Uses In the form ferroniobium (produced by silicon reduction of columbite) to alloy stainless steels and metals for welding rods. Getter in electronic vacuum tubes.
Occurrence In the minerals columbite, pyrochlore and tantalite.
Approximately as abundant in Earth's crust as nickel (*c.* 0.018%).

Physical properties

M. Pt. 2468°C **B. Pt.** 4927°C **Specific gravity** 8.57
Solubility Organic solvents: fused alkalis, hot sulfuric acid

Mammalian & avian toxicity

Acute data
LD_{50} oral (potassium niobate) rat 3000 mg kg^{-1} (1).
LD_{50} oral (niobium pentachloride) mouse 940 mg kg^{-1} (2).
LD_{50} intraperitoneal (potassium niobate) mouse, rat 13, 92 mg kg^{-1}, respectively (1,3).
LD_{50} intraperitoneal (niobium pentachloride) mouse 61 mg kg^{-1} (2).
50 mg kg^{-1} sodium niobate caused severe intoxication in rat (route unspecified) (4).
Acute toxicity symptoms (salt, dose and species unspecified) include urination, defecation, a milky-exudate from the anus, decreased respiration and lethargy. The first deaths were recorded after 2 days with deaths occurring to 7 days (2).

Sub-acute and sub-chronic data

Intraperitoneal (duration unspecified) rat, rabbit, dog 10-50 mg kg^{-1} day^{-1} (niobium pentachloride); 10 mg kg^{-1} caused no effect on body weight gain, at doses above this a dose-related decrease in body weight gain was observed. 3/5 rats of the dose group 30 mg kg^{-1} day^{-1} had died after 15 injections and all animals in the dose group 50 mg kg^{-1} day^{-1} had died by 14 injections. Dose-response renal changes were also observed including increased weight, intratubular brown pigmentation, tubular necrosis and regenerative proliferation (1,3).
Intraperitoneal (potassium niobate) rat 10-95 mg kg^{-1} day^{-1} suffered similiar dose-response effects on body weight, renal damage and mortality to those given nobium pentachloride. All rats survived 11 injections of 10 mg kg^{-1}. 2/5 died from 4 injections of 57 mg kg^{-1}. No rats survived 4 injections of 95 mg kg^{-1}. Renal damage was more pronounced than in nobium pentachloride treated groups (1,3).

Carcinogenicity and chronic effects

Oral (lifetime study) rat, mouse 1.62 ppm in diet mainly as a component of corn oil and 5 ppm in drinking water as sodium niobate. In rats glycosuria and lowered amounts of urinary protein were observed in ♂ and ♀. ♂ also reduced lifespan, decreased heart weight and increased body weights. Mice showed similar but not identical effects, older mice had reduced body weight compared with the controls. ♀ had reduced lifespan and hepatic fatty lesions were frequently observed (5,6).
Life-time studies in mice and rats showed no increased incidences of tumours (5,6).

Irritancy

Dermal rabbit application of niobium pentachloride to unabraded skin caused oedema and erythema within 24 hr which persisted for 72 hr. An eschar 25-30 mm in diameter formed with skin loss in the area by 7 days which had not healed by 14 days. Irritation was more severe on abraded skin. By 7 days ulcers of 25-30 mm in diameter had formed with penetration through the skin to the muscle layers (1).
Instillation of niobium pentachloride into rabbit eye caused very slight irritation (dose duration unspecified) (1).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Nobium metal is completely unreactive with body fluids and would not be expected to exhibit toxicity when given acutely (1).

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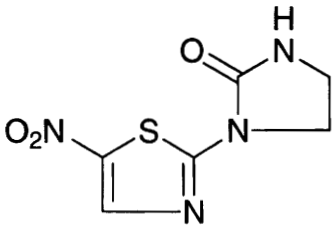
N62 niridazole



$C_6H_6N_4O_3S$ **Mol. Wt.** 214.20 **CAS Registry No.** 61-57-4

Synonyms 1-(5-nitro-2-thiazolyl)-2-imidazolidinone; Ambilhar; Nitrothiamidazole; Nitrothiazol

EINECS No. 200-512-6 **RTECS No.** NJ 1050000

Uses Anthelmintic drug, effective against the three common schistosomes that may infect man. Amoebicide.

Physical properties

M. Pt. 260-262°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 0.9, 2.5 g kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal mouse 220 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Oral (30 wk) ♀ Swiss mice 0.1% in diet caused significant growth retardation (4).

Oral (duration unspecified) Swiss mice 0.2 or 0.4%, Syrian golden hamsters 0.32 or 0.64% in diet caused a reduction in body weight and severe testicular atrophy (5).

Carcinogenicity and chronic effects

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

Oral (18 month) ♂, ♀ Swiss mouse 0.0125, 0.025, 0.5% in diet caused a significant increase in the incidences of lung adenomas, carcinomas of the forestomach and in ♀ mice of mammary carcinomas and ovarian granulosa-cell tumours (4).

Oral (18 month) ♂, ♀ Swiss mouse 0.0125, 0.025, 0.5% in diet, 2 submucosal atypical cellular masses were found in the urinary bladder of lower dose group ♂ and were identified as smooth-muscle tumours (7).

Oral (duration unspecified) ♂, ♀ Swiss mice infected with 40 *Schistosoma mansoni* cercariae and non-infected mice 0.05, 0.025 or 0.0125% in diet, after 25 wk the dose was doubled. Both infected and non-infected mice developed tumours, including lung adenomas, papillomas and carcinomas of the forestomach and bladder and in ♀ carcinomas of the mammary gland and ovary (5).

Oral (duration unspecified) ♂, ♀ Syrian golden hamsters infected with 30 *Schistosoma mansoni* and non-infected 0.04-0.24% in diet. Both infected and non-infected hamsters developed significantly increased incidences of tumours of the forestomach except at doses of 0.04%, mainly papillomas and transitional-cell papillomas of the bladder in doses ≥0.08% (5).

Teratogenicity and reproductive effects

Has been shown to cause necrosis of mesenchymal tissue near the cepalic end of the neural tube and thinning of the neuro-epithelium on the right side of the tube in developing embryos. Cell homogenates and liver microsomal fractions from 10-day-old rat embryos had an increase in oxygen uptake when niridazole was added. It was hypothesised that redox treatment-effects on cycling form the basis of the *in vitro* teratogenic action of niridazole (8).

Metabolism and toxicokinetics

Oral rat, dog, rabbit [^{14}C]niridazole slowly but thoroughly absorbed and excreted in urine and faeces within a few days (9).

In vitro degradation by rat tissue occurred most rapidly in liver and kidney homogenates and at a lesser rate in testes, spleen, heart, lung, brain, muscle and thymus. This order corresponds to nitroreductase activity levels in the tissues (9).

In *in vitro* rat liver microsomes the principal metabolite is *N*-(hydroxyamino)thiamidazole, formed by reduction of the nitro group of niridazole (10).

Oral human metabolised in the liver and eliminated mainly in urine and faeces (11).

In vitro intact rat embryos generated a stable metabolite by reduction in the presence of 5% oxygen. Embryo and yolk sac homogenates or liver microsomes required anaerobic conditions (12).

Genotoxicity

Salmonella typhimurium TA100, TA1538 without metabolic activation positive (13).

Saccharomyces cerevisiae D5 mitotic recombination positive at 100-200 μg ml^{-1} (metabolic activation unspecified) (14).

In vivo dominant lethal test in mice, significant decrease in number of pregnant animals and in total implants per pregnancy (15).

In vivo rat, mice bone marrow cells no chromosomal abnormalities (16,17).

In vivo mice bone marrow cells, no induction of micronuclei (18).

Other effects

Other adverse effects (human)

Suppresses delayed hypersensitivity (19).

Patients undergoing treatment with niridazole have common side-effects, including anorexia, nausea, vomiting, diarrhoea, abdominal pain, dizziness and headache. Central nervous system effects are less common but more serious (20).

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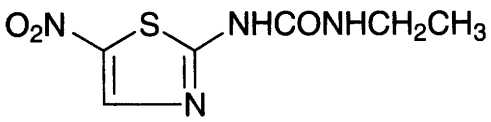
N63 nithiazide



$C_6H_8N_4O_3S$ **Mol. Wt.** 216.22 **CAS Registry No.** 139-94-6

Synonyms *N*-ethyl-*N'*-(5-nitro-2-thiazolyl)urea; 1-ethyl-3-(5-nitro-2-thiazolyl)urea; Hepzide

EINECS No. 205-387-1 **RTECS No.** YT 3500000

Uses Antiprotozoal agent (veterinary).

Physical properties

M. Pt. 288°C (decomp.) **Partition coefficient** log P_{ow} –0.1205 (1)
Solubility Water: 30 mg l^{-1}

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 2150 mg kg^{-1} (2).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (3).
Oral (104 wk) ♂, ♀ B6C3F1 mice 2500 or 5000 mg kg^{-1} for 61 wk, followed by a control diet for 9 wk then original dose resumed for 33 wk and then a control diet for 1 wk. There was no significant dose-related trend in mortality. ♂ had significant dose-related increase in hepatocellular carcinomas/adenomas. ♀ had a non-statistically significant increase in pooled hepatocellular carcinomas/adenomas (4).
Oral (104 wk) ♂, ♀ Fischer 344 rat, 625 or 1250 mg kg^{-1} for 38 wk followed by a control diet for 9 wk then original dose resumed for 33 wk followed by a control diet for 1 wk. There was no significant dose-related trend in mortality. ♀ had statistically significant dose-related increased incidences of fibroadenomas/cystadenomas of skin, subcutaneous tissue and mammary gland and chromophobe/acidophil adenomas of the pituitary. ♂ showed no significant increased incidences of tumours (4).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive; TA98, TA1535, TA1537 without metabolic activation positive (5).

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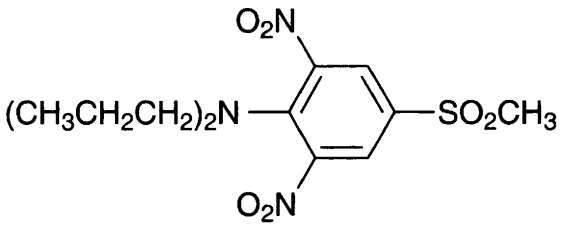
N64 nitralin



$C_{13}H_{19}N_3O_6S$ **Mol. Wt.** 345.38 **CAS Registry No.** 4726-14-1

Synonyms 4-(methylsulfonyl)-2,6-dinitro-*N*,*N*-dipropylbenzenamine; 4-(methylsulfonyl)-2,6-dinitro-*N*,*N*-dipropylaniline; Nitraline; Planavin; Planuin

EINECS No. 225-219-0 **RTECS No.** CY 0380000

Uses Superseded herbicide.

Physical properties

M. Pt. 150-151°C **Specific gravity** 1.39 **Volatility** v.p. 9.3×10^{-9} mmHg at 20°C
Solubility Water: 0.6 ppm at 22°C. Organic solvents: acetone, benzene, dimethyl sulfoxide

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) rainbow trout >4.5 mg l^{-1} (1).

Environmental fate

Degradation studies
Markedly degraded by bacteria (type unspecified) in mineral salt medium. The major metabolites were formed by reduction of the nitro groups (2).
$t_{1/2}$ dry soil 54 day (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >2 g kg^{-1} (3).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

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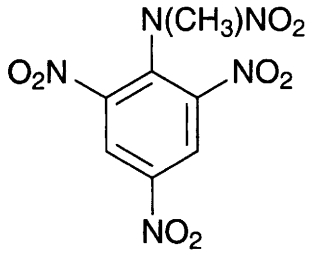
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

N65 nitramine



$C_7H_5N_5O_8$ **Mol. Wt.** 287.15 **CAS Registry No.** 479-45-8

Synonyms 2,4,6-trinitrophenylmethylnitroamine; *N*-methyl-*N*,2,4,6-tetranitrobenzenamine; Tetryl; picrylmethylnitramine

EINECS No. 207-531-9 **RTECS No.** BY 6300000

Uses Insecticide. Miticide. Indicator.

Physical properties

M. Pt. 130°C **B. Pt.** 187°C (explodes) **Specific gravity** 1.57 at 19°C

Occupational exposure

FR-VLE 1.5 mg m^{-3}

UK-LTEL 1.5 mg m^{-3} **UK-STEL** 3 mg m^{-3}

US-TWA 1.5 mg m^{-3}

Supply classification explosive, toxic

Risk phrases Risk of explosion by shock, friction, fire or other sources of ignition – Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R2, R23/24/25, R33)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – This material and its container must be disposed of in a safe way – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S35, S45)

Environmental fate

Degradation studies

7 day biodegradation test, 0% degradation in culture (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} subcutaneous dog 5000 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (3).

Other effects

Any other adverse effects

Causes sensitisation dermatitis and irritation of upper respiratory tract, anaemia and liver and kidney damage (species, route and duration 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).
Included in the UK List of Classified and Authorised Explosives 1994. UK Class and Division 3.2. Competent Authority Reference GB 32142 (7).

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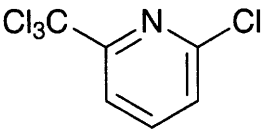
N66 nitrapyrin



$C_6H_3Cl_4N$ **Mol. Wt.** 230.91 **CAS Registry No.** 1929-82-4

Synonyms 2-chloro-6-(trichloromethyl)pyridine; N-Serve; CP; N-Serve 24E; Dowco 163

EINECS No. 217-682-2 **RTECS No.** US 7525000

Uses Fertilizer additive to prevent loss of soil nitrogen and to control nitrification.

Physical properties

M. Pt. 62.5-62.9°C **B. Pt.** 136-137.5°C at 11 mmHg **Specific gravity** 1.579 at 25°C
Partition coefficient log P_{ow} 3.325 **Volatility** v.p. 4.8×10^{-3} mmHg at 25°C
Solubility Water: 40 mg l^{-1} at 22°C. Organic solvents: ethanol, acetone, dichloromethane, xylene

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} **US-STEL** 20 mg m^{-3}
Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin (S2, S24)

Ecotoxicity

Fish toxicity
LC_{50} channel catfish 5.8 mg l^{-1} (1)

Invertebrate toxicity
10 mg l^{-1} caused no mortality to *Daphnia* sp. or ramshorn snail (1).

Bioaccumulation
5lb active ingredient $acre^{-1}$ applied to soil prior to planting with strawberries. No nitrapyrin residues were detected in strawberries (≥0.04 ppm). The metabolite 6-chloropicolinic acid was detected in strawberries at 0.09 ppm (2).

Environmental fate

Nitrification inhibition
75% inhibition of ammonia oxidation by activated sludge at 100 mg l^{-1} (3).
50% inhibition of ammonia oxidation by pure culture at 11.0 mg l^{-1} (4).
50% inhibition of nitrification in recirculating system at 50 mg l^{-1} tested over 6 days (5).

Degradation studies
6-Chloropicolinic acid is the sole detectable metabolite, other than carbon dioxide, in soil (6).
Degradation in soil was fastest soon after application and decreased with time. Degradation was less in a silty clay loam soil, which had a relatively high level of organic matter, than in silt loam soil (7).

Abiotic removal
Undergoes hydrolysis in buffered distilled water with a $t_{1/2}$ 1.7-4.0 day at 35°C, depending on concentration.
Undergoes photolysis in natural water with a $t_{1/2}$ 12 hr (6).

Adsorption and retention
Field studies with Drummer silty clay loam and Cisne silt loam found that nitrapyrin did not move beyond 7.5 cm of the point of application in the soil. The highest concentrations were found within 2.5 cm of the point of application and a concentration gradient existed out to 7.5 cm, movement was less in silty clay loam soil. There was no indication that soil accumulation would occur from a once a yr application (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral chicken 235 mg kg^{-1} (1).
LD_{50} dermal rabbit 850 mg kg^{-1} (8).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral Japanese quail, mallard duck 820, 1466 mg kg^{-1}, respectively (1).
LD_{50} (8 days) oral rabbit, mouse, rat 500-940 mg kg^{-1} (8-10).
No-effect level (94 day) oral rat, dog 300, 600 mg kg^{-1}, respectively (1).

Teratogenicity and reproductive effects
Oral rat 0-50 mg kg^{-1} day^{-1} on gestation days 6-15, no foetotoxic or teratogenic effects observed (11).
Oral rabbit 0-30 mg kg^{-1} day^{-1} on gestation days 6-15. Foetuses of the 30 mg kg^{-1} day^{-1} dose group had an increased incidence of crooked hyoid bone which was considered to indicate foetotoxicity but not genotoxicity (11).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive, TA100 without metabolic activation and TA1535 with and without metabolic activation negative (12).

Legislation

Subject to registration or re-registration in USA (13).
Log P_{ow} exceeds the European Union recommended limit of 3.0 (14).

Other comments

Nitrification inhibition reviewed (15).
Toxicity reviewed (16).
As well as inhibiting nitrification, nitrapyrin restricted the growth of radishes and lowered their calcium and magnesium tissue concentrations.

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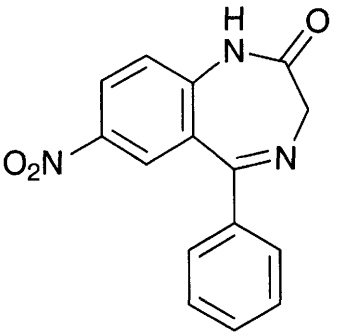
N67 nitrazepam



$C_{15}H_{11}N_3O_3$ **Mol. Wt.** 281.27 **CAS Registry No.** 146-22-5

Synonyms 1,3-dihydro-7-nitro-5-phenyl-2*H*-1,4-benzodiazepin-2-one; Mogadon; Epibenzalin; Neozopam; Sonebon; Relact

EINECS No. 205-665-2 **RTECS No.** DF 2450000

Uses Anticonvulsant. Hypnotic.

Physical properties

M. Pt. 224-226°C
Solubility Organic solvents: acetone, chloroform, ethanol, ethyl acetate

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 745-905 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse, rat 275, 733 mg kg^{-1}, respectively (2,3).
LD_{50} intravenous mouse, rabbit 130, 520 mg kg^{-1}, respectively (2,4).

Teratogenicity and reproductive effects

Oral Sprague-Dawley rats 100-300 mg kg^{-1} on day 10-14 of gestation, foetuses were examined on day-20 of gestation. Malformations were predominantly limb reduction defects which were produced at high frequency by treatment on day 12 or 13 of gestation, but also included exencephaly, cleft palate, micrognathia and short or kinky tail. Microscopic examination of limb buds revealed haemorrhage and mesenchymal cell necrosis (5).

Metabolism and toxicokinetics

Readily absorbed from the gastro-intestinal tract in humans. Metabolised in the liver, mainly by nitro-reduction followed by acetylation. Only a small amount is excreted unchanged in urine, with the majority of elimination being of metabolites (6).
Elimination $t_{1/2}$ 24 hr, in humans (6).
Can cross placental and blood-brain barriers and small amounts have been detected in breast milk, in humans (6).

Genotoxicity

Salmonella typhimurium TA98, TA102, TA1535, TA1537 with and without metabolic activation negative. TA100 with metabolic activation weakly positive (7).
Escherichia coli WP2 uvrA with and without metabolic activation negative (7).
In vivo Drosophila melanogaster sex-linked recessive lethal test and ♀ germ-line-mosaic test, genotoxicity was demonstrated (8).
In vivo mouse bone marrow micronucleus test negative (9).

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N68 nitric acid

$$HNO_3$$

HNO_3 **Mol. Wt.** 63.01 **CAS Registry No.** 7697-37-2

Synonyms hydrogen nitrate; aqua fortis

EINECS No. 231-714-2 **RTECS No.** QU 5775000

Uses Manufacture of nitrates and nitro compounds for use as fertilizers, dye intermediates, explosives and organic chemicals. Pharmaceutical acidifier. Veterinary cauterising agent for warts.

Physical properties

M. Pt. –42°C **B. Pt.** 86°C **Specific gravity** 1.50269 at 25°C with respect to water at 4°C

Occupational exposure

DE-MAK 2 ppm (5.2 mg m^{-3})
FR-VME 2 ppm (5 mg m^{-3}) **FR-VLE** 4 ppm (10 mg m^{-3})
JP-OEL 2 ppm (5.2 mg m^{-3})
SE-LEVL 2 ppm (5 mg m^{-3}) **SE-STEL** 5 ppm (13 mg m^{-3})
UK-LTEL 2 ppm (5.2 mg m^{-3}) **UK-STEL** 4 ppm (10 mg m^{-3})
US-TWA 2 ppm (5.2 mg m^{-3}) **US-STEL** 4 ppm (10 mg m^{-3})

UN No. 2031 (other than red fuming)

UN No. 2032 (red fuming)

UN No. 1796 (mixtures containing >50% and <50% nitric acid) **HAZCHEM Code** 2PE **Conveyance classification** corrosive substance **Conveyance classification** corrosive substance, fire intensify hazard, toxic (red fuming)
Supply classification oxidising, corrosive
Risk phrases ≥70% – Contact with combustible material may cause fire – Causes severe burns (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)

Mammalian & avian toxicity

Acute data
LD_{Lo} oral human 430 mg kg^{-1} (1).

Teratogenicity and reproductive effects
Teratogenic effects reported in rats after oral administration of a total dose of 21150 mg kg^{-1} on days 1-21 after birth. Reproductive effects reported in rats after oral administration of 2345 mg kg^{-1} on day-18 after birth (2).

Sensitisation
Corrosive and irritant to rabbits' skin (dose and duration unspecified) (3).

Other effects

Other adverse effects (human)
Several cases of occupational asthma in a mineral analysis laboratory were attributed to acid, including nitric acid, vapours (4).
Occupational exposure to the liquid can cause eye burns and permanent visual impairment; concentrated liquid or vapours can cause severe skin burns, and dilute nitric acid causes mild skin irritation (5).
Chronic occupational exposure, or exposure to high concentrations can cause chronic bronchitis and chemical pneumonitis, respectively, and dental erosion (6-9).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (10).
Hazards reviewed (11-13).

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N69 nitric oxide

NO

NO **Mol. Wt.** 30.01 **CAS Registry No.** 10102-43-9

Synonyms nitrogen monoxide; mononitrogen monoxide

EINECS No. 233-271-0 **RTECS No.** QX 0525000

Uses Manufacture of nitric acid; bleaching rayon; stabiliser for propylene and methyl ether.

Physical properties

M. Pt. –163.6°C **B. Pt.** –151.7°C **Specific gravity** 1.229 g l^{-1} at 20°C and 760mmHg
Solubility Water: 4.6% v/v at 20°C and 760 mmHg

Occupational exposure

FR-VME 25 ppm (30 mg m^{-3})
SE-LEVL 25 ppm (30 mg m^{-3}) **SE-STEL** 50 ppm (60 mg m^{-3})
UK-LTEL 25 ppm (31 mg m^{-3}) **UK-STEL** 35 ppm (44 mg m^{-3})
US-TWA 25 ppm (31 mg m^{-3})

UN No. 1660 **Conveyance classification** toxic gas, fire intensify hazard, corrosive
Supply classification toxic
Risk phrases Very toxic by inhalation – Very toxic in contact with skin (R26, R27)
Safety phrases 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) (S7/9, S26, S45)

Environmental fate

Degradation studies
Nitric oxide release in soil was stimulated by ammonium and inhibited by nitrapyrin (1).

Mammalian & avian toxicity

Acute data
LC_{50} (duration unspecified) inhalation rat 1068 mg m^{-3} (2).
LC_{Lo} (duration unspecified) inhalation mouse 320 ppm (3).

Carcinogenicity and chronic effects

♂ rats exposed to up to 1500 ppm for 15 months, or 1000 ppm for 30 months suffered no lung inflammation (4).

Metabolism and toxicokinetics

In rats, inhaled nitric oxide reacts with haemoglobin, forming nitrosyl-haemoglobin from which nitrate and nitrite are generated. Most nitrate is excreted via urine but some enters the oral cavity via saliva and is microbially transformed to nitrite, part of which interacts with secondary amines and amides to form nitroso compounds. Nitrate in the intestine is partly reduced by microflora activity to ammonia via nitrite, reabsorbed and converted into urea. Most metabolites are excreted within 48 hr (5).

Other comments

Nitric oxide and superoxide are free radicals that appear to contribute to the pathogenesis of a number of brain disorders, and cerebral endothelial cells are a potential target of these agents. Together, the compounds appear to act synergistically, resulting in enhanced toxicity (6).

Carcinogenicity reviewed (7).

Soil microbial metabolism, atmospheric chemistry, sources and sink, and flux between soil and the atmosphere reviewed (8).

Environmental health criteria reviewed (9).

Review (10).

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N70 nitrilotriacetic acid

$$N(CH_2CO_2H)_3$$

$C_6H_9NO_6$ **Mol. Wt.** 191.14 **CAS Registry No.** 139-13-9

Synonyms aminotriacetic acid; *N,N*-bis(carboxymethyl)glycine; triglycine; triglycollamic acid

EINECS No. 205-355-7 **RTECS No.** AJ 0175000

Uses Chelating and sequestering agent; eluting agent in purification of rare earth elements.

Physical properties

M. Pt. 246°C (decomp.)

Solubility Water: 1.28 g l^{-1} at 22.5°C

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 92.3 mg l^{-1} (1).

LC_{50} (24 hr) fathead minnow >100 mg l^{-1} (2).

Invertebrate toxicity

LOEC *Scenedesmus quadricauda* 8.3 mg l^{-1} (3).

LC_{50} (24 hr) *Daphnia magna* >100 mg l^{-1} (2).

EC_{50} (15 min) *Photobacterium phosphoreum* 1003 ppm Microtox test (4).

Toxicity threshold *Pseudomonas putida* >10000 mg l^{-1} (3); *Microcystis aeruginosa* 510 mg l^{-1} (5); *Entosiphon sulcatum* 800 mg l^{-1} (3); *Uronema parduczi Chatton-Lwoff* >800 mg l^{-1} (6).

1 or 10 mg l^{-1} had no effect and 100 mg l^{-1} a marginal inhibitory effect on *Selenastrum capricornutum* (7).

In studies on the effect of growth medium composition on algal toxicity, the lowest concentration significantly reducing growth in Bolds basal medium was 50 mg l^{-1} for *Selenastrum capricornutum* (1-3, 1-4 or 1-5 days) and 80 mg l^{-1} for *Scenedesmus subspicatus* (1-5 days) and *Chlorella vulgaris* (1-3 or 1-5 days). The lowest concentration reducing growth on EPA and OECD media was 5 mg l^{-1} for all species (8).

Toxicity to other species

Not teratogenic in the frog embryo teratogenicity assay: *Xenopus* (FETAX) (9).

Environmental fate

Degradation studies

BOD^{20}_5 nil (non-acclimated seed organisms); BOD^{20}_{20} 0.65-0.72 at 2-10 mg O_2 l^{-1} (acclimated organisms) (10).

ThOD 1.08 mg O_2 l^{-1}, COD 0.75, nitrogenous oxygen demand 0.33 mg O_2 l^{-1}; analytical reflux COD 90.7% recovery, BOD_5 0.014, BOD_5/COD 0.021 (7).

Biodegraded to glycerate and ammonia via iminodiacetic acid and glycine (11).

A Gram-negative bacteria isolated from river sediment was able to grow with nitrilotriacetic acid as a combined carbon, nitrogen and energy source in the absence of molecular oxygen, using nitrate as the terminal electron acceptor. It was tentatively located in the γ-subclass of Proteobacteria close to, but separate from, *Xanthomonas* (12).

In studies of microbial degradation in groundwater, laboratory studies found under aerobic conditions >90% of an initial concentration of 105-600 μg l^{-1} nitrilotriacetic acid was removed during column passage. Under denitrifying conditions partial breakthrough of nitrilotriacetic acid into column effluent occurred; after 5 days adaption, again >90% was degraded (13).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1470, 3160 mg kg^{-1}, respectively (14).

LD_{Lo} intraperitoneal mouse 125 mg kg^{-1} (15).

Carcinogenicity and chronic effects

NTP tested rats and mice via feed. Clear evidence of carcinogenicity in rats and mice, causing kidney, bladder and urinary tract tumours (16).

Irritancy

Classified as a skin irritant by calculation and by the pH-acid/alkali reserve method (17).

Genotoxicity

Salmonella typhimurium TA98, TA97, TA100, TA102, TA1535, TA1537 (activation unspecified) negative (18).

Did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells with or without metabolic activation (19).

Induced mitotic recombination and possibly aneuploidy in *Drosophila melanogaster* (20).

Nitrilotriacetic acid has a synergistic effect on Cr(VI) mutagenicity in *Salmonella typhimurium* and *Drosophila melanogaster* (21).

Other comments

Isolated as contaminant in sewage effluent.
Properties of nitrilotriacetate-degrading bacteria reviewed (22).
Physiology, biochemistry and ecology of microbiol degradation of chelating agents used in detergents, including nitrilotriacetic acid, reviewed (23).

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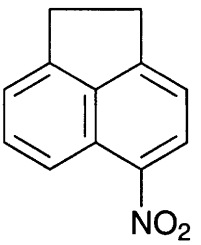
N71 5-nitroacenaphthene



$C_{12}H_9NO_2$ **Mol. Wt.** 199.21 **CAS Registry No.** 602-87-9

Synonyms 1,2-dihydro-5-nitroacenaphthylene; 5-nitronaphthaleneethylene; 5-NAN

EINECS No. 210-025-0 **RTECS No.** AB 1060000

Uses In manufacture of naphthalimide dyes, plastics, pesticides.

Physical properties

M. Pt. 90-95°C **B. Pt.** 279°C

Occupational exposure

Supply classification toxic
Risk phrases May cause cancer (R45)
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) brown trout, rainbow trout, bluegill sunfish, fathead minnow 0.58-1.70 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* 41 mg l^{-1} (2).

Environmental fate

Adsorption and retention
25% of 100 μg l^{-1} adsorbed onto smectite clay particles (50 mg l^{-1}) from simulated sea water (3).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (4).
NTP tested rats and mice via feed. Clear evidence of carcinogenicity in rats and ♀ mice, causing tumours in the lung, liver ovary and mammary glands (5).
Oral administration of 1% to ♀ rats or ♀ hamsters for 4 and 6 months, respectively, caused small intestinal adenomas and mammary carcinomas. Intraperitoneal injection of 6 mg kg^{-1} 2 × wk^{-1} for 18 months produced leukaemia and reticulum cell sarcomas in mice (6).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (7).
Escherichia coli WP2 *uvrA* with metabolic activation positive (8).
DNA repair test with rat or mouse hepatocytes positive (9).

Other comments

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

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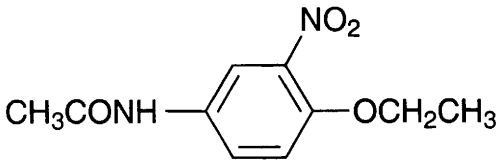
N72 3-nitro-*p*-acetophenelide



$C_{10}H_{12}N_2O_4$ **Mol. Wt.** 224.22 **CAS Registry No.** 1777-84-0

Synonyms 4-acetylamino-2-nitrophenetole; *N*-(4-ethoxy-3-nitrophenyl)acetamide; 5-nitro-*p*-acetophenetidide

EINECS No. 217-211-0 **RTECS No.** AM 4550000

Physical properties

M. Pt. 103-104°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 664 mg kg^{-1} (1).

Carcinogenicity and chronic effects

NTP tested rats and mice in feed. Clear evidence of carcinogenicity in ♂ mice, causing liver tumours no evidence of carcinogenicity in rats (1).

Irritancy

100 mg (duration unspecified) caused moderate irritation to rabbits' eyes (2).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (3).

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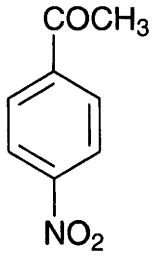
N73 4′-nitroacetophenone



$C_8H_7NO_3$ **Mol. Wt.** 165.15 **CAS Registry No.** 100-19-6

Synonyms 1-(4-nitrophenyl)-ethanone; 4-acetylnitrobenzene; *p*-acetylnitrobenzene; methyl *p*-nitrophenyl ketone; *p*-nitroacetophenone; *p*-nitrophenyl methyl ketone

EINECS No. 202-827-4 **RTECS No.** AM 9627000

Physical properties

M. Pt. 78-80°C **B. Pt.** 202°C

Environmental fate

Carbonaceous inhibition

EC_{50} (30 min) *Photobacterium phosphoreum* 27.4 ppm Microtox test (1).

Degradation studies

Rate of biodegradation was 5.2 mg COD g^{-1} hr^{-1} when it was the carbon source for microbes in the inoculum (adapted activated sewage sludge) (2).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation positive, TA100, TA1535, TA1537 with and without metabolic activation negative (3-8).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**, 361-431.
2. Pitter, P. *Water Res.* 1976, **10**, 231-235.
3. Zeiger, E. et al *Environ. Mol. Mutagen.* 1987, **9** (Suppl. 9), 1-109.
4. Mullin, C. A. et al *Mutat. Res.* 1987, **188**(4), 267-274.
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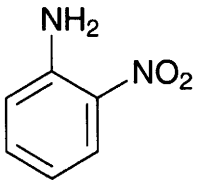
N74 2-nitroaniline



$C_6H_6N_2O_2$ **Mol. Wt.** 138.13 **CAS Registry No.** 88-74-4

Synonyms *o*-nitroaniline; 1-amino-2-nitrobenzene; C.I. 37025

EINECS No. 201-855-4 **RTECS No.** BY 6650000

Uses Dyestuff intermediate

Physical properties

M. Pt. 73-76°C **B. Pt.** 284.5°C **Flash point** 168°C **Specific gravity** 0.9015 at 25°C with respect to water at 4°C **Volatility** v.p. 1 mmHg at 104°C ; v.den. 4.77

Solubility Water: slightly soluble. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1661 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification toxic

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R33, R52/53)

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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity

10 mg l^{-1} (24 hr) was neither lethal nor toxic to unspecified freshwater fish species (1).

Log LC_{50} (14 day) guppy 1.85 (LC_{50} expressed in μmol l^{-1}) (2).

Invertebrate toxicity

EC_{50} (60 hr) *Tetrahymena pyriformis* 116 mg l^{-1} (3).

EC_{50} (5-30 min) *Photobacterium phosphoreum* 7.25 ppm Microtox test (4).

Bioaccumulation

Non or low accumulative (5).

Environmental fate

Degradation studies

Non-biodegradable (5).

Pseudomonas putida biotype A is reportedly capable of utilising aniline derivatives as sole source of carbon (6). No degradation occurred in 23 days in the static (Zahn-Wellens) test (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral quail 750 mg kg^{-1} (8).

LD_{50} oral mouse, rat, guinea pig 1070-2350 mg kg^{-1} (9,10).
LD_{50} dermal rabbit 20 g kg^{-1} (11).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (12,13).
DNA repair test with cultured rat hepatocytes negative (14).

References

1. Newsome, L. et al *QSAR Environ. Toxicol. Proc. Int. Workshop 2nd* 1986, 231-250.
2. Deneer, J. W. et al *Aquat. Toxicol.* 1987, **10**(2/3) 115-129.
3. *The list of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* 1987, Chemicals Inspection & Testing Institute, Japan.
4. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
5. Schultz, T. W. et al *Ecotoxicol. Environ. Saf.* 1985, **10**, 97-111.
6. Park, Y. K. et al *Sanop Misaengmul Hakhoechi* 1988, **16**(5), 413-420.
7. Wellens, V. H. *Z. Wasser Abwasser Forsch.* 1990, **23**(3), 85-98.
8. *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355.
9. *Gig. Tr. Prof. Zabol.* 1981, **25**(8), 50.
10. *Vopr. Kommunaln. Gig.* 1966, **6**, 89.
11. *Toxicol. Appl. Pharmacol.* 1977, **42**, 417.
12. Chiu, C. W. et al *Mutat. Res.* 1978, **58**, 11-22.
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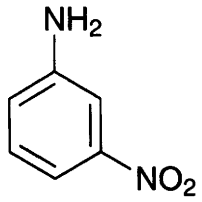
N75 3-nitroaniline



$C_6H_6N_2O_2$ **Mol. Wt.** 138.13 **CAS Registry No.** 99-09-2

Synonyms *m*-nitroaniline; 1-amino-3-nitrobenzene; *m*-nitroaminobenzene; 3-nitrobenzenamine; *m*-nitrophenylamine; C.I. 37030

EINECS No. 202-729-1 **RTECS No.** BY 6825000

Uses Dyestuff intermediate.

Physical properties

M. Pt. 114°C **B. Pt.** 306°C **Flash point** 199°C **Specific gravity** 0.9011 at 25°C with respect to water at 4°C
Volatility v.p. 1 mm Hg at 119°C
Solubility Water: 1.25 g l^{-1}. Organic solvents: ethanol, methanol

Occupational exposure

UN No. 1661 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R33, R52/53)
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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity
Highest test concentration (24 hr) causing neither sickness nor death in unspecified freshwater fish species 5 mg l^{-1} (1).
LC_{50} (14 day) guppy 372 μmol l^{-1} (2).

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 30.2 ppm Microtox test (3).

Bioaccumulation
Non or low accumulative (4).

Environmental fate

Degradation studies
Non-biodegradable (4).
No (0%) degradation in 23 days in the static (Zahn-Wellens) test (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral quail 562 mg kg^{-1} (6).
LD_{50} oral mouse, guinea pig, rat 308, 450, 535 mg kg^{-1}, respectively (7,8).
LD_{Lo} intraperitoneal dog 70 mg kg^{-1} (9).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation positive, TA100 without metabolic activation negative (10).
Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (11).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (12).

References

1. Newsome, L. D. et al *QSAR Environ. Toxicol. Proc. Int. Workshop 2nd* 1987, 231-250.
2. Deneer, J. W. et al *Aquat. Toxicol.* 1987, **10**(2/3), 115-129.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
4. *The list of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* 1987, Chemicals Inspection & Testing Institute, Japan.
5. Wellens, V. H. Z. *Wasser Abwasser Forsch.* 1990, **23**(3), 85-98.
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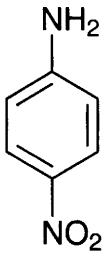
N76 4-nitroaniline



$C_6H_6N_2O_2$ **Mol. Wt.** 138.13 **CAS Registry No.** 100-01-6

Synonyms *p*-nitroaniline; *p*-aminonitrobenzene; 1-amino-4-nitrobenzene; *p*-nitrophenylamine; C.I. 37035

EINECS No. 202-810-1 **RTECS No.** BY 7000000

Uses Intermediate for dyes, antioxidants, gasoline gum inhibitors, poultry medicinals, corrosion inhibitor.

Physical properties

M. Pt. 149-51°C **B. Pt.** 260°C at 100 mmHg **Flash point** 165°C **Specific gravity** 1.424
Volatility v.p. 1 mmHg at 142.4°C
Solubility Water: 1 g 1250 ml^{-1}. Organic solvents: benzene, ethanol, ether, methanol

Occupational exposure

DE-MAK 1 ppm (5.7 mg m^{-3})
FR-VME 3 mg m^{-3}
JP-OEL 3 mg m^{-3}
UK-LTEL 6 mg m^{-3}
US-TWA 3 mg m^{-3}

UN No. 1661 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R33, R52/53)
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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) *Leuciscus idus* 35 mg l^{-1} (1).
LC_{50} (96 hr) *Brachydanio rerio*, fathead minnow 87.6, 106 mg l^{-1} (2).

Invertebrate toxicity
LOEC *Microcystis aeruginosa, Uronema parduczi* 0.35, 31 mg l^{-1}, respectively (3).
EC_{50} (60 hr) *Tetrahymena pyriformis* 10 mg l^{-1} (4).
EC_{50} (30 min) *Photobacterium phosphoreum* 1.02 ppm Microtox test (5).

Bioaccumulation
Non or low accumulative (6).

Environmental fate

Degradation studies

Biodegraded by soil microflora in >64 days (7).

Low biodegradability.

Mammalian & avian toxicity

Acute data

LD_{50} oral quail 1 g kg^{-1} (8).

LD_{50} oral guinea pig, rat, mouse 450-810 mg kg^{-1} (9-11).

LD_{Lo} intraperitoneal rat 600 mg kg^{-1} (12).

LD_{50} intraperitoneal, intramuscular mouse 250, 800 mg kg^{-1}, respectively (13,14).

Carcinogenicity and chronic effects

The National Toxicology Program tested mice via gavage. Equivocal evidence for carcinogenicity in ♂, no evidence for carcinogenicity in ♀ (15).

0-9 mg kg^{-1} day^{-1} by gavage for 2 yr had no effect on tumour incidence in ♂ or ♀ rats. 9 mg kg^{-1} day^{-1} caused increased methaemoglobinaemia and spleen weight (16).

Teratogenicity and reproductive effects

0-9 mg kg^{-1} day^{-1} by gavage for 14 or 18 wk prior to mating, through to lactation had no consistent effect on mating, pregnancy or fertility in ♂ and ♀ rats (16).

1-100 mg kg^{-1} by gavage caused reduced sperm motility and increased relative epididymis weight in ♂ mice (17). Reduced litter viability, liveborn per litter and pup survival in a proposed short-term *in vivo* assay, in which mice were dosed with 1200 mg kg^{-1} day^{-1} on days 6-13 of pregnancy (17).

Metabolism and toxicokinetics

Absorbed through skin or inhalation. Metabolites oxidise haemoglobin to methaemoglobin (species unspecified) (18).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (19).

Other effects

Other adverse effects (human)

Cases of poisoning and cyanosis have been reported (18).

Legislation

Criteria for setting UK occupational exposure limit summarised (18).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (20).

References

1. Wellens, H. Z. *Wasser Abwasser Forsch.* 1982, **15**, 49.
2. Curtis, M. W. et al *J. Hydrol.* 1981, **51**, 359.
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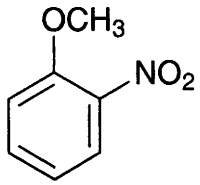
N77 2-nitroanisole



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 91-23-6

Synonyms *o*-nitroanisole; 2-methoxynitrobenzene; 1-methoxy-2-nitrobenzene; *o*-nitrophenyl methyl ether

EINECS No. 202-052-1 **RTECS No.** BZ 8790000

Uses Dye intermediate; organic synthesis.

Physical properties

M. Pt. 9.5-10.5°C **B. Pt.** 273°C **Flash point** >110°C **Specific gravity** 1.254 at 20°C with respect to water at 4°C

Solubility Water: insoluble in water. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2730 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance

Supply classification toxic

Risk phrases May cause cancer – Harmful if swallowed (R45, R22)

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

Ecotoxicity

Invertebrate toxicity

EC_{50} (24 hr) *Daphnia magna* 13 mg l^{-1} (nominal value) (1).

E_BC_{10} (72 hr) *Scenedesmus subspicatus* 3.9 mg l^{-1} (2).

Bioaccumulation
Non- or low accumulative (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 1450, 1980 mg kg^{-1}, respectively (4).

Carcinogenicity and chronic effects
National Toxicology Program classification: reasonably anticipated to be a human carcinogen (5).
Oral rat (2 yr) 0, 222, 666, 2000 ppm in feed induced mononuclear cell leukaemia in the haemopoietic system; urinary bladder papilloma and carcinoma; adenomas/carcinomas of the intestine; and papilloma/carcinoma in kidney (6).
Oral mice (2 yr) 0, 666, 2000, 6000 in feed induced liver adenomas and carcinomas (6).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (7); TA98 without metabolic activation positive (8).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).

References

1. Kuehn, R. et al *Water Res.* 1989, **23**(4), 501-510.
2. Kuehn, R. et al *Water Res.* 1990, **24**(1), 31-38.
3. *The list of the existing chemical substances on biodegradability by microorganisms or bioaccumulation in fish body* 1987, Chemicals Inspection & Testing Institute, Japan.
4. *Gig. Tr. Prof. Zabol.* 1981, **25**(8), 50.
5. *Eighth Report on Carcinogens* 1998, National Toxicology Program, NIEHS, Research Triangle Park, NC 27709, USA.
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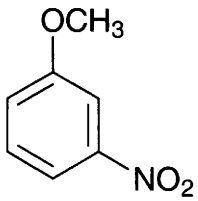
N78 3-nitroanisole



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 555-03-3
Synonyms 3-methoxynitrobenzene; *m*-nitroanisole; 1-methoxy-3-nitrobenzene
EINECS No. 209-079-8

Physical properties

M. Pt. 36-38°C **B. Pt.** 258°C **Flash point** >110°C **Specific gravity** 1.373
Solubility Water: insoluble. Organic solvents: ethanol

Occupational exposure

UN No. 2730 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance

Ecotoxicity

Bioaccumulation
Non- or low accumulative (1).

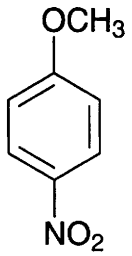
Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (2).

References

1. *The list of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* 1987, Chemicals Inspection & Testing Institute, Japan.
2. Chiu, C. W. et al *Mutat. Res.* 1978, **58**, 11-22

N79 4-nitroanisole



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 100-17-4
Synonyms *p*-nitroanisole; 1-methoxy-4-nitro-benzene; 4-methoxynitrobenzene; 4-nitrophenyl methyl ether
EINECS No. 202-825-3 **RTECS No.** BZ 8800000

Physical properties

M. Pt. 54°C **B. Pt.** 258-260/274°C **Specific gravity** 1.233 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.03 (1) **Volatility** v.den. 5.29
Solubility Water: 70 mg l^{-1} at 15°C. Organic solvents: diethyl ether, ethanol, petroleum ether

Occupational exposure

UN No. 2730 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* concentration 16.4 mg l^{-1} Microtox test (2).
EC_{50} (24 hr) *Daphnia magna* 7.0 mg l^{-1} (3).
EC_{50} (48 hr) *Scenedesmus subspicatus* 39 mg l^{-1} (4).
NOEC (2 day) *Daphnia magna* 2.0 mg l^{-1} (3).

Environmental fate

Degradation studies

Decomposition by a soil microflora in >64 days (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 2600 and 1710 mg kg^{-1}, respectively (6).
LD_{50} intraperitoneal mouse 698 mg kg^{-1} (7).
LD_{50} intraperitoneal rat 1400 mg kg^{-1} (8).

Metabolism and toxicokinetics

During recirculation of autologous blood perfusion (in ♂ rats) total absorption occurred during the first passage and it was eluted rapidly with the 1st peak at 0.92 min (9).
Not metabolised by non-parenchymal cell homogenates treated with *p*-nitroanisole (species unspecified) (10).
The rate of *O*-demethylation decreased by 41% in aged rats (11).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation positive, without metabolic activation equivocal; TA100 with metabolic activation positive, without metabolic activation negative (12).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).

Other comments

Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicology and exposure limits listed (14).

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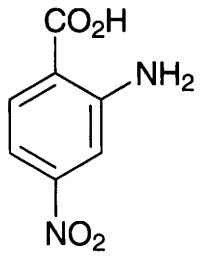
N80 4-nitroanthranilic acid



$C_7H_6N_2O_4$ **Mol. Wt.** 182.14 **CAS Registry No.** 619-17-0

Synonyms 2-amino-4-nitrobenzoic acid

EINECS No. 210-583-5 **RTECS No.** CB 3675000

Uses Dye intermediate.

Physical properties

M. Pt. 268-270°C decomposes

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 640 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral (110 wk) ♂/♀ Fischer 344 rats and B6C3F1 mice, high and low doses were 1.5 and 0.46% and 1.0 and 0.46% for rats and mice, respectively. Evidence of carcinogenicity was negative in both sexes and species (2).

Genotoxicity

Salmonella typhimurium TA98 without metabolic activation positive, mutagenicity was enhanced with metabolic activation (3,4).

In vitro Chinese hamster ovary cells, micronucleus test with and without metabolic activation negative (5).

In vitro Chinese hamster ovary cells, HGPRT with and without metabolic activation negative (5).

Legislation

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

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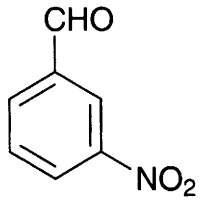
N81 3-nitrobenzaldehyde



$C_7H_5NO_3$ **Mol. Wt.** 151.12 **CAS Registry No.** 99-61-6

Synonyms *m*-nitrobenzaldehyde

EINECS No. 202-772-6 **RTECS No.** CU 7250000

Physical properties

M. Pt. 58°C **B. Pt.** 164°C at 23 mmHg

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Environmental fate

Degradation studies

Adapted activated sludge at 20°C: 94% COD removal at 10 mg COD g^{-1} dry inoculum hr^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 180 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA98 and TA100 with and without metabolic activation positive and negative, respectively (3).

Legislation

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

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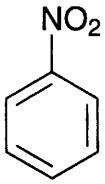
N82 nitrobenzene



$C_6H_5NO_2$ **Mol. Wt.** 123.11 **CAS Registry No.** 98-95-3

Synonyms essence of mirbane; mirbane oil; nitrobenzol

EINECS No. 202-716-0 **RTECS No.** DA 6475000

Uses Manufacture of aniline. In soaps. Shoe polishes. Refining lubricating oils. Manufacture pyroxylin compounds. Solvent in TNT production.

Occurrence It may be formed in the atmosphere from the photochemical reaction of benzene with oxides of nitrogen (1).

Physical properties

M. Pt. 5-6°C **B. Pt.** 210-211°C **Flash point** 88°C (closed cup) **Specific gravity** 1.205 at 15°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.85 (2) **Volatility** v.p. 0.15 mmHg at 20°C ; v.den. 4.25

Solubility Water: 1900 mg l^{-1} at 20°C. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

FR-VME 1 ppm (5 mg m^{-3})
JP-OEL 1 ppm (5 mg m^{-3})
SE-LEVL 1 ppm (5 mg m^{-3}) **SE-STEL** 2 ppm (10 mg m^{-3})
UK-LTEL 1 ppm (5.1 mg m^{-3}) **UK-STEL** 2 ppm (10 mg m^{-3})
US-TWA 1 ppm (5 mg m^{-3})

UN No. 1662 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification toxic, dangerous for the environment

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Possible risk of irreversible effects – Toxic: danger of serious damage to health by prolonged exposure through inhalation and in contact with skin – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment – Possible risk of impaired fertility (R23/24/25, R40, R48/23/24, R51/53, R62)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) juvenile rainbow trout 0.002 mg l^{-1} (3).
LC_{50} (96 hr) fathead minnow 0.6-7 mg l^{-1} (4).
LC_{50} (96 hr) bluegill sunfish 43 mg l^{-1} (5).
LC_{50} (96 hr) sheepshead minnow 59 mg l^{-1} (6).
LC_{50} (48 hr) ide 60-89 mg l^{-1} (7).
IC_{50} (96 hr) fathead minnow 120 mg l^{-1} (8).

Invertebrate toxicity

Toxicity threshold (cell multiplication inhibition test) *Microcystis aeruginosa* 1.9 mg l^{-1} (9).

EC_{50} *Daphnia magna* 24 hr, 48 hr, 14 day 24, 27, 27 mg l^{-1}, respectively (10,11).

EC_{50} (30 min) *Photobacterium phosphoreum* concentration 34.7 mg l^{-1} Microtox test (12).

Toxicity threshold (cell multiplication inhibition test): *Pseudomonas putida* 7 mg l^{-1}; *Scenedesmus quadricauda* 33 mg l^{-1}; *Entosiphon sulcatum* 1.9 mg l^{-1} (13).

Bioaccumulation

Confirmed to be non-accumulative or low accumulative (14).

The log bioconcentration factor in golden orfe was <1.0 in a 3-day static test (15).

The log bioconcentration factor in fathead minnow was 1.18 in a 28-day test (16).

No biomagnification was observed in an aquatic ecosystem containing algae *Daphnia magna*, mosquito larvae, snails and mosquito fish (17).

A negative correlation was found between the amount of accumulation and cell growth rate in *Chlorella fusca* (18).

Environmental fate

Nitrification inhibition

IC_{50} *Nitrosomonas* sp. (25 day) 0.92 mg l^{-1} (8).

Carbonaceous inhibition

Inhibition of glucose degradation by *Pseudomonas fluorescens* at 30 mg l^{-1} (19).

Inhibition of glucose degradation by *Escherichia coli* at 600 mg l^{-1} (20).

Anaerobic effects

Inhibition of anaerobic digestion, laboratory scale, species unspecified, 50 g l^{-1}, 46% at 5 hr and 0% at 285 hr (20).

Inhibition of anaerobic digestion, laboratory scale, species unspecified 100 mg l^{-1}, 80% at 5 hr and 3% at 285 hr (20).

Anaerobic toxicity assay, IC_{50} methanogens (from an enrichment culture) 13 mg l^{-1} (8).

Degradation studies

Under anaerobic conditions using a sewage inoculum, 50% degradation occurred in 14 days, including an 8-day lag period (21).

In an anaerobic reactor with a 2 to 10 hr hydraulic retention time and an inoculum maintained on acetate, 81% of utilisation was obtained after 110 days (22).

Decomposition by soil microflora in >64 days (23).

BOD_5 nil using standard dilute sewage at <440 mg O_2 l^{-1} (24).

ThOD 1.95 mg O_2 l^{-1} (24).

Adapted activated sludge at 20°C: 98.0% COD removal at 14 mg COD g^{-1} dry inoculum hr^{-1} (25).

In model waste stabilisation ponds that were continuously fed with a synthetic waste feed stock and retained for 12 days, 89.5% of the added nitrobenzene was degraded, 4.9% volatilised, 2.3% adsorbed to sediment, 2.3% lost in effluent, and 1% remained in the water column (26).

100% degradation in 7 days with a sewage inoculum (27).

99.6 and 20% degradation after 6 days using municipal and industrial sewage seeds, respectively (28).

No degradation in 10 days with an activated sludge inoculum (29).

Complete removal was obtained when Rhine river water underwent bank filtration. The removal was ascribed to microbial processes (30).

$t_{1/2}$ in silt loam and sandy loam soils was 9.1 days (31).

$t_{1/2}$ in Rhine river in the Netherlands was estimated to be 1 day (30).

Abiotic removal

In organic solvents containing abstractable hydrogen atoms, it undergoes photoreduction when irradiated with UV light (32).

26% degradation occurred in 5 hr using a petroleum solvent and light >290 nm; azobenzene and aniline were the main products formed (32).

In near-surface pure water at 40°C North latitude, the average annual photolytic $t_{1/2}$ is estimated to be 133 days (33).

The photolysis of humic substances in natural water gives rise to hydrated electrons that can reduce organic compounds; the calculated $t_{1/2}$ due to this reaction in an eutrophic Swiss lake is 22 days (34).
In a clear shallow body of water rich in nitrate (14 mg nitrate-N l^{-1}), the $t_{1/2}$ of nitrobenzene exposed to midsummer, midday sunlight was 11 hr (34).
It will degrade in the atmosphere primarily by photolysis, 38% degradation in 5 hr in laboratory tests (35).
Adsorbability on activated carbon 0.196 g g^{-1} carbon. 95.6% reduction influent: 1023 mg l^{-1}; effluent: 44 mg l^{-1} (36).

Adsorption and retention
Moderately adsorbed to soil and should leach into the ground if released on land (37).
In three Norwegian soils, one low organic content sandy soil and two organic soils, the soil adsorption coefficient and retardation factor for the sandy soil was 30.6 and 1.27, while for the two organic soils the soil adsorption coefficients were 42.8 and 69.6 and the retardation factors were 3.36 and 5.52, respectively (37).
Soil adsorption coefficients for two Danish subsoils were 170 and 370 (38).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat and dog 590-750 mg kg^{-1} (39-41).
LD_{50} dermal rat 2100 mg kg^{-1} (42).
LD_{Lo} dermal rabbit 600 mg kg^{-1} (42).
LD_{50} intraperitoneal rat 640 mg kg^{-1} (43).
LD_{50} subcutaneous rat 800 mg kg^{-1} (43).
LD_{50} intravenous dog 150 mg kg^{-1} (43).

Sub-acute and sub-chronic data
Administration of 0.7 ml kg^{-1} day^{-1} to rabbits for 23 wk increased megakaryocytes in bone marrow and spleen. Degenerative changes to the adrenal glands were also noted (43).
Inhalation (duration unspecified) rats at 0.8 mg m^{-3} for 100 days caused disturbances between antagonist muscles, increased blood cholinesterase, methaemoglobin formation and decreases in total blood haemoglobin (44).

Carcinogenicity and chronic effects
Inhalation (2 yr) ♂/♀ B6C3F1 mice 0, 5, 25 or 50 ppm and ♂/♀ F344 rats 0, 1, 5 or 25 ppm. Survival was not adversely affected by the exposure and only mild exposure related decreases in body weight were observed (45).

Teratogenicity and reproductive effects
Degeneration of the testes occurred in rats exposed to 50 ppm, but this effect was not noted in mice at the same dose (duration unspecified) (46).
Inhalation rat 0, 1, 10 or 40 ppm. No effects on reproduction at 1 or 10 ppm. At 40 ppm a decrease in fertility index of the F_0 and F_1 generations was observed due to alterations in the male reproductive organs. Weights of testes and epididymis were reduced and seminiferous tubule atrophy, spermatocyte degeneration and the presence of giant syncytial spermatocytes were observed (47).
Antenatal development of rat embryos was observed after exposure. Embryogenesis was adversely affected; in addition, a general toxic effect on blood indexes and organ weights occurred (48).
Pregnant rats given 7-13 subcutaneous injections of 125 mg kg^{-1} from days 4-6 or from days 9-12 of gestation showed significant signs of disturbed embryogenesis and abnormal placental metabolism (49).

Metabolism and toxicokinetics
In boar spermatazoa fortified with glucose, no acetylation, deacetylation or monooxygenation of nitrobenzene was found (50).
Workers exposed to nitrobenzene can be monitored by measuring 4-nitrophenol in the urine. Levels reach a maximum 4 hr after exposure and may be detected up to 100 hr later (51).
Oxidation-reduction cycling can form nitrosobenzene and phenylhydroxylamine with haemoglobin or autoreduction of quinone intermediate such as *p*-aminophenol with ultimate production of hydrogen peroxide. The nitroxide radical can also be formed via the generation of the superoxide radical which dismutates to form hydrogen peroxide (43,52).

Irritancy
Liquid is irritating to the eyes. The vapours cause irritation and, as a result of action on the central nervous system, visual disturbances (53).

Sensitisation
It may produce dermatitis by primary irritation or sensitisation (53).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (54-56).
Increased sex linked recessive lethal mutations in *Drosophila melanogaster* (57).
In vitro hamster V-79 cells mutagenicity positive (58).
It was not mutagenic in mice after intragastric administration, using the micronucleus test and metaphase analysis for chromosomal aberrations in bone marrow cells (59).

Other effects

Other adverse effects (human)
It is highly toxic, ingestion of 1 g may be fatal. Effects from ingestion are usually delayed for several hours and may include nausea, prostration, burning headache, methaemoglobinaemia with cyanosis, haemolytic anaemia, vomiting, convulsions and coma, ending in death after a few hr (60).
It is rapidly absorbed through the skin (61).
Acute effects in man include haemolymphoretic toxicity, neurotoxicity and hepatotoxicity (43).
Transient leucocytopenia also recorded in humans (62).
The vapour is more toxic than the liquid with the onset of toxic symptoms from inhalation occurring rapidly (48).

Any other adverse effects
Heinz bodies are noted in red blood cells following prolonged exposures at low concentrations (63).
Found to be toxic to *in vitro* cultured African green monkey kidney cells (62).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (64).
Maximum admissible concentration (former USSR) 0.2 mg l^{-1} (65).
US likely to recommend 30 µg l^{-1} using taste/odour criteria (66).

Other comments

May be released to the environment in emissions and in wastewater during its production and use (67).
Reviews on human health effects, experimental toxicity, environmental effects, ecotoxicology, exposure levels, epidemology and work experience listed (68).
Uptake is passive in terrestial plants and the major route of chemical loss is via volatilisation from leaves (69).
Autoignition temperature 482°C.

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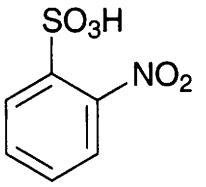
N83 2-nitrobenzenesulfonic acid



$C_6H_5NO_5S$ **Mol. Wt.** 203.18 **CAS Registry No.** 80-82-0

EINECS No. 201-311-6

Occupational exposure

UN No. 2305 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Environmental fate

Degradation studies

Decomposed by a soil microflora in >64 days (1).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (2).

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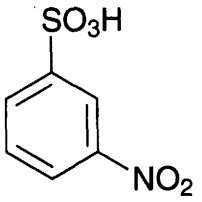
N84 3-nitrobenzenesulfonic acid



$C_6H_5NO_5S$ **Mol. Wt.** 203.18 **CAS Registry No.** 98-47-5

Synonyms 3-nitrophenylsulfonic acid

EINECS No. 202-671-7 **RTECS No.** DB 7190000

Physical properties

M. Pt. 70°C **B. Pt.** decomp.

Solubility Organic solvents: ethanol

Occupational exposure

UN No. 2305 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Environmental fate

Degradation studies

Decomposed by a soil microflora in >64 days (1).

Mammalian & avian toxicity

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation, 2 mg (24 hr) instilled into rabbit eye caused severe irritation (2).

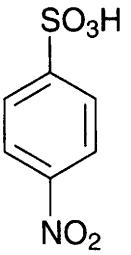
Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (3).

References

1. Alexander, M. et al *J. Agric. Food Chem.* 1966, **14**, 410.
2. Marhold, J. V. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, Prague, Czechoslovakia.
3. Kawai, A. et al *Sangyo Igaku* 1987, **29**(1), 34-54

N85 4-nitrobenzenesulfonic acid



$C_6H_5NO_5S$ **Mol. Wt.** 203.18 **CAS Registry No.** 138-42-1

Synonyms *p*-nitrophenylsulfonic acid

EINECS No. 205-329-5

Physical properties

M. Pt. 95°C

Occupational exposure

UN No. 2305 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Environmental fate

Degradation studies

Decomposition by a soil microflora in >64 days (1).

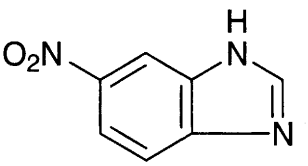
Genotoxicity

Salmonella typhimurium TA98 and TA100 with and without metabolic activation negative (2).

References

1. Alexander, M. et al *J. Agric. Food Chem.* 1966, **14**, 410.
2. Kawai, A. et al *Sangyo Igaku* 1987, **29**(1), 34-54

N86 5(6)-nitrobenzimidazole



$C_7H_5N_3O_2$ **Mol. Wt.** 163.14 **CAS Registry No.** 94-52-0

Synonyms 5-nitro-1*H*-benzimidazole

EINECS No. 202-341-2 **RTECS No.** DD 9800000

Uses In photographic developers.

Physical properties

M. Pt. 209-210°C
Solubility Organic solvents: benzene, chloroform, diethyl ether

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* concentration 11.3 mg l^{-1}; Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 500 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Oral (107 wk and 96 wk) ♂/♀ Fischer 344 rats and B6C3F1 mice, 0.5 and 0.12% and 0.24 and 0.12% in diet, respectively. Non-neoplastic lesions of the eyes and of the Harderian glands were observed. It was not carcinogenic to Fischer 344 rats, but was carcinogenic to B6C3F1 mice, causing hepatocellular carcinomas in both sexes (3).

Genotoxicity

Salmonella typhimurium TA100, with and without metabolic activation positive (4,5).
Salmonella typhimurium TA98 without metabolic activation equivocal, with metabolic activation negative; TA1537 without metabolic activation negative, with metabolic activation equivocal (4).
Escherichia coli WP2 *uvrA* with and without metabolic activation negative (4).

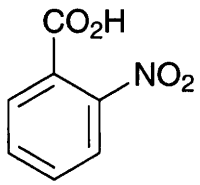
Legislation

Included in Schedule 4 (Release into Air: 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. *Natl. Acad. Sci.* 1953, **5**, 22.
3. *National Toxicology Program Research and Testing Division* 1992, Report No.TR-117, NIEHS, Research Triangle Park, NC, USA.
4. Dunkel, V. C. *Environ. Mol. Mutagen.* 1985, **7**(Suppl. 5) 1-248.
5. Mortelmans, K. *Environ. Mol. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
6. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

N87 2-nitrobenzoic acid



$C_7H_5NO_4$ **Mol. Wt.** 167.12 **CAS Registry No.** 552-16-9
Synonyms *o*-nitro-benzoic acid
EINECS No. 209-004-9 **RTECS No.** DH 5050000

Physical properties

M. Pt. 147.5°C **Specific gravity** 1.575 at 20°C **Partition coefficient** log P_{ow} 1.04 (1)
Solubility Water: 6800 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Environmental fate

Anaerobic effects

Anaerobic digesting sludge, 2-3 g l^{-1}, the net gas production was ~2% after >80 days, showed inhibiting effect on anaerobic biodegradation (2).

Degradation studies

Decomposition by a soil microflora in 8 days (3).
Adapted activated sludge at 20°C: 93.4% COD removal at 20 mg COD g^{-1} O_2 dry inoculum hr^{-1} (4).
Lag period for degradation of 16 mg kg^{-1} by soil suspension and wastewater at pH 7.3 and 30°C, 14-25 and 3-5 days, respectively (5).
It is degraded by *Pseudomonas pseudoalcaligenes* via reduction of the NO_2 group by a nonspecific nitrate reductase (6).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (7).
Salmonella typhimurium TA97, TA98, TA1535 with and without metabolic activation negative; TA100 with and without metabolic activation positive (8).

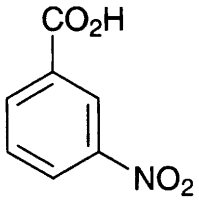
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (9).

References

1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold Co., New York, USA.
2. Battersby, N. S. et al *Appl. Environ. Microbiol.* 1989, **55**(2), 433-439.
3. Alexander, M. et al *J. Agric. Food Chem.* 1966, **14**, 410.
4. Pitter, P. *Water Res.* 1976, **10**, 231-235.
5. Haller, H. D. *J. Water Pollut. Control Fed.* 1978, 2771-2777.
6. Mironov, A. D. et al *Prikl. Biokhim. Mikrobiol.* 1991, **27**(4), 571-576.
7. Kawai, A. et al *Sangyo Igaku* 1987, **29**(1), 34-54.
8. Zeiger, E. et al *Environ. Mol. Mutagen.* 1987, **9** (Suppl. 9), 1-109.
9. *S. I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

N88 3-nitrobenzoic acid



$C_7H_5NO_4$ **Mol. Wt.** 167.12 **CAS Registry No.** 121-92-6

Synonyms *m*-nitrobenzenecarboxylic acid

EINECS No. 204-508-5 **RTECS No.** DH 5000000

Physical properties

M. Pt. 140-142°C **Specific gravity** 1.469 at 20°C **Partition coefficient** log P_{ow} 1.83 (1)
Solubility Water: 3100 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies

Decomposition by a soil microflora in >64 days (2).

Adapted activated sludge at 20°C: 93.4% COD removal at 20 mg O_2 kg^{-1} dry inoculum hr^{-1} (3).

Lag period for degradation of 16 mg l^{-1} by waste water at pH 7.3, 30°C (3-5 days) and by soil suspension at pH 7.3, 30°C (14-25 days) (4).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous, intraperitoneal rat, mouse 610, 680 mg kg^{-1}, respectively (4).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation negative, TA100 with and without metabolic activation positive (5).

Salmonella typhimurium TA97, TA100, TA1537 with and without metabolic activation positive; TA98, TA1535 with and without metabolic activation negative (6).

Salmonella typhimurium TA98 and TA100 with and without metabolic activation negative (7).

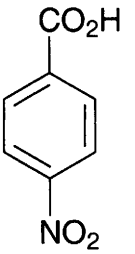
Legislation

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

References

1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold Co. Inc., NY, USA.
2. Alexander, M. et al *J. Agric. Food Chem.* 1966, **14**, 410.
3. Pitter, P. *Water Res.* 1976, **10**, 231-235.
4. Haller, H. D. *J. Water Pollut. Control Fed.* 1978, 2771-2777.
5. Kawai, A. et al *Sangyo Igaku* 1987, **29**(1), 34-54.
6. Zeiger, E. et al *Environ. Mol. Mutagen.* 1989, **13**, 116-127.
7. Dellarco, V. L. et al *Environ. Mol. Mutagen.* 1989, **13**, 116-127.
8. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

N89 4-nitrobenzoic acid



$C_7H_5NO_4$ **Mol. Wt.** 167.12 **CAS Registry No.** 62-23-7

Synonyms *p*-nitrobenzenecarboxylic acid; nitrodracylic acid

EINECS No. 200-526-2 **RTECS No.** DH 5075000

Physical properties

M. Pt. 242.4°C **B. Pt.** sublimes **Specific gravity** 1.550 at 32°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.89 (1)
Solubility Water: 420 mg l^{-1} at 25°C

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* concentration 15.95 mg l^{-1} Microtox test (2).
In vitro Aspergillus flavus 500, 700, 1000 or 2000 ppm caused 45.5, 70.0, 80.0 or 100% mycelial inhibition, respectively (3).

Environmental fate

Anaerobic effects
Anaerobic digesting sludge, 2-3 g l^{-1} the net gas production was ~19% after >80 days, showed inhibiting effect on anaerobic biodegradation (4).

Degradation studies
Decomposition by soil microflora in 4 days (5).
Adapted activated sludge at 20°C, 92% COD removal at 19.7 mg COD g^{-1} O_2 dry inoculum hr^{-1} (6).
Lag period for degradation of 16 mg l^{-1} by wastewater or by soil at pH 7.3 and 30°C; 3-5 days (7).
Closed bottle test, 5 mg l^{-1} 74% ThOD after 4 wk (8).
Streptomyces antibioticus and *Streptomyces violaceoniger* degraded 4-nitrobenzoic acid to 4-aminobenzoic acid (9).

Adsorption and retention
It is not strongly adsorbed onto non-crystalline iron hydroxide and geothite (10).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1960 mg kg^{-1} (11).
LD_{50} intraperitoneal mouse, rat 880, 1210 mg kg^{-1}, respectively (11).
LD_{50} intravenous mouse 770 mg kg^{-1} (11).

Genotoxicity

Salmonella typhimurium (strain and metabolic activation unspecified) positive (12).
Chinese hamster ovary cells, chromosomal aberrations and sister chromatid exchanges positive (12).

Salmonella typhimurium TA100 with and without metabolic activation positive, TA98 with and without metabolic activation negative (13).
Salmonella typhimurium TA98, TA1535, TA1537 with and without metabolic activation negative (14).
Salmonella typhimurium TA98 with and without metabolic activation negative, TA100 with and without metabolic activation positive (15).

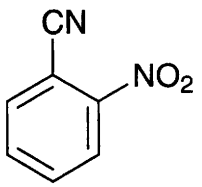
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).

References

1. Verschueren, K. *Handbook of Environmental Data on Organic Chemicals* 2nd ed., 1983, Van Nostrand Reinhold Co. Inc., NY, USA.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. Dube, S. et al *Pesticides* 1988, **22**(3), 11-12.
4. Battersby, N. S. et al *Appl. Environ. Microbiol.* 1989, **55**(2), 433-439.
5. Alexander, M. et al *J. Agric. Food Chem.* 1966, **14**, 410.
6. Pitter, P. *Water Res.* 1976, **10**, 231-235.
7. Robertson, D. J. et al *J. Air Pollut. Control Assoc.* 1979, **29**(1), 50-51.
8. Richterich, K. et al *Chemosphere* 1989, **19**(10/11), 1643-1654.
9. Kergomard, A. et al *Agric. Biol. Chem.* 1986, **50**(11), 2913-2914.
10. Kung, K. H. et al *Soil Sci. Soc. Am. J.* 1989, **53**(6), 1673-1678.
11. *C. R. Seances Soc. Biol. Ses Fil.* 1966, **160**, 1097.
12. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(3), 269-280.
13. Kawai, A. et al *Sangyo Igaku* 1987, **29**(1), 34-54.
14. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl.9), 1-109.
15. Dellarco, V. L. et al *Environ. Mol. Mutagen.* 1989, **13**, 116-127.
16. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

N90 2-nitrobenzonitrile



$C_7H_4N_2O_2$ **Mol. Wt.** 148.12 **CAS Registry No.** 612-24-8

Synonyms 2-cyanonitrobenzene

EINECS No. 210-301-0 **RTECS No.** DI 4903000

Physical properties

M. Pt. 107-109°C **B. Pt.** 165°C at 16 mmHg

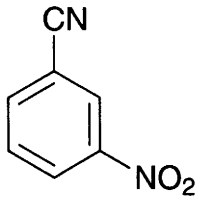
Genotoxicity

Salmonella typhimurium TA100 without metabolic activation negative; TA98 without metabolic activation positive (1).
Bacillus subtilis HA, M45 rec assay positive (2).

References

1. Chin, C. W. et al *Mutat. Res.* 1978, **58**, 1-10.
2. Shimizu, M. et al *Mutat. Res.* 1986, **170**, 11-22

N91 3-nitrobenzonitrile



$C_7H_4N_2O_2$ **Mol. Wt.** 148.12 **CAS Registry No.** 619-24-9

Synonyms 3-cyanonitrobenzene

EINECS No. 210-587-7 **RTECS No.** DI 4900000

Physical properties

M. Pt. 117-118°C

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 3276

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 60.2 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 48.1 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 250 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA98, TA1538 without metabolic activation positive with metabolic activation negative; TA100 with and without metabolic activation positive; TA1535, TA1537 with and without metabolic activation negative (3).

Bacillus subtilis H17, M45 rec assay positive (4).

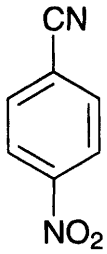
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (5).

References

1. Pearson, J. G. et al *Aquatic Toxicology; ASTM STP 667*, 1979, 284-301.
2. *Summary Tables of Biological Tests* 1954, **6**, 216, National Research Council, Chemical-Biological Coordination Center.
3. Spanggord, R. J. et al *Environ. Mutagen.* 1982, **4**, 163-179.
4. Schimizu, M. et al *Mutat. Res.* 1986, **170**, 11-22.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

N92 4-nitrobenzonitrile



$C_7H_4N_2O_2$ **Mol. Wt.** 148.12 **CAS Registry No.** 619-72-7

Synonyms 4-cyanonitrobenzene

EINECS No. 210-610-0 **RTECS No.** DI 4903500

Physical properties

M. Pt. 146-149°C

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 24.4 mg kg^{-1} (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 49.4 mg kg^{-1} (1).

EC_{50} (30 min) *Photobacterium phosphoreum* concentration 2.4 mg l^{-1} Microtox test (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 30, 140 mg kg^{-1}, respectively (3,4).

LD_{50} intraperitoneal mouse 100 mg kg^{-1} (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (5).

Bacillus subtilis H17, M45 rec assay positive (6).

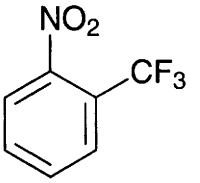
Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

References

1. Pearson, J. G. et al *Aquatic Toxicology, ASTM STP 667* 1979, 284-301.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. *Zentralbl. Arbeitsmed. Arbeitsschutz* 1969, **19**, 225.
4. *Ann. Pharm. Fr.* 1983, **41**, 391.
5. Spanggord, R. J. et al *Environ. Mutagen.* 1982, **4**, 163-179.
6. Shimizu, M. et al *Mutat. Res.* 1986, **170**, 11-22.
7. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

N93 2-nitrobenzotrifluoride



$C_7H_4F_3NO_2$ **Mol. Wt.** 191.11 **CAS Registry No.** 384-22-5

Synonyms 1-nitro-2-trifluoromethylbenzene; 2-nitro-α,α,α-trifluorotoluene

EINECS No. 206-855-8

Uses Organic synthesis.

Physical properties

M. Pt. 31-32°C **B. Pt.** 104-105°C at 20 mmHg **Flash point** 95°C
Solubility Organic solvents: acetone, benzene, diethyl ether

Occupational exposure

UN No. 2306 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Environmental fate

Abiotic removal
Sunlight induced photodegradation (1).

Genotoxicity

Bacillus subtillis recE4 DNA damage and repair test negative (2).
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (2).
Saccharomyces cerevisiae 6117 with and without metabolic activation gene conversion and mitotic crossing over negative (2).

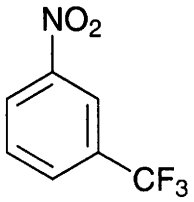
Legislation

Halogens and their covalent compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (3).

References

1. Simmons, M. S. et al *Water Res.* 1986, **20**(7), 899.
2. Mazza, G. et al *Farmaco, Ed. Prat.* 1986, **41**(7), 215-225.
3. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

N94 3-nitrobenzotrifluoride



$C_7H_4F_3NO_2$ **Mol. Wt.** 191.11 **CAS Registry No.** 98-46-4

Synonyms 3-nitro-α,α,α-trifluorotoluene; *m*-nitrotrifluorotoluene; *m*-(trifluoromethyl)nitrobenzene; 3-trifluoromethylnitrobenzene

EINECS No. 202-670-1 **RTECS No.** XT 3500000

Uses Bactericide.

Physical properties

M. Pt. –5°C **B. Pt.** 200-205°C **Flash point** 102°C (open cup) **Specific gravity** 1.437 at 15.5°C with respect to water at 15.5°C **Volatility** v.p. 0.3 mmHg at 25°C

Solubility Organic solvents: acetone, benzene, diethyl ether

Occupational exposure

UN No. 2306 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Environmental fate

Abiotic removal

Sunlight induced photodegradation (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 520, 610 mg kg^{-1}, respectively (2).

LC_{50} (2 hr) inhalation mouse 800 mg m^{-3} (3).

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

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (5).

Bacillus subtilis recE4 DNA damage and repair test negative (5).

Saccharomyces cerevisiae 6117 with and without metabolic activation, gene conversion and mitotic crossing-over negative (5).

Drosophila melanogaster larvae administered in food increased the incidence of dominant lethal mutations among the offspring and increased the percentage of unfertilised eggs (6).

Legislation

Halogens and their covalent compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (7).

Other comments

Reviews on human health effects and experimental toxicology listed (8).

References

1. Simmons, M. S. et al *Water Res.* 1986, **20**(7), 899.
2. *Toxicology of New Industrial Chemical Sciences* 1968, **10**, 131.
3. Izmerov, N. F. *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, Moscow, USSR.
4. *NTIS Report* AD 277-689, Nat. Tech. Inf. Serv., Springfield, VA, USA.
5. Mazza, G. et al *Farmaco. Ed. Prat.* 1986, **41**(7), 215-225.
6. Ilichkina, A. G. et al *Mol. Mekh. Genet. Protsessov.* 1976, 291, (Ital.) (*Chem. Abstr.* **86**, 157742g).
7. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

N95 4-nitrobenzotrifluoride

$C_7H_4F_3NO_2$ **Mol. Wt.** 191.11 **CAS Registry No.** 402-54-0

Synonyms 1-nitro-4-trifluoromethylbenzene; 4-nitro-α,α,α-trifluorotoluene; 4-(trifluoromethyl)nitrobenzene

EINECS No. 206-948-3

Physical properties

M. Pt. 38-40°C **B. Pt.** 81-83°C at 10 mmHg

Occupational exposure

UN No. 2306 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 15.2 mg l^{-1} Microtox test (1).

Toxicity to other species

LD_{Lo} subcutaneous frog 870 mg kg^{-1} (2).

Environmental fate

Degradation studies

Sunlight induced photodegradation (3).

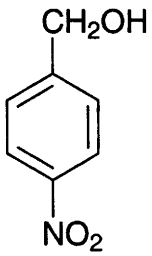
Legislation

Halogens and their covalent compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (2).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Canada* 1991, **26**(3), 361-431.
2. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
3. Simmons, M. S. et al *Water Res.* 1986, **20**(7), 899

N96 4-nitrobenzyl alcohol



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 619-73-8

Synonyms 4-nitrobenzenemethanol; *p*-nitrobenzyl alcohol; *p*-(hydroxymethyl)nitrobenzene; (4-nitrophenyl)methanol

EINECS No. 210-611-6 **RTECS No.** DP 0657100

Physical properties

M. Pt. 92-94°C **B. Pt.** 185°C at 12 mmHg

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 35.9 ppm. Microtox test (1).

Genotoxicity

Syrian hamster embryo cell transformation positive (metabolic activation unspecified). Also enhanced intercellular communication between Syrian hamster embryo cells in a dye transfer assay (2).

Other comments

Covered by a QSAR study of acute toxicity (3).

Toxicity to *in vitro* rat hepatocytes studied (4).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. *Cancer Lett. (Shannon, Irel.)* 1990, **52**(3), 203.
3. Kaiser, K. L. E. *QSAR Environ. Toxicol. Proc. Int. Workshop, 2nd 1986* 1987, 169-188, Kaiser, K. L. E. (Ed.), Reidel, Dordrecht, Netherlands.
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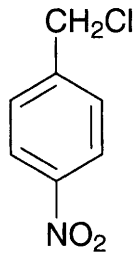
N97 4-nitrobenzyl chloride



$C_7H_6ClNO_2$ **Mol. Wt.** 171.58 **CAS Registry No.** 100-14-1

Synonyms α-chloro-4-nitrotoluene; α-chloro-*p*-nitrotoluene; *p*-nitrobenzyl chloride

EINECS No. 202-822-7 **RTECS No.** XS 9093000

Physical properties

M. Pt. 70-73°C

Occupational exposure

UN No. 2433 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 2.6 mg l^{-1} Microtox test (1).

Mammalian & avian toxicity

Acute data

LC_{Lo} (4 hr) inhalation rat 280 mg m^{-3} (2).

Genotoxicity

Salmonella typhimurium TA100, TA98 without metabolic activation positive (3).
Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (4).
Salmonella typhimurium TA100 without metabolic activation weakly positive (5).
In vitro Chinese hamster ovary cells sister chromatid exchange equivocal (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine guide level 1 μg l^{-1} (7).
Halogens and their covalent compounds are included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Genotoxicity, biological properties and human exposure limits reported (9).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Canada* **26**(3), 361-431.
2. *Toxicologist* 1984, **4**, 66.
3. Ball, J. C. et al *Mutat. Res.* 1984, **138**(2-3), 145-151.
4. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
5. Shimizu, M. et al *Mutat. Res.* 1986, **170**(1-2), 11-22.
6. Hemminki, K. et al *J. Appl. Toxicol.* 1983, **3**(4), 203-207.
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.
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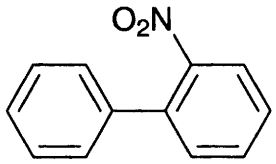
N98 2-nitrobiphenyl



$C_{12}H_9NO_2$ **Mol. Wt.** 199.21 **CAS Registry No.** 86-00-0

Synonyms 2-nitro-1,1'-biphenyl; 2-nitrodiphenyl; *o*-nitrobiphenyl; ONB

EINECS No. 201-646-8 **RTECS No.** DV 5530000

Uses Plasticiser for cellulose acetate and nitrate, polystyrenes and resins. Textile fungicide. Wood preservative. Dye intermediate.

Physical properties

M. Pt. 36.7°C **B. Pt.** 325°C **Flash point** 179°C **Specific gravity** 1.44 at 25°C with respect to water at 4°C
Volatility v.p. 2 mmHg at 140°C ; v.den. 5.9
Solubility Organic solvents: acetone, carbon tetrachloride, dimethylformamide, ethanol, methanol, perchloroethylene, tetrahydrofurfuryl alcohol, turpentine

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, rabbit 1230, 1580 mg kg^{-1}, respectively (1).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (2).
In vitro mouse lymphoma L5178Y tk^+/tk^- with metabolic activation positive (3).
In vitro mouse lymphoma L5178Y tk^+/tk^- DNA alkaline unwinding assay with metabolic activation positive (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (6).

References

1. *J. Ind. Hyg. Toxicol.* 1947, **29**, 1.
2. Zeiger, E. et al *Environ. Mol. Mutagen.* 1988, **11** (Suppl. 12), 1-157.
3. Wangenheim, J. et al *Mutagenesis* 1988, **3**(3), 193-205.
4. Garberg, P. et al *Mutat. Res.* 1988, **203**, 155176.
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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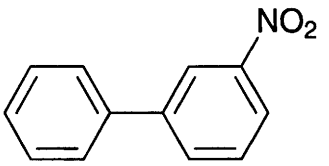
N99 3-nitrobiphenyl



$C_{12}H_9NO_2$ **Mol. Wt.** 199.21 **CAS Registry No.** 2113-58-8

Synonyms 3-nitro-1,1'-biphenyl; 3-nitrodiphenyl; *m*-nitrobiphenyl

EINECS No. 218-305-4 **RTECS No.** DV 5570000

Occurrence Air pollutant (1).

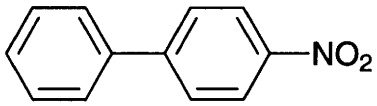
Genotoxicity

Salmonella typhimurium TA98, TA98NR, TA98/1, 8DNP$_6$ without metabolic activation negative (2).

References

1. Atkinson, R. et al *Report ARB-R-88/366* 1988, Order No. PB88-247481, Avail. NTIS.
2. Hirayama, T. H. et al *Mutat. Res.* 1986, **163**, 101-107

N100 4-nitrobiphenyl



$C_{12}H_9NO_2$ **Mol. Wt.** 199.21 **CAS Registry No.** 92-93-3

Synonyms 4-nitro-1,1'-biphenyl; 4-nitrodiphenyl; PNB; *p*-nitrobiphenyl

EINECS No. 202-204-7 **RTECS No.** DV 5600000

Physical properties

M. Pt. 113.7°C **B. Pt.** 340°C

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2811

Supply classification toxic

Risk phrases May cause cancer (R45)

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

Tetrahymena pyriformis GL-C Static assay had not reached 50% growth inhibition at saturation (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, rat 1970, 2230 mg kg^{-1}, respectively (2).

LD_{50} intraperitoneal mouse 347 mg kg^{-1} (3).

Carcinogenicity and chronic effects

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

Listed as a carcinogen by US Occupational Safety and Health Act (5).

Metabolism and toxicokinetics

Metabolically reducible to an arylamine. When administered orally to rabbit was metabolised to the corresponding *N*-arylformamide and *N*-arylacetamide (6).

Under anaerobic conditions the following reductive metabolites of 4-nitrophenyl by S9 rat liver fraction were isolated: 4-aminobiphenyl (79% of total metabolites) and hydroxylaminobiphenyls were the major metabolites, and 4-acetylaminobiphenyl, *N*-hydroxy-4-acetylaminobiphenyl, *x*-hydroxy-4-nitrobiphenyl, biphenylene and *N*-formyl-4-aminobiphenyl were the minor metabolites (7).

Genotoxicity

Salmonella typhimurium TA98 with metabolic activation mutagenicity enhanced (8).

In vitro Chinese hamster ovary cells with and without metabolic activation HGPRT mutation negative (9).

Other effects

Other adverse effects (human)

In vitro human urothelial cells with metabolic activation cytotoxic in concentration and duration-dependent manner (10).

Other comments

Reviews on experimental toxicology, epidemiology human health effects, workplace experience and physico-chemical properties listed (11).
Air pollutant (12).

References

1. Schultz, T. W. et al *ASTM Spec. Tech. Publ.* 1988, **1007**(Aquat. Toxicol. Environ. Fate II Vol.) 410-423.
2. *J. Ind. Hyg. Toxicol.* 1947, 29, 1.
3. *J. Natl. Cancer Inst.* 1979, 62, 911.
4. *IARC Monograph* 1987, **Suppl. 7**, 97.
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6. Tatsumi, K. et al *Cancer Res.* 1989, **49**(8), 2059-2064.
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12. Pacific Environmental Services, Inc. *US Environ. Prot. Agency, Off-Air Qual. Plann. Stand.* 1987, EPA450/4-87-023a

N101 1-nitrobutane

$$CH_3CH_2CH_2CH_2NO_2$$

$C_4H_9NO_2$ **Mol. Wt.** 103.12 **CAS Registry No.** 627-05-4

EINECS No. 210-980-3 **RTECS No.** EK 5075000

Physical properties

M. Pt. -81°C **B. Pt.** 152-153°C **Flash point** 47°C **Specific gravity** 0.9710 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.47
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 54.1 ppm Microtox test (1).

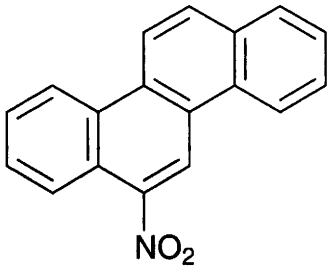
Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with and without metabolic activation negative (2).
In vivo rat liver DNA and RNA damage negative (3).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Loefroth, G. et al *Prog. Clin. Biol. Res.* 1986, **209B** 149-155.
3. Conaway, C. C. et al *Can. Res.* 1991, **51**, 3143-3147

N102 6-nitrochrysene



$C_{18}H_{11}NO_2$ **Mol. Wt.** 273.29 **CAS Registry No.** 7496-02-8

Synonyms

Uses As an internal standard in the chemical analysis of nitroarenes.

Physical properties

M. Pt. 209°C **B. Pt.** sublimes without decomposition

Solubility Organic solvents: slightly soluble in cold carbon disulfide, diethyl ether, ethanol

Environmental fate

Degradation studies

Metabolised by human faecal anaerobic bacteria to 6-nitrosochrysene, 6-aminochrysene, *N*-formyl-6-aminochrysene and 6-acetyl aminochrysene (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to animals, inadequate evidence for carcinogenicity to humans, IARC classification Group 2B (2).

National Toxicology Program classification: reasonably anticipated to be a human carcinogen (3).

Dermal ♀ mice 0.1 mg on alternate days to a total dose of 1 mg. Ten days after this initiation treatment completed, dosed and control mice received 2.5 µg 12-*O*-tetradecanoylphorbol 13-acetate 3 × wk for 25 wk. At the end of this treatment 12/20 treated mice and 1/20 controls had developed skin tumours (4).

Intraperitoneal mice (26 wk) received a total of 38.5 or 189 µg 6-nitrochrysene over days 1, 8 and 15 after birth. All treated mice developed multiple lung tumours (p <0.0001) and 70% had adenocarcinomas. A few lymphomas and nodular hyperplasia of the liver were found in treated but not control animals (5).

♀ weanling CD rats were administered 2.04 µmol 6-nitrochrysene into each of the 6 mammary glands on the left side and DMSO into the 6 mammary glands on the right. Positive control rats received the same doses of 4-nitropyrene (the most active mammary carcinogen among the mononitropyrene isomers). After 43 wk the rats dosed with 6-nitrochrysene had developed fibroadenomas, adenocarcinomas and spindle cell sarcomas of the mammary glands. Significantly higher numbers of the 6-nitrochrysene-treated animals developed malignant tumours compared with positive controls and animals receiving DMSO alone. The total number of malignant tumours was also significantly higher in the experimental group (6).

Intraperitoneal CD rats administered the first dose within 24 hr of birth and then 5 weekly injections to a total of 14.8 μmol were killed at 32 wk. Adenocarcinomas and dysplasias and/or adenomas of the colon were observed as was elevated aryl hydrocarbon hydroxylase activity in both target and non-target organs (6).

Metabolism and toxicokinetics

♀ CD rats administered [3,4,9,10-^{3}H]6-nitrochrysene intraperitioneally excreted 1.3% of the dose in the 24-hr urine and 23.0% in the 24-hr faeces. After 3 days the total excretions in urine and faeces were 2.8% and 34.9%, respectively. 24.85% of the total radioactivity was retained in various organs after 3 days. The following metabolites were identified: in the faeces – *trans*-1,2-dihydro-1,2-dihydroxy-6-nitrochrysene, chrysene-5,6-quinone, and 6-aminochrysene; in the urine – 6-aminochrysene, *trans*-1,2-dihydro-1,2-dihydroxy-6-nitrochrysene and *trans*-9,10-dihydroxy-6-nitrochrysene in free forms and as glucuronide and/or sulfate conjugates (7).

Genotoxicity

Salmonella typhimurium TA98, TA100 with or without metabolic activation positive (8).
Induced morphological transformation in cultured Syrian hamster embryo cells (9).
Mutagenic in Chinese hamster ovary CHO-K1 and CHO-UV5 cells (10).

Other effects

Any other adverse effects

Two DNA adducts, *N*-(deoxyguanosin-8-yl)-6-aminochrysene and *N*-(deoxyguanosin-8-yl)-6-aminochrysene, and *N*-(deoxyinosin-8-yl)-6-aminochrysene were formed when primary cultures of rat liver hepatocytes were incubated with 6-nitrochrysene (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (12).

Other comments

Identified in ambient air, Upper Frankonia, Germany, at a level of *c.* 1 ng m^{-3} (13).
Carcinogenic risks to humans evaluated (2).

References

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9. Sala, M. et al *Carcinogenesis* 1987, **8**, 503-507.
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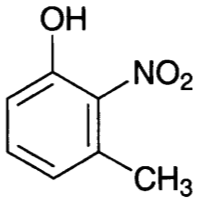
12. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
13. Garner, R. C. et al *Environ. Mutagenesis* 1986, **8**, 109-117

N103 2-nitro-*m*-cresol



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 4920-77-8

Synonyms 3-methyl-2-nitrophenol; 2-nitro-3-methyl phenol; 3-hydroxy-2-nitrotoluene

EINECS No. 225-546-9

Physical properties

M. Pt. 35-39°C **B. Pt.** 106-108°C at 9.5 mmHg **Partition coefficient** log K_{ow} 2.29 (1)

Occupational exposure

UN No. 2446 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 46.1 mg l^{-1} (2).

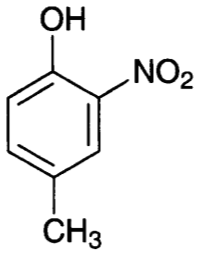
Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 18.8 mg l^{-1} (2).

References

1. Schwarzenbach, R. P. et al *Environ. Sci. Technol.* 1988, **22**, 83-92.
2. Pearson, J. G. et al *Aquatic Toxicology* 1979, Marking, L. L. et al (Ed.), ASTM STP 667

N104 2-nitro-*p*-cresol



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 119-33-5

Synonyms 4-methyl-2-nitrophenol; 2-nitro-4-methylphenol; 4-hydroxy-3-nitrotoluene; *o*-nitro-*p*-methylphenol

EINECS No. 204-315-6 **RTECS No.** GP 2800000

Physical properties

M. Pt. 32-35°C **B. Pt.** 125°C at 22 mmHg **Flash point** 108°C **Specific gravity** 1.240 at 28.6°C
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2446 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity
LOEC *Scenedesmus quadricauda* 3.8 mg l^{-1} (1).
LOEC *Entosiphon sulcatum* 0.42 mg l^{-1} (1).
Cell multiplication inhibition test *Microcystis aeruginosa* 32 mg l^{-1} (2).
Cell multiplication inhibition test *Uronema parduczi* 5.8 mg l^{-1} (3).
EC_0 (24 hr) *Daphnia magna* 19 mg l^{-1} (4).
EC_{50} (24 hr) *Daphnia magna* 52 mg l^{-1} (4).

Bioaccumulation
The absorption rate constants for goldfish body surface and gills are, respectively, 5.070 and 8.958 (min^{-1} g^{-1}) × 10^4 (5).
Confirmed to be non-accumulative or low accumulative (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3360 mg kg^{-1} (7).

Other comments

As pollutant in atmospheric deposition (8).

References

1. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
2. Bringmann, G. et al *GWF, Gas-Wasserfach: Wasser/Abwasser* 1976, **117**(9).
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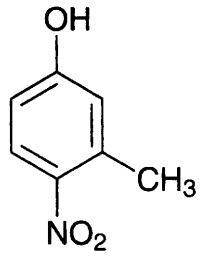
5. Sakiya, Y. et al *Int. J. Pharm.* 1988, **47**, 185-194.
6. *The list of the existing chemical substances tested on biodegradability by microorganisms or bioaccumulation in fish body* 1987, Chemicals Inspection and Testing Institute, Japan.
7. Huntingdon Research Center *Report* 1972, Brooklandville, MD 21022, USA.
8. Welch, D. I. et al *Int. J. Environ. Anal. Chem.* 1990, **38**, 185-198

N105 4-nitro-*m*-cresol



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 2581-34-2

Synonyms 3-methyl-4-nitrophenol; 2-nitro-5-hydroxytoluene; 4-nitro-3-methylphenol; 4-nitro-5-methylphenol; 5-hydroxy-2-nitrotoluene; 5-methyl-4-nitrophenol; *p*-nitro-*m*-cresol; *p*-nitro-*m*-methylphenol

EINECS No. 219-952-5 **RTECS No.** GP 2625000

Physical properties

M. Pt. 129°C

Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2446 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

Cell multiplication inhibition test *Uronema parduczi* 0.26 mg l^{-1} (1).

Cell multiplication inhibition test *Entosiphon sulcatum* 5.8 mg l^{-1} (2).

EC_{50} (30 min) *Photobacterium phosphoreum* 1.30 ppm Microtox test (3).

Bioaccumulation

Confirmed to be non-accumulative or low accumulative (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4410 mg kg^{-1} (5).

LD_{Lo} intraperitoneal mouse 500 mg kg^{-1} (6).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (7).

Other comments

A urinary metabolite of the organophosphorus insecticide fenitrothion in rats (8).

References

1. Bringmann, G. et al Z. *Wasser Abwasser Forsch.* 1980, **1**, 26-31 (Ger.).
2. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
3. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.

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7. Corbett, M. D. et al *Toxicol. Lett.* 1987, **35**, 201-207.
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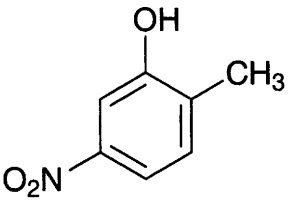
N106 5-nitro-*o*-cresol



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 5428-54-6

Synonyms 5-nitro-2-methylphenol; 5-nitro-2-cresol; 2-hydroxy-4-nitrotoluene; 2-methyl-5-nitrophenol

EINECS No. 226-580-7

Physical properties

M. Pt. 115-118°C **B. Pt.** 180°C at 15 mmHg

Solubility Water: slightly soluble. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2446 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Bioaccumulation

Non- or low accumulative (1).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (2).

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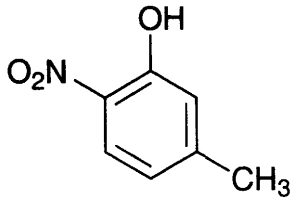
N107 6-nitro-*m*-cresol



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 700-38-9

Synonyms 5-methyl-2-nitrophenol

EINECS No. 211-843-0

Physical properties

M. Pt. 53-56°C **Flash point** 109°C

Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2446 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 47 mg l^{-1} (1).

Invertebrate toxicity

LOEC *Scenedesmus quadricauda* 7 mg l^{-1} (2).

LOEC *Entosiphon sulcatum* 1.3 mg l^{-1} (2).

EC_{50} (48 hr) *Daphnia magna* 21.3 mg l^{-1} (1).

Cell multiplication inhibition test *Uronema parduczi* 5.3 mg l^{-1} (3).

Other comments

As pollutant of air and water (4,5).

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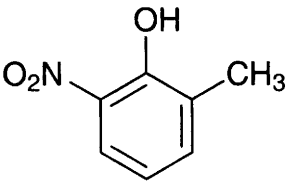
N108 6-nitro-*o*-cresol



$C_7H_7NO_3$ **Mol. Wt.** 153.14 **CAS Registry No.** 13073-29-5

Synonyms 2-methyl-6-nitrophenol; 2-hydroxy-3-methylnitrobenzene; 2-hydroxy-3-nitrotoluol; 6-methyl-2-nitrophenol

Physical properties

M. Pt. 70°C **B. Pt.** 250-260°C (decomp.)
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2446 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

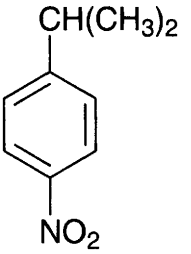
Ecotoxicity

Fish toxicity
Non-toxic at 5 ppm (24 hr) for trout, bluegill sunfish, yellow perch and goldfish. Test conditions; pH 7; 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).

References

1. Wood, E. M. *The Toxicity of 3400 Chemicals to Fish* 1987, EPA 560/6-87-002, PB 87-200-275, US EPA/Office of Toxic Substances, Washington, DC, USA

N109 *p*-nitrocumene



$C_9H_{11}NO_2$ **Mol. Wt.** 165.19 **CAS Registry No.** 1817-47-6

Synonyms 1-(1-methylethyl)-4-nitrobenzene; *p*-isopropylnitrobenzene; 4-nitroisopropylbenzene; 2-(*p*-nitrophenyl)propane

EINECS No. 217-326-6

Physical properties

M. Pt. 106-107°C at 11 mmHg **B. Pt.** >110°C **Specific gravity** 1.090

Ecotoxicity

Bioaccumulation

In algae and fish relative bioaccumulation rates 120 and 190, respectively (1,2).

Environmental fate

Degradation studies

Relative biodegradation rate in activated sludge 0.2% CO_2 (relative to dose applied) (2).

Other comments

Experimental toxicology, human health effects and workplace experience under consideration for study by Berufsgenossenschaft der Chemischen Industrie (BG Chemie), Germany (3).

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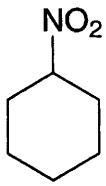
N110 nitrocyclohexane



$C_6H_{11}NO_2$ **Mol. Wt.** 129.16 **CAS Registry No.** 1122-60-7

EINECS No. 214-354-0 **RTECS No.** GV 6600000

Physical properties

M. Pt. -34°C **B. Pt.** 205/206°C at 768 mmHg **Flash point** 81/88°C (open cup) **Specific gravity** 1.061
Volatility v.den. 4.5

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 250 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat 150 mg m^{-3} (1).
LC_{Lo} (2 hr) inhalation mouse 10 mg m^{-3} (1).

References

1. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, CIP, Moscow, USSR

N111 nitroethane

$CH_3CH_2NO_2$

$C_2H_5NO_2$ **Mol. Wt.** 75.07 **CAS Registry No.** 79-24-3

EINECS No. 201-188-9 **RTECS No.** KI 5600000

Uses Solvent.

Physical properties

M. Pt. -90°C **B. Pt.** 114-115°C **Flash point** 27/28°C **Specific gravity** 1.041 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 0.18 **Volatility** v.p. 15.6 mmHg at 20°C ; v.den. 2.58

Solubility Water: 4.5 ml 100 ml^{-1} at 25°C. Organic solvents: miscible with diethyl ether, ethanol, methanol

Occupational exposure

DE-MAK 100 ppm (310 mg m^{-3})

FR-VME 100 ppm (310 mg m^{-3})

SE-LEVL 20 ppm (60 mg m^{-3}) **SE-STEL** 50 ppm (150 mg m^{-3})

UK-LTEL 100 ppm (312 mg m^{-3})

US-TWA 100 ppm (307 mg m^{-3})

UN No. 2842 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Supply classification harmful

Risk phrases Flammable – Harmful by inhalation and if swallowed (R10, R20/22)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Avoid contact with the eyes – In case of fire and/or explosion do not breathe fumes (S2, S9, S25, S41)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 860, 1100 mg kg^{-1}, respectively (1,2).

LD_{Lo} oral rabbit 500 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 310 mg kg^{-1} (4).

Carcinogenicity and chronic effects

♂, ♀ rat exposed at 100 or 200 ppm, 7 hr day^{-1}, 5 days wk^{-1} for 2 yr. No pharmacological or mortality effects were observed. There were no effects on haematology, clinical chemistry or organ weights and no significant neoplastic or non-neoplastic pathology (5).

Teratogenicity and reproductive effects

Smaller litters were produced in rats in a three generation study; stillbirths and malformations were not significantly increased (6).

Metabolism and toxicokinetics

Rapidly excreted through the lungs and is completely eliminated within 30 hr (7).

Irritancy

Respiratory tract irritation and narcosis (species unspecified) (3).

Eye irritant and may cause corneal damage. Weak skin irritant (species unspecified) (8).

Genotoxicity

Salmonella typhimurium TA92, TA98, TA100, TA1537 with and without metabolic activation negative (9).

In vivo Charles River (CD-1) mouse bone marrow micronucleus induction negative (9).

Other effects

Any other adverse effects

Only low levels of methaemoglobin were induced even in cases of acute poisoning (species unspecified) (10). Moderately toxic by ingestion producing kidney and liver damage in experimental animals (11).

Other comments

Reviews on experimental toxicology, epidemiology, human health effects, workplace experience and physico-chemical properties listed (12).

Low estimated affinity for a series of biological materials including fat, serum and psoriasis scales (13).

Autoignition temperature, 410/414°C.

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2. *Gig. Sanit.* 1967, **32**(9), 9.
3. Machle, W. et al *J. Ind. Hyg. Toxicol.* 1940, **22**, 315.
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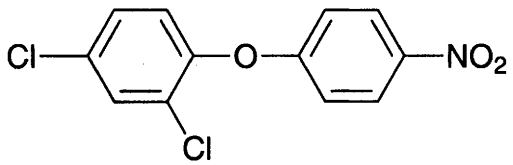
N112 nitrofen



$C_{12}H_7Cl_2NO_3$ **Mol. Wt.** 284.10 **CAS Registry No.** 1836-75-5

Synonyms 2,4-dichloro-1-(4-nitrophenoxy)benzene; 2,4-dichlorophenyl *p*-nitrophenyl ether; FW925; Mezotox; Niclofen; Nitrophen; Tok; Triziliu

EINECS No. 217-406-0 **RTECS No.** KN 8400000

Uses Superseded herbicide.

Physical properties

M. Pt. 70-71°C **Partition coefficient** log P_{ow} 5.0 (1) **Volatility** v.p. 8×10^{-6} mmHg at 40°C

Solubility Water: 0.7-1.2 mg l^{-1} at 22°C. Organic solvents: acetone, methanol, xylene

Occupational exposure

Supply classification toxic
Risk phrases May cause cancer – May cause harm to the unborn child (R45, R61)
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} (48 hr) common carp 2.1 mg l^{-1} (2).
LC_{50} (48 hr) goldfish 1.4 mg l^{-1} (2).
LC_{50} (96 hr) rainbow trout 7.0 mg l^{-1} (3).
LC_{50} (96 hr) orfe 26.0 mg l^{-1} (3).
LC_{50} (96 hr) guppy 1.6 mg l^{-1} (3).

Invertebrate toxicity
LC_{50} (48 hr) *Asellus aquaticus* 1.6 mg l^{-1} (3).
IC_{50} (10 day) *Ankistrodesmus falcatus* 0.086 mg l^{-1} (3).
LC_{50} (48 hr) *Ceriodaphnia dubia* 0.22 mg l^{-1} (4).
IC_{50} (4, 7 day) *Ceriodaphnia dubia* 0.14-0.15 and 0.13-0.14 mg l^{-1}, respectively (5).

Environmental fate

Carbonaceous inhibition
2.5 kg ha^{-1} as spray did not affect soil respiration when applied as TOK 50 WP; at 10 kg ha^{-1} soil respiration was depressed. Spraying twice in a year severely depressed all groups of soil microorganisms, as detected 356 days after the second spray (5).

Degradation studies
687 days after spraying 2.5 kg ha^{-1} as TOK 50 WP the soil nitrogen residue was 0.112 mg kg^{-1} and 0.353 mg kg^{-1} when applied at 10 kg ha^{-1} (5).
Degraded by mixed cultures of bacterial soil isolates. Degradation was reduced by addition of sterilised field soil to the culture, indicating that adsorption can be responsible for field persistence. Non-toxic to the microorganisms (6).
Degraded by mixed bacterial populations isolated from arable soil, with acetate, within 4-5 wk. Degradation proceeds endogeneously after ATP-dependent uptake followed by a temporary accumulation. Application of glucose as substance blocks degradation and peptone and algae biomass retard degradation (7).
Paddy-field soils $t_{1/2}$, 2.9-24.3 days. Soil type affected degradation rate. B-C horizon of forest soil $t_{1/2}$, 86.6 days. Degradation rate was correlated with the redox potentials of the soils not with the physical and chemical properties (8).

Abiotic removal
Photodecomposes in aqueous solution to form: 2,4-dichlorophenol, *p*-nitrophenol, 2,4-dichlorophenyl *p*-aminophenyl ether, 4,4'-bis(2,4-dichlorophenoxy)azobenzene, hydroquinone, and 4-nitrocatechol by rapid cleavage of the ether link. Other pathways include: ring hydroxylation, denitration prior to cleavage of the ether linkage, and replacement of the ring chlorines by hydroxyl or hydrogen. ~10% remained after 4 wk exposure to sunlight (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 450, 740 mg kg^{-1}, respectively (10).
LD_{50} oral rabbit 1620 mg kg^{-1} (11).
LD_{Lo} oral cat 300 mg kg^{-1} (10).
LC_{Lo} (4 hr) inhalation cat 620 mg m^{-3} (10).
LD_{50} dermal rat 5000 mg kg^{-1} (12).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (13).

Oral Osborne-Mendel rat and B6C3F1 mouse 3656 or 2300 ppm for ♂ rat, 2600 or 1300 ppm for ♀ rat and 4696 or 2348 ppm for both sexes of mice, in feed for 78 wk. ♀ rats showed a statistically significant dose-related increased incidence of pancreatic carcinomas. Poor ♂ rat survival prevented evaluation. At both doses and for both sexes the mice showed statistically highly significant incidences of hepatocellular carcinomas. Haemangiosarcoma of the liver had a statistically significant relationship with dietary concentration (14).

Oral B6C3F1 mouse (78 wk) at 1775-2500 or 3550-5000 mg kg^{-1} dissolved in corn oil. Weight gain was depressed in both ♀ groups and in the high-dose ♂ groups. There was no positive association with mortality. Incidence of hepatocellular carcinomas was significantly increased. Haemangiosarcomas of the spleen and liver were also observed (15).

The incidences in ♂ and ♀ B6C3F1 mice of hepatocellular adenomas and carcinomas fed 3000 or 6000 mg kg^{-1} (78 wk) were statistical different in a dose-related manner. Fischer 344 rats fed 3000 or 6000 mg kg^{-1} (78 wk) showed no statistically difference in incidence of tumours compared with controls (16,17).

Teratogenicity and reproductive effects

Offspring of CD-1 mice given 100 mg kg^{-1} body weight day^{-1} on days 7-17 of pregnancy developed hydrocephaly and microphthalmia (18,19).

Stomach intubation of 10, 20 or 50 mg kg^{-1} body weight day^{-1} to Sherman rats on day 7-15 of pregnancy caused an increase in stillbirths, reduced pup viability at 20 mg kg^{-1}. At the high dose, term foetuses had poorly expanded lungs (20).

Reduced pup weight at birth, high post-natal mortality and foetal malformations including cardiac deformities, diaphragmatic hernia and hydronephrosis reported in Long Evans rats. Administered as single oral dose of 150 mg kg^{-1} body weight on day 9, 10, 11 or 12 of pregnancy (21).

2000 and 500 ppm were administered in diet to, respectively, ICR mice and CD rats. Embryos/foetuses showed general growth retardation. Lung development was bilaterally retarded. In mice the left lung was more hypoplastic than the right one, while the opposite occurred (22).

The lung cells of rat foetuses showed abnormal DNA, RNA and protein content which interfered with ontogenic acquisition of cells when the mother was administered 20 or 40 mg kg^{-1} day^{-1} on gestation days 10-13. Adrenal catecholamines and red blood cell concentration were reduced (23).

Metabolism and toxicokinetics

Oral sheep administered 40 mg kg^{-1} body weight had excreted 76.2% in faeces and urine after 99 hr in a radiolabel study. After 100 hr, radioactivity was highest in fat. The liver, adrenal gland, kidney, lung, muscle, thyroid, mammary gland, spleen and skin contained lower levels. The predominant metabolites were, 2,4-dichlorophenyl 4-aminophenyl ether, 2, 4-dichlorophenol, 2,4-dichloro-5-hydroxyphenyl 4-nitrodiphenyl ether, 2-chlorophenyl 4-nitrophenyl ether, and conjugates (24).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate to severe erythema and moderate oedema and 100 mg instilled into rabbit eye (24 hr) caused severe irritation (25).

Irritating effects on the skin and eye were seen in occupationally exposed workers (26,27).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (28).

Salmonella typhimurium TA100 without metabolic activation negative, with metabolic activation positive. TA1535, TA1538 with and without metabolic activation negative (29).

Bacillus subtilis H17*rec*+ M45*rec*– without metabolic activation negative (30).

Escherichia coli SOS Chromotest with and without metabolic activation negative (31).

Escherichia coli prophage λ without metabolic activation negative, with metabolic activation positive (32).

In vivo rat bone marrow cells no significant increase in chromosomal aberrations (33).

In vivo mouse bone marrow no micronuclei induction (34).

Other effects

Any other adverse effects

Acute toxicity effects in laboratory animals are mainly neurological and respiratory (35,36).
Liver:body weight ratios have been reported as significantly raised in rats and beagles (37).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (38).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (39).
Included in Schedule 4 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (39).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (40).

Other comments

Has been detected as a contaminant in ground water in areas where used (41).
Detected as a contaminant in vegetables (42,43).
Teratogenicity mechanism reviewed (44).

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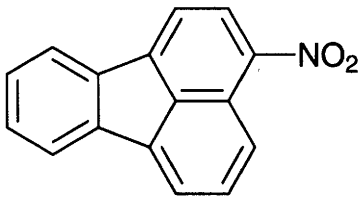
N113 3-nitrofluoranthene



$C_{16}H_9NO_2$ **Mol. Wt.** 247.25 **CAS Registry No.** 892-21-7

RTECS No. LL 4750000

Physical properties

M. Pt. 157-159°C

Solubility Organic solvents: acetone, benzene, dichloromethane

Environmental fate

Abiotic removal

3-Nitrofluoranthene exposed to light of wavelength ≥310 nm, either in dimethyl sulfoxide or after coating onto silica, decomposed with $t_{1/2}$ 12.5 and >20 days, respectively (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (2).

Subcutaneous rat, the lowest toxic dose, 120 mg kg^{-1}, given for 8 wk intermittently induced sarcomas at the injection site in 40% of rats (3).

Metabolism and toxicokinetics

Rat liver microsomes metabolise 3-nitrofluoranthene *in vitro*, under aerobic conditions, by ring hydroxylation. Under anaerobic conditions reduction by both microsomal and cytosolic rat liver enzymes occurs (4).

In vitro nitro-reduction of 3-nitrofluoranthene by rabbit liver aldehyde oxidase requires the presence of flavin mononucleotide or flavin adenine dinucleotide and is inhibited by oxygen in a concentration-dependent manner. K_m and V_{max} values for the reaction were 1.9 μM and 5.4 pmol min^{-1} $unit^{-1}$ enzyme, respectively (5).
3-nitrofluoranthene incubated *in vitro* with rat lung cytosol or microsomes, under anaerobic conditions, is metabolised to its amino derivative. Under aerobic conditions with lung microsomes 1 major (possibly 3-nitrofluoranthene-8-ol) and 3 minor metabolites were detected (6).

Genotoxicity

Salmonella typhimurium TA100 positive; TA100NR and TA100-Tn5-1,8DNP1012 negative (7).
Hamster embryo cells 4100 nmol l^{-1} oncogenic transformation positive (8).
Rat and mouse hepatocyte DNA-repair tests positive (9).
Chinese hamster V-79 cells with metabolic activation (by S9 or S100) positive (10).
Escherichia coli PQ37 (SOS Chromotest) without metabolic activation positive (11).

Other comments

Investigated for mutagenicity or carcinogenicity as an airborne particulate pollutant and as a component of diesel emissions (12-16).
Physico-chemical properties, human health effects, experimental toxicology, workplace experience, epidemiology, exposure levels (environment and workplace), environmental effects and environmental fate reviewed (17,18).

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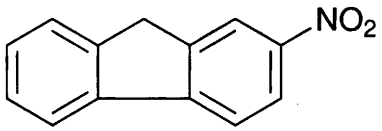
N114 2-nitrofluorene



$C_{13}H_9NO_2$ **Mol. Wt.** 211.22 **CAS Registry No.** 607-57-8

Synonyms 2-nitro-9*H*-fluorene

EINECS No. 210-138-5 **RTECS No.** LL 8225000

Physical properties

M. Pt. 157-158°C

Solubility Organic solvents: acetone, benzene, tetrahydrofuran, toluene

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 1600 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Possibly carcinogenic to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (2).

Oral (8 months) Holtzman rats 342 mg kg^{-1} in diet. Squamous-cell carcinomas and multiple papillomas in the forestomach developed in most animals. 2/9 ♀ exhibited mammary gland tumours. A group of ♂ rats were then fed 342 mg kg^{-1} diet for 12 months, of the survivors 17/18 had squamous-cell carcinomas of the forestomach, 13 had liver tumours, 4 had tumours of the ear duct, 2 had tumours of the small intestinal epithelium and one had a tumour of the mammary gland (3).

In another study 2/9 Minnesota rats (♀) exhibited one adenocarcinoma of the mammary gland and one squamous-cell carcinoma of the ear duct after a 23 wk oral study, 500 mg kg^{-1} in diet (4).

Metabolism and toxicokinetics

2-Formylaminofluorene, 2-aminofluorene and 2-acetylaminofluorene were excreted in urine for 3 days following oral administration to ♂ albino rabbits. The latter two compounds are carcinogenic in animal experiments, In ♂ Wistar rats the same metabolites were found in the faeces but not in the urine (5).

Following single oral dose to Sprague-Dawley rats approximately 60% was excreted in the urine and 30% in faeces in an 8-day period. The metabolites were: *N*-, 1-, 3-, 5-, 7-, 8-, and 9-hydroxy-2-acetylaminofluorenes; the two major metabolites were 5- and 7-hydroxy-2-acetylaminofluorenes. *N*-Hydroxy-2-acetylaminofluorene and 9-hydroxy-2-acetylaminofluorene are carcinogenic in laboratory animals (6,7).

Rat liver microsomes and rabbit liver microsomes and cytosol under anaerobic conditions catalysed reduction to the carcinogens 2-aminofluorene and *N*-hydroxy-2-aminofluorene (8-11).

The liver excretes hydroxy-2-nitrofluorene as non-mutagenic glucuronide conjugates. When excreted via the bile, intestinal β-glucuronidase can liberate direct-acting mutagens in the gut (12).

In rats given a single oral dose, intestinal microflora reduced excretion of mutagenic metabolites (13).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1538 without metabolic activation positive (14).

Saccharomyces cerevisiae D3 mitotic recombination positive (15).

Saccharomyces cerevisiae D4 mitotic recombination negative (16).

Initiator tRNA acceptance assay with metabolic activation positive (17).

Escherichia coli PQ37 SOS Chromotest with metabolic activation weakly positive (18).

In vitro mouse lymphoma L5178Y tk^+/tk^- positive (19).
In vivo oral Chinese hamster bone marrow cells increased incidence of sister chromatid exchange. No such effect was observed after intraperitoneal administration (20).
Induced morphological transformation of Syrian hamster embryo cells in presence of hamster hepatocytes (21).
In vivo DNA-repair host-mediated assay negative for liver, lungs, kidneys or spleen following intraperitoneal administration (22).

Other effects

Any other adverse effects
Covalent binding to haemoglobin has been reported in Sprague-Dawley rats (23).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 $\mu g\ l^{-1}$ (24).

Other comments

Occurs in diesel exhaust (25-27). In airborne particulates (28-30). In emissions from heaters and burners (29,31). In river sediment (29).
In vivo metabolism reviewed (29).
Genotoxicity reviewed (32,33).
Toxicity, genotoxicity, carcinogenicity and biological effects reviewed (34).

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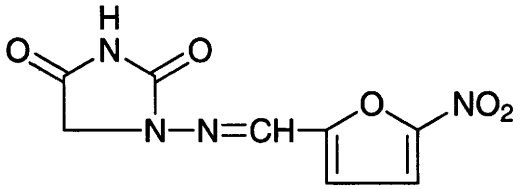
N115 nitrofurantoin



$C_8H_6N_4O_5$ **Mol. Wt.** 238.16 **CAS Registry No.** 67-20-9

Synonyms 1-[[(5-nitro-2-furanyl)methylene]amino]-2,4-imidazolidinedione; 1-[(5-nitro-2-furfurylidene)amino]hydantoin; Berkfurin; Furadantin; Furalan; Macrodantin; Urantoin; Urolong; Zoofurin

EINECS No. 200-646-5 **RTECS No.** MU 2800000

Uses Antibacterial agent.

Physical properties

M. Pt. 270-272°C (decomp.) **Partition coefficient** log P_{ow} -0.0270 (1)
Solubility Water: 19 mg 100 ml^{-1}. Organic solvents: acetone, dimethylformamide, ethanol, glycerol, peanut oil

Ecotoxicity

Invertebrate toxicity
Vibrio cholerae 10 and 37% survival doses, respectively, 18.0 and 5.5 μg ml^{-1} hr^{-1}. Causes filamentation of the cells (2).

Environmental fate

Degradation studies
The kinetic constants have been calculated for a continuous flow, completely mixed activated sludge process that treats pharmaceutical wastewater containing the substance and two other drugs. Maximum species substrate degradation rate, 1.5 day^{-1}; saturation constant, 35.2 mg l^{-1}; yield 0.368; microorganism self-oxidation rate, 0.045 day^{-1}; substrate oxygen-consumption coefficient, 0.25; and interval RQ, 0.1 day^{-1} (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 360, 604 mg kg^{-1}, respectively (4,5).
LD_{50} intraperitoneal mouse, rat 100, 112 mg kg^{-1}, respectively (5,6).

Sub-acute and sub-chronic data

Oral (14 day, 13 wk) F344/N rat, B6C3F1 mouse 5000-20000 ppm in diet showed weight loss and some of the mice died. Renal tubular epithelial necrosis occurred in ♂ mice at 5000 ppm (7).

At 116 mg kg^{-1} day^{-1} ♀ Sprague-Dawley rats showed decreased weight-gain. At this concentration for ♀ and at 81 mg kg^{-1} day^{-1} for ♂ there was an increase in sciatic nerve degeneration, testicular degeneration and fibrosis and an increase in focal biliary proliferation in the ♀. There was no evidence of renal toxicity (8).

Carcinogenicity and chronic effects

Oral F344/N rat, B6C3F1 mouse (103 wk) 1300 or 2500 ppm and ♀ rat 600 or 1300 ppm. Kidney tubular cell adenomas were significantly increased in ♂ rats. Tubular cell carcinomas occurred in two high-dose ♂s only. Interstitial cell adenomas of the testis occurred with a negative trend in rats. The incidence of clitoral gland neoplasms increased in low-dose rats. One low-dose and two high-dose ♂ rats exhibited osteosarcomas. Subcutaneous tissue neoplasm incidence was increased in ♂ rats. ♀ rats and ♂ mice showed no compound-related neoplastic lesions. ♀ mice showed ovary tubular cell adenomas, benign mixed tumours, granulosa cell tumours (one malignant) and malignant lymphomas. There was one case from both dose groups of adenocarcinoma of the uterus. Hepatocellular neoplasms at increased incidence were seen at high dose and an Ito cell tumour of the liver occurred at both concentrations. The study concluded that there was some evidence for carcinogenic activity in the ♂ rat and clear evidence of carcinogenic activity in the ♀ mouse. ♀ rat and ♂ mouse showed no evidence of carcinogenic activity (7).

When administered to Sprague-Dawley rats at doses ranging from 12-116 mg kg body $weight^{-1}$ day^{-1} there was no increase in the incidence of neoplasms at any site (duration unspecified) (8).

Teratogenicity and reproductive effects

Degeneration of the germinal epithelium of the seminiferous tubules of the testis was observed in F344/N rats and B6C3F1 mice that received, respectively, 2500-10000 and 1300-5000 ppm in an oral study. Necrosis of the ovarian follicles occurred at 2500-10,000 ppm in rats and at 5000 ppm in mice (7).

Metabolism and toxicokinetics

Readily absorbed from the gastro-intestinal tract. Concentrations in body tissues and blood are low due to rapid elimination. The placenta and blood-brain barrier are crossed and the compound has been detected in breast milk. Reported protein binding figures range from 60 to 95%. $t_{1/2}$, 0.3-1 hr. Metabolism occurs in the liver and most body tissues while 30 to 50% is excreted quickly unchanged in the urine (9).

Six lactating women were given either 50 or 100 mg 3 × day^{-1}, 2-5 days after giving birth. At both concentrations elimination $t_{1/2}$ and plasma clearance were, respectively, 0.8 hr and 27.6 1 hr^{-1}. 22-57 µg (0.05-0.11% of dose) and 61-284 µg (0.06-0.28%) was excreted within 6 hr at the two doses. The concentration ratio of the breast milk to the plasma collected at 3 hr was 2.2 and 2.3 (10).

Sensitisation

Skin rashes, fever, pruritus, urticaria, angioedema, erythema multiforme, exfoliative dermatitis, pancreatitis and arthralgia occur. Acute asthmatic attacks may affect patients with a history of asthma and acute pulmonary sensitivity reactions have been reported (9).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive; TA1535, TA1537 with and without metabolic activation negative (7).

Vibrio cholerae DNA Cross-links positive (2).

In vitro mouse lymphoma L5178Y tk^+/tk^- without metabolic activation positive (7).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges and chromosomal aberrations positive (7).

Drosophila sex-linked recessive lethal assay by feeding or injection negative (7).

Other effects

Other adverse effects (human)

Nausea, vomiting, anorexia, diarrhoea and abdominal pain affect the gastro-intestinal tract. Neurological effects

include headache, drowsiness, vertigo and dizziness. Peripheral polyneuropathy had been reported. Long-term use may give rise to sub-acute or chronic pulmonary symptoms which may not be reversible (9).
In glucose-6-phosphate dehydrogenase-deficient individuals it may initiate a haemolytic reaction (10).

Any other adverse effects

In a 2-yr cancer study of F344/N rats and B6C3F1 mice non-neoplastic lesions included chronic nephropathy, hyperplasia of the parathyroid gland, mineralisation of the glandular stomach and fibrous osteodystrophy of the bone in ♂ rats, testicular degeneration in rats and mice and ovarian atrophy and hyperplasia of the adrenal cortex spindle of ♀ mice (7).
Reduced mitogen responsiveness of both B- and T-lymphocytes of human peripheral blood lymphocytes and mouse spleen cells *in vitro* in a concentration-dependent manner. *In vivo* study showed no mouse spleen cell transformation in response to mitogen (11).
In rodent studies non-neoplastic ovarian changes included hypoplasia, atrophy, tubular hyperplasia and follicular necrosis (12).
Caused *in vitro* rat liver protein thiol and glutathione tissue levels to fall to, respectively, 49 and 17% of initial concentrations (13).

Other comments

Pharmacology, pharmacokinetics and bioavailability reviewed (14).

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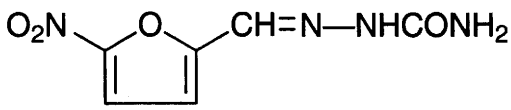
N116 nitrofurazone



$C_6H_6N_4O_4$ **Mol. Wt.** 198.14 **CAS Registry No.** 59-87-0

Synonyms 5-nitro-2-furancarboxaldehyde semicarbazone; 5-nitro-2-furaldehyde semicarbazone; 5-nitro-2-furfural semicarbazone; 2-[(5-nitro-2-furanyl)methylene]hydrazinecarboxamide; (5-nitro-2-furfurylideneamino)-urea; Vabrocid; Furacin; Furazone

EINECS No. 200-443-1 **RTECS No.** LT 7700000

Uses Antiseptic. Organic synthesis.

Physical properties

M. Pt. 242-244°C (decomp.) **Partition coefficient** log P_{ow} –0.0612 (1)
Solubility Water: ~0.25 mg l^{-1}. Organic solvents: acetone, dimethylformamide, ethanol, propylene glycol, methanol

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) channel catfish 19 mg l^{-1}. Skin and muscle lesions were observed (2).
LC_{50} (96 hr) goldfish 71 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 250, 590 mg kg^{-1}, respectively (3-5).
LD_{50} subcutaneous mouse, rat 750, 3000 mg kg^{-1}, respectively (3,6).
LD_{50} intraperitoneal mouse, rat 96, 150 mg kg^{-1}, respectively (7,8).

Sub-acute and sub-chronic data
Oral rat and mouse (13 wk) 70-2500 mg kg^{-1} diet. High doses caused convulsive seizures and gonadal hypoplasia in both species. Evidence of toxicity in rats also included degenerative arthropathy (9).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (10).
Oral rat, mouse (2 yr) 0, 310 or 620 ppm diet for rats, 0, 150 or 310 ppm diet for mice. Clear evidence of carcinogenicity was shown in ♀ rats by a markedly increased incidence of fibroadenomas of the mammary gland, and in ♀ mice as shown by increased incidences of benign mixed tumours and granulosa cell tumours of the ovary. Equivocal evidence of carcinogenicity was observed in ♂ rats by the occurrence of sebaceous gland adenomas and trichoepitheliomas of the skin, mesotheliomas of the tunica vaginalis, and preputial gland tumours. There was no evidence of carcinogenic activity in ♂ mice (9).
Oral rat (66 wk) 1000 mg kg^{-1} diet for 46 wk. Mammary fibroadenomas developed in 22/29 treated rats compared with 2/29 controls (11).
Transplacental mouse, 75 mg kg^{-1} day^{-1} on days 13, 15 and 17 of gestation. Offspring were foster-nursed by untreated dams. At 32 wk 67/145 treated animals and 548/844 controls were still alive. At this time the incidence of lung tumours was not significantly different from controls (12).

Teratogenicity and reproductive effects
Oral rabbit, 0, 5, 10, 15 or 20 mg kg^{-1} day^{-1} on days 6-19 of gestation. The high dose was associated with maternal mortality (2/26), reduced maternal body weight gain increased maternal liver weight, increased resorption and increased incidence of malformed live foetuses (13).
Gavage ♂ rat, 100 mg kg^{-1} day^{-1} for 7 days caused testicular atrophy (14).

Metabolism and toxicokinetics
Following oral administration to rats, urinary metabolites included 4-hydroxynitrofurazone, 4-hydroxyfurazolidone and 4-hydroxynitrofurantoin (15).
Within 24 hr after oral administration of ^{14}C-nitrofurazone to rats, ~67% of the radioactivity appeared in the urine, 26% in the faeces and ~1% expired as carbon dioxide. Complete recovery of the administered dose was observed after 96 hr, <15% of the radio-label was recovered as unchanged substance (16).
In humans nitrofurazone is not significantly absorbed from the skin or mucous membranes after local administration (17).

Sensitisation
Sensitisation and generalised allergic skin reactions have been reported in human patients following topical application (18).

Genotoxicity

CASE structure-activity methodology predicted it to be mutagenic in *Salmonella typhimurium* (19).
Drosophila melanogaster sex-linked recessive lethal assay negative (20).
In vitro mouse lymphoma L5178Y cells without metabolic activation tk^+/tk^- positive (9).
In vitro Chinese hamster ovary cells with and without metabolic activation, sister chromatid exchanges positive; with metabolic activation chromosomal aberrations equivocal, without metabolic activation positive (21).
In vitro mouse lymphoma L5178Y cell mutation assay positive (metabolic activation unspecified) (21).
In vitro rat and mouse hepatocytes, DNA repair test negative (22).
In vivo rat bone marrow cells chromosomal aberrations negative (23).
Intraperitoneal mouse, 15-150 mg kg^{-1} day^{-1} for 5 days did not induce sperm abnormalities (24).

Other effects

Other adverse effects (human)

Nitrofurazone had been reported to cause haemolytic anaemia in individuals with glucose-6-phosphate dehydrogenase deficiency (25).
Polyneuropathy is common among trypanosomiasis patients treated with nitrofurazone (26).
In a collaborative perinatal study in which exposure of pregnant women was studied, 15 malformed children were born to 234 women exposed during the first trimester of pregnancy, giving a standardised relative risk of 0.99 (27).

Any other adverse effects

Effects of nitrofurazone were studied in isolated perfused rat liver. A perfusion medium containing 120 mg l^{-1} and lacking the GSH precursors, glycine, glutamic acid and cysteine, caused a marked increase in bile flow, a massive biliary efflux of glutathione disulfide and a sharp decline in the caval efflux of GSH and the tissue level of GSH. 30 mg l^{-1} with or without amino acid supplementation, and 120 mg l^{-1} with supplementation induced less dramatic effects. The author suggested that the toxicity of the reactive oxygen species generated by the redox cycling of the nitro group and the reactive metabolites generated by further reduction of nitrofurazone can be mitigated by adequate GSH levels, but that livers deficient in GSH may be damaged (28).

Other comments

Physical properties, use, analysis, mammalian toxicity and metabolism reviewed (29,30).

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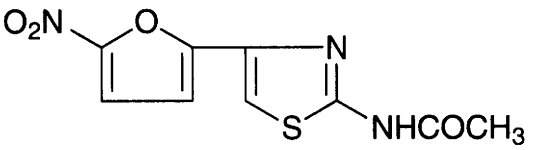
N117 *N*-[4-(5-nitro-2-furyl)-2-thiazolyl]acetamide



$C_9H_7N_3O_4S$ **Mol. Wt.** 253.24 **CAS Registry No.** 531-82-8

Synonyms 2-acetylamino-4-(5-nitro-2-furyl)thiazole; 2-acetylamino-4-(5-nitro-2-furyl)thiazole; furathiazole; NFTA

RTECS No. AC 6650000

Uses Formerly used in treatment of cystitis and urinary calculi with secondary infection; its use is now almost exclusively veterinary.

Physical properties

M. Pt. 296°C

Solubility Water: insoluble. Organic solvents: dimethylacetamide, dimethylformamide

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate data on carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (1).

Carcinogenic in mice, rats and hamsters after oral administration, producing lymphosarcomas and forestomach tumours in mice, lung and renal pelvis carcinomas in rats, urinary bladder carcinomas and forestomach tumours in hamsters. The mice were fed diets containing 1000 ppm for 14 wk, the rats up to 200 mg kg^{-1} day^{-1} for 46 wk, and the hamsters 1000 ppm for 48 wk (2).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive; TA1535 without metabolic activation negative (3).

Other comments

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

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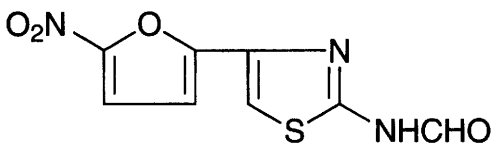
N118 *N*-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide



$C_8H_5N_3O_4S$ **Mol. Wt.** 239.21 **CAS Registry No.** 24554-26-5

Synonyms FANFT; 2-(formylamino)-4-(5-nitro-2-furyl)thiazole

RTECS No. LQ 3150000

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Rats, mice and hamsters, but not guinea pigs, are susceptible to bladder carcinogenesis by FANFT (1). Administration of 0.188% in the diet for 20 wk increased incidence of bladder carcinomas in ♀ rats; co-administration with 3% uracil reduced incidence of bladder tumours but increased incidence of pelvic and uterine tumours (2).

Metabolism and toxicokinetics

2-Amino-4-(5-nitro-2-furyl)thiazole (ANFT) was detected in urine of rats, mice and hamsters fed 0.188% FANFT for 1 wk (1).

In rats and guinea pigs administered radiolabelled FANFT, highest concentrations of radioactivity occurred in urine and intestines. FANFT was not detected in urine of either species. A unique metabolite, ANFT *N*-glucuronide, was detected in guinea pig but not rat urine. A unique UDP-glucuronosyl-transferase appears partly responsible for the reduced amount of free ANFT excreted by guinea pigs compared with rats, and this reduced level of urinary ANFT in guinea pigs may partially explain their resistance to FANFT-induced bladder carcinogenesis (3).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive; TA1535, TA1537, TA1538 with and without metabolic activation negative. *Escherichia coli* WP2 *uvr* A with and without metabolic activation positive (4).

Urine from rats, mice, hamsters and guinea pigs fed 0.188% for 1 wk was mutagenic to *Salmonella typhimurium* TA100; there was a positive correlation between bladder carcinogenesis susceptibility by FANFT and urinary ANFT excretion, but none between this susceptibility and urine mutagenesis (1).

Other comments

Mechanism of bladder carcinogenesis reviewed (5,6).

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N119 nitrogen

N_2

N_2 **Mol. Wt.** 28.01 **CAS Registry No.** 7727-37-9

Synonyms azote

EINECS No. 231-783-9 **RTECS No.** QW 9700000

Uses Food preservative (through the elimination of oxygen). Manufacture of ammonia and nitric acid. In incandescent bulbs. Liquid nitrogen is used in food freezing process and in cryogenic studies.
Occurrence Formed from inorganic nitrogen containing compounds by denitrifying bacteria throughout the environment. Incorporated into organic material by Leguminosae plants. Constitutes ~75.5% by weight, or 78% by volume of Earth's atmosphere.

Physical properties

M. Pt. –210°C **B. Pt.** –195.8°C **Specific gravity** 1.25046 at 0°C and 1 atm
Volatility v.p. 760 mmHg at –195°C ; v.den. 0.97
Solubility Water: sparingly soluble in water. Organic solvents: liquid ammonia, ethanol

Occupational exposure

UN No. 1066 (compressed), 1977 (refrigerated liquid) **HAZCHEM Code** 2T (compressed)
HAZCHEM Code 2RE (refrigerated liquid) **Conveyance classification** non-flammable non-toxic gas

Mammalian & avian toxicity

Acute data
Inhalation mouse, atmosphere containing ~89% v/v nitrogen at 30°C (~10% oxygen) caused incapacitation in 35-45 min, while concentrations of ~91% (~8% oxygen) caused incapacitation in 10-15 min (1).

Other effects

Other adverse effects (human)
Exposure can cause nausea, headache and vomiting (2).
Contact with liquid nitrogen can cause severe frostbite or "burns" to the skin (3).

Nitrogen narcosis had been reported from nitrogen breathed at high pressure, as in deep sea diving. Under high pressure nitrogen dissolves in the blood and lipid . If decompression is too rapid, nitrogen effervesces from body stores producing gas emboli, leading to the syndrome of decompression sickness (4).

Any other adverse effects

Acts as a simple asphyxiant at high concentrations by displacing oxygen (2,5).

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N120 nitrogen dioxide

NO_2

NO_2 **Mol. Wt.** 46.01 **CAS Registry No.** 10102-44-0

Synonyms nitrogen oxide (NO_2); nitrogen peroxide

EINECS No. 233-272-6 **RTECS No.** QW 9800000

Uses Intermediate in nitric and sulfuric acid production. Organic synthesis.

Physical properties

M. Pt. –11.2°C **B. Pt.** 21.15°C **Specific gravity** 1.4494 at 20°C with respect to water at 20°C
Volatility v.p. 440 mmHg at 10°C ; v.den. 1.58
Solubility Water: miscible. Organic solvents: carbon disulfide, chloroform

Occupational exposure

DE-MAK 5 ppm (9.5 mg m^{-3}) **FR-VLE** 3 ppm (6 mg m^{-3})
JP-OEL (pending)
SE-LEVL 2 ppm (4 mg m^{-3}) **SE-CEIL** 5 ppm (10 mg m^{-3})
UK-LTEL 3 ppm (5.7 mg m^{-3}) **UK-STEL** 5 ppm (9.6 mg m^{-3})
US-TWA 3 ppm (5.6 mg m^{-3}) **US-STEL** 5 ppm (9.4 mg m^{-3})

UN No. 1067 (liquefied) **HAZCHEM Code** 2PE (liquefied) **Conveyance classification** toxic gas, fire intensifying hazard, corrosive (liquefied)
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 – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S26, S28, S36/37/39, S45)

Mammalian & avian toxicity

Acute data

LC_{50} (10 min) inhalation mouse 1000 ppm (1).
LC_{50} (1 hr) inhalation guinea pig 30 ppm (2).

Sub-acute and sub-chronic data

Inhalation (2 wk) rabbit, continuous exposure to 0.15-1.0 ppm suppressed incorporation of carbon dioxide into serine (3).
Inhalation mouse (1 hr) 9.5-19 mg m^{-3} caused a decrease in the erythrocyte and haemoglobin content of the blood, with increased levels of methaemoglobin and bilirubin (4).
Inhalation rabbit (22 wk) 7 mg m^{-3} for 2 hr day^{-1} for 15 wk resulted in a reduction in body weight and a decreased erythrocyte count accompanied by a reduced haemoglobin content and increased leucocyte count. Histological examination showed thickening of the alveolar septa with an accumulation of neutral mucopolysaccharides. The bronchial cells showed cellular infiltration and localised development of granulation tissue with an accumulation of acidic and neutral mucopolysaccharides and collagen formation (5).
Inhalation rat (4 hr) 9, 20 or 60 mg m^{-3}. The high-dose exposure caused disorientation, reduced breathing rate by ~30% and a three-fold increase in the quantity of detached cells in lung rinses. The 20 mg m^{-3} exposure caused a two-fold increase in the quantity of detached cells in lung rinses (6).
Inhalation (7 days) rats exposed to 10 ppm showed an influx of macropahges into the airways. Increased total inflammation of respiratory bronchioles and alveoli, but no influx of inflammatory cells in the main bronchi, was seen. There was a loss of cilia in the epithelium of small airways and ectasia of alveolar capillaries. No alterations were detected to microvascular permeability or modification of bronchial smooth muscle responsiveness (7,8).
Inhalation rat (6 month) 5.7 mg m^{-3} 6 × wk^{-1} caused changes in the conditioned reflex activity (9).

Teratogenicity and reproductive effects

Inhalation mouse 0, 22 or 45 ppm from gestation day 7-18. Exposure did not affect the number of live pups $litter^{-1}$ but it significantly decreased birth weight. Neuromuscular coordination of the pups was affected as demonstrated by the altered righting reflex (10).
Inhalation ♀ rat, 0.13 or 2.4 mg m^{-3} 12 hr day^{-1} for 3 months. The high dose increased the oestrus cycle from 5.3 to 9.1 days (11).

Metabolism and toxicokinetics

As a result of formation of nitrous and nitric acid following absorption, nitrate may accumulate in the blood (4).
Uptake by isolated rat lungs was proportional to atmosphere concentration and temperature, but became saturated with exposures >14 μg nitrogen dioxide min^{-1}. This suggests that uptake, in part, is rate limited by chemical reaction with epithelial surface constituents rather than by direct physical solubility (12).

Irritancy

Inhalation rat (4 hr) threshold for irritation of the upper respiratory tract 20 mg m^{-3} (6).
Inhalation guinea pig, 0.5 ppm 6 days wk^{-1} for 2 wk, sensitisation with albumen was demonstrated after 44 exposures (13).

Genotoxicity

Salmonella typhimurium TA100 (metabolic activation unspecified) positive (14).
Escherichia coli WP2 (metabolic activation unspecified) positive (15).
Escherichia coli K12, SOS-chromotest (metabolic activation unspecified) positive (15).
In vivo rat peripheral blood lymphocytes, sister chromatid exchanges negative (16).
In vivo rat tracheal epithelium, DNA strand break negative (17).

Other effects

Other adverse effects (human)

Inhalation man, 4, 7 or 10 mg m^{-3} for 20 min. All doses caused an inflammatory cell response in bronchoalveolar lavage fluid. An increase in the number of lymphocytes in the fluid was observed for the two high doses. A dose-dependent increase in the number of mast cells was also observed (18).

Atmospheric nitrogen dioxide induced lipid oxidation and oxidative damage of human erythrocyte membrane *in vitro* (19).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (20).

Other comments

Reaction product with oxygen in combustion processes. Released into the atmosphere from industrial processes, including the manufacture of nitric acid and fertilisers (21).
Physical properties, occurrence, mammalian toxicity and environmental impact of nitrogen oxides reviewed (22).
Flux of nitrogen oxides between the soil and atmosphere, and soil microbial action reviewed (23).
Relationship between nitrogen dioxide exposure and potentiation of asthma and cancer reviewed (24,25).
Environmental health criteria reviewed (26).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (27).
Exists as a mixture of nitrogen dioxide and dinitrogen tetroxide (31% NO_2 at 40°C; 88% NO_2 at 100°C; 100% NO_2 at 140°C).

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N121 nitrogen trifluoride

NF_3

F_3N **Mol. Wt.** 71.00 **CAS Registry No.** 7783-54-2

Synonyms nitrogen fluoride

EINECS No. 232-007-1 **RTECS No.** DX 1925000

Uses Etchant. Fluorination agent. Laser gas.

Physical properties

M. Pt. –208.5°C **B. Pt.** –129°C **Specific gravity** 1.885 at –129°C with respect to water at 4°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
FR-VME 10 ppm (30 mg m^{-3})
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 10 ppm (30 mg m^{-3}) **UK-STEL** 15 ppm (44 mg m^{-3})
US-TWA 10 ppm (29 mg m^{-3})

UN No. 2451 **Conveyance classification** toxic gas, fire intensifying hazard

Environmental fate

Abiotic removal

Removed from waste gases by adsorption and/or catalysis by titanium oxide (1).

Mammalian & avian toxicity

Acute data

LC_{50} (1 hr) inhalation rat, dog, monkey 6700-9600 ppm (2,3).
LC_{50} (4 hr) inhalation mouse 2000 ppm (4).

Sub-acute and sub-chronic data

Inhalation rat, 100 ppm 7 hr day^{-1} for 18 wk caused mild pathological changes in the liver and kidneys. There was no significant effect on the spleen or in haematology. There was no evidence of fluorosis in the teeth or bones (5).

Other effects

Other adverse effects (human)

Prolonged exposure may cause mottled teeth and skeletal changes, which are characteristic of fluoride toxicity (6).

Any other adverse effects

Intraperitoneal rat, single dose of 8-15 mg kg^{-1} of the gas caused the animals to become cyanotic and develop enlarged spleens, possibly as a secondary response to methaemoglobinaemia (5).
Dogs surviving acute exposure to 9600 ppm for 60 min exhibited Heinz body anaemia (7).

Legislation

Included in Schedule 6 (Release into Air: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (9).

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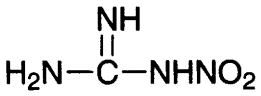
N122 nitroguanidine



$CH_4N_4O_2$ **Mol. Wt.** 104.07 **CAS Registry No.** 556-88-7

Synonyms α-nitroguanidine; 1-nitroguanidine; picrite (the explosive)

EINECS No. 209-143-5 **RTECS No.** MF 4600000

Uses Manufacture of explosives and propellants. Organic synthesis.

Physical properties

M. Pt. 239°C (decomp.) **Partition coefficient** log P_{ow} 0.148 (1)

Solubility Water: 4.4 g l^{-1} at 25°C. Organic solvents: diethyl ether, ethanol, methanol

Occupational exposure

UN No. 1336 **Conveyance classification** flammable solid

Environmental fate

Degradation studies

Catabolised by *Anabaena flos-aquae* and *Selenastrum capricornutum* (1).

Abiotic removal

Photolysis $t_{1/2}$ 0.6 days in summer and 2.3 days in winter at 40° North (1).

Effectively removed from waste water by adsorption onto activated carbon. Cation exchange beds removed the guanidinium ion (2).

Adsorption and retention

K_{oc} <0.1 indicates that nitroguanidine is readily mobile in soils (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1030-4300 mg kg^{-1} (3,4).

LD_{50} oral rat >5000 mg kg^{-1} (5).

LD_{50} intraperitoneal mouse 48 mg kg^{-1} (6).

Sub-acute and sub-chronic data

Oral rat and mouse 0, 100, 320 or 1000 mg kg^{-1} day^{-1} for 90 days. No toxic effects were observed in mice. In rats food consumption was reduced and water consumption increased. Reduced weight gain was observed in high dose ♀ rats. The increased water consumption suggested that nitroguanidine, which was excreted unchanged in the urine, may act as an osmotic diuretic (7,8).

Teratogenicity and reproductive effects

Gavage rat 0, 100, 320 or 1000 mg kg^{-1} day^{-1} on days 6-15 of gestation. The high dose caused some maternal deaths and maternal weight loss. Foetuses in this group were smaller than controls, with retarded ossification. No developmental toxicity was observed. In rabbits administered the same dosages on days 6-18 of gestation, the high dose had similar effects. An increased incidence of resorption was also observed in all treated rabbits (9,10).

Metabolism and toxicokinetics

Following oral administration to rats nitroguanidine was excreted unchanged in the urine (8).

Irritancy

Non-irritating to rabbit skin in modified Draize method (11).

Reported to be irritating to the skin, eyes, mucous membranes and upper respiratory tract (species unspecified) (12).

Sensitisation

Skin sensitisation in ♂ guinea pigs using the Buehler Dermal sensitisation method negative (13).

Genotoxicity

Drosophila melanogaster sex-linked recessive lethal assay negative (14).

In vitro mouse lymphoma cells, tk^+/tk^- with and without metabolic activation negative (15).

In vitro Chinese hamster ovary cells, sister chromatid exchanges with and without metabolic activation negative (16).

Legislation

Included in the UK List of Classified and Authorised Explosives 1994. UK Class and Division 3.2. Competent Authority Reference GB 32087 (17).

Other comments

Health advisories for nitroguanidine in drinking water discussed (18).

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N123 3-nitro-3-hexene

$$CH_3CH_2C(NO_2)=CHCH_2CH_3$$

$C_6H_{11}NO_2$ **Mol. Wt.** 129.16 **CAS Registry No.** 4812-22-0

RTECS No. MP 7350000

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 420 mg kg^{-1} (1).

LD_{Lo} dermal rabbit 940 mg kg^{-1} (1).

LD_{Lo} intraperitoneal rat 80 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Adenocarcinomas of the lung reported in 4/40 mice exposed to 0.2 ppm 6 hr day^{-1}, 5 days wk^{-1} for 15 months. One adenocarcinoma occurred in controls. Rates of bacterial infection were high and cannot be ruled out as a contributory factor (3).

Irritancy

Severe eye and skin irritant in rabbits (dose and duration unspecified) (4).

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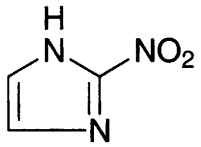
N124 2-nitroimidazole



$C_3H_3N_3O_2$ **Mol. Wt.** 113.08 **CAS Registry No.** 527-73-1

Synonyms azomycin; 2-nitro-1*H*-imidazole

EINECS No. 208-425-5 **RTECS No.** NI 7875000

Uses Organic synthesis. Antibiotic.

Occurrence Isolated from *Streptomyces* species.

Physical properties

M. Pt. 287°C (decomp.) **Partition coefficient** log P_{ow} 1.4 (1)

Solubility Organic solvents: acetone, butyl acetate, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 320 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 320 mg kg^{-1} (2).

LD_{50} intravenous mouse 80 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 80 mg kg^{-1} (4).

Irritancy

Irritating to skin, eyes, mucous membrane and upper respiratory tract (species, dose and duration unspecified) (5).

Genotoxicity

Salmonella typhimurium TA98, TA100 without metabolic activation positive (1).

Escherichia coli and phage ϕX174 electrolytically and radiolytically reduced 2-nitroimidazole induced DNA damage (6).

Other comments

2-Nitroimidazole did not inhibit liver glutathione peroxidase, or glutathione reductase in yeasts (7).

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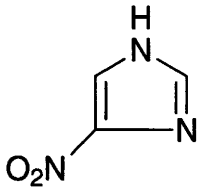
N125 4-nitroimidazole



$C_3H_3N_3O_2$ **Mol. Wt.** 113.08 **CAS Registry No.** 3034-38-6

Synonyms 4-nitro-1*H*-imidazole

EINECS No. 221-224-7 **RTECS No.** NI 7892000

Uses Organic synthesis. Component of photographic developer and emulsions.

Physical properties

M. Pt. 303°C (decomp.)

Solubility Organic solvents: dimethylformamide, ethanol

Genotoxicity

CASE structure-activity methodology predicted it to be positive for mutagenicity to *Salmonella typhimurium* (1).

In vitro Chinese hamster ovary cells, chromosomal aberrations (metabolic activation unspecified) positive (2).

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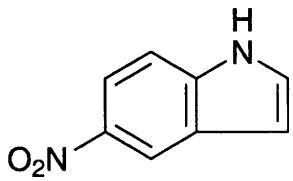
N126 5-nitroindole



$C_8H_6N_2O_2$ **Mol. Wt.** 162.15 **CAS Registry No.** 6146-52-7

Synonyms 5-nitro-1*H*-indole

EINECS No. 228-153-0 **RTECS No.** NM 1168200

Physical properties

M. Pt. 140-142°C

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 0.093 ppm, Microtox test (1).

Genotoxicity

CASE structure-activity methodology predicted it to be positive for mutagenicity to *Salmonella typhimurium* (2).

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N127 nitromethane

CH_3NO_2

CH_3NO_2 **Mol. Wt.** 61.04 **CAS Registry No.** 75-52-5

Synonyms nitrocarbol

EINECS No. 200-876-6 **RTECS No.** PA 9800000

Uses Rocket fuel. Organic synthesis. Solvent. Corrosion inhibitor.

Physical properties

M. Pt. –29°C **B. Pt.** 101°C **Flash point** 35°C (closed cup) **Specific gravity** 1.1322 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} –0.33 **Volatility** v.p. 27.8 mmHg at 20°C ; v.den. 2.11
Solubility Water: 9.5% at 20°C. Organic solvents: acetone, diethyl ether, dimethylformamide, ethanol

Occupational exposure

DE-MAK 100 ppm (250 mg m^{-3})
FR-VME 100 ppm (250 mg m^{-3})
SE-LEVL 20 ppm (50 mg m^{-3}) **SE-STEL** 50 ppm (130 mg m^{-3})
UK-LTEL 100 ppm (254 mg m^{-3}) **UK-STEL** 150 ppm (381 mg m^{-3})
US-TWA 20 ppm (50 mg m^{-3})

UN No. 1261 **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Heating may cause an explosion – Flammable – Harmful if swallowed (R5, R10, R22)
Safety phrases Keep out of reach of children (if sold to general public) – In case of fire and/or explosion do not breathe fumes (S2, S41)

Ecotoxicity

Fish toxicity
Not toxic to brown trout, bluegill sunfish, yellow perch and goldfish at 5 mg l^{-1} for 24 hr (1).

Bioaccumulation
Bioconcentration factor in three-day experiment in fish 1.4 (species not specified) (2).
Bioconcentration factor for *Chlorella fusca* 960 in a 24 hr study (2).

Environmental fate

Degradation studies
36% mineralisation occurred after a five-day incubation with activated sludge (2).

Abiotic removal

Photolytic $t_{1/2}$ 4-9 hr at >290 nm (3).

Reaction with photochemically produced hydroxyl radicals in the atmosphere $t_{1/2}$ 100 days (4,5).

Estimated volatilisation $t_{1/2}$ 29 hr in model river water and 13 days in model pond water (6-9).

Adsorption and retention

Estimated k_{oc} 0.28-15 indicates that adsorption to soil and sediments would not be significant (9).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 940-950 mg kg^{-1} (10).

LC_{50} (6 hr) inhalation rabbit 5000 ppm (11).

LD_{50} intraperitoneal mouse 110 mg kg^{-1} (12).

LD_{Lo} intravenous dog, rabbit 750-800 mg kg^{-1} (13).

Sub-acute and sub-chronic data

Oral rat, 0.10 or 0.25% in drinking water for 15 wk caused some fatalities, a decrease in body weight gain and liver abnormalities (11).

Inhalation ♂ rat and rabbit (6 month) 98 or 750 ppm 5 days wk^{-1} for 24 wk. The high dose caused a decrease in body weight gain, an increase in thyroid weight and a decrease in serum thyroxin levels (14).

Metabolism and toxicokinetics

Absorbed through human skin (15).

Metabolised *in vitro* to acetone and nitrate by rat liver microsomes in the presence of NADPH and oxygen (16).

Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (15).

Sensitisation

Reported to induce dermatitis in humans (17).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (18,19).

Drosophila melanogaster sex-linked recessive lethal assay negative (19).

In vivo rat and mouse bone marrow, induction of micronuclei negative (19).

Other effects

Other adverse effects (human)

Leads to the formation of methaemoglobin, which in sufficient concentrations causes cyanosis (15).

Any other adverse effects

Intraperitoneal rat single dose of 200 mg kg^{-1} induced an increase in acid proteinase activity in the brain 4 hr after administration. This was accompanied by a marginal increase in cerebral glutathione concentration. Hepatic effects were restricted to a decrease in cytochrome c reductase activity with proliferation of smooth endoplasmic reticulum (20).

Legislation

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

Other comments

Occurs in car exhaust condensate and cigarette smoke. Has been identified as a contaminant in human milk samples (22,23).

Physical properties, use, toxicity, mutagenicity and safety precautions reviewed (24-26).

Autoignition temperature 400°C.

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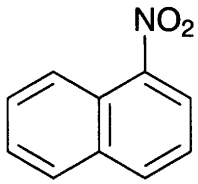
N128 1-nitronaphthalene



$C_{10}H_7NO_2$ **Mol. Wt.** 173.17 **CAS Registry No.** 86-57-7

Synonyms α-nitronaphthalene; nitrol (pesticide)

EINECS No. 201-684-5 **RTECS No.** QJ 9720000

Uses Organic synthesis. Fluorescence quencher for mineral oils. Vapour phase corrosion inhibitor. Fungicide. Wood preservative. Manufacture of explosives and dyestuffs. Corrosion inhibition.

Physical properties

M. Pt. 59-60°C **B. Pt.** 304°C **Flash point** 164°C **Specific gravity** 1.332 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.32 (1) **Volatility** v.p. 4.8×10^{-4} mmHg at 25°C ; v.den. 5.96
Solubility Water: 18 mg l^{-1}. Organic solvents: carbon disulfide, chloroform, diethyl ether, ethanol, pyridine

Occupational exposure

UN No. 2538 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) silver carp 1.6 mg l^{-1} (2).
In vitro cichlid peripheral erythrocytes, induction of micronuclei positive (3).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 0.21-0.27 ppm, Microtox test (4).

Bioaccumulation
The calculated bioconcentration factor is 120-160 (5).

Environmental fate

Carbonaceous inhibition
IC_{50} (5 days) aerobic heterotrophic bacterial culture isolated from activated sludge 380 mg l^{-1} (6).

Anaerobic effects
IC_{50} (50 days) methanogenic bacterial culture 16 mg l^{-1} (6).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 5.5 days (7).
Estimated volatilisation $t_{1/2}$ 15.8 days in model river water and 2.5 yr in model pond water (5,8).

Adsorption and retention
Estimated K_{oc} of 900-1300 indicates that 1-nitronaphthalene will have a low mobility in soils (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 120 mg kg^{-1} (9).
LD_{50} intraperitoneal rat 86 mg kg^{-1} (10).
Intraperitoneal rat, single injection of 87 mg kg^{-1} caused lesions throughout the lung epithelium similar to those caused by toxic gases such as methyl isocyanate (11).
Intraperitoneal ♂ rat, single injection of 25-200 mg kg^{-1} caused respiratory distress within 24 hr, (ED_{50} 60 mg kg^{-1}). At necroscopy at 24 hr, there was diffuse, irregular red mottling in the pleural surface of the lungs and necrosis of non-ciliated bronchiolar epithelial cells. Hepatotoxicity was also observed after administration of 100 mg kg^{-1}, increasing in severity over 74 hr after injection (10).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (12).
Oral rat and mouse (2 yr) 0.05-0.18% diet for 78 wk. >80% treated animals survived to 80 wk. Tumours were observed in the respiratory, digestive and endocrine systems in both treated and control animals. The incidences did not differ significantly between the groups of treated animals and controls. No toxic effects were observed in rat administered up to 0.12% diet and in mice administered up to 0.18% diet (13).

Metabolism and toxicokinetics
Metabolised in mouse lung tissues *in vitro* by cytochrome P_{450} enzymes via an oxidative pathway leading to binding to tissue macromolecules (14).

Following intraperitoneal administration to ♂ rats, 1-naphthylamine was detected in the urine (15).
Under aerobic conditions, metabolised to dihydrodiol and phenol metabolites in rat liver *in vitro*. Under anaerobic conditions 1-naphthylamine was formed (16,17).

Irritancy
Irritating to the skin, eyes, mucous membranes and upper respiratory tract (species, dose, duration unspecified) (18).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive; TA98, TA1537 with and without metabolic activation negative; TA1535 without metabolic activation negative, with metabolic activation weakly positive (19).
Escherichia coli PQ37, SOS-chromotest negative (20).
Drosophila melanogaster sex-linked recessive lethal assay negative (21).
In vitro Chinese hamster ovary cells chromosomal aberrations positive, sister chromatid exchanges negative (metabolic activation unspecified) (22).
In vitro Chinese hamster V79 lung cells without metabolic activation, sister chromatid exchanges positive (23).

Other effects

Other adverse effects (human)
Has been reported to cause cyanosis (18).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (24).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (25).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (26).

Other comments

Occurs in vehicle exhausts and in some batches of carbon black (12).
Physical properties, occurrence, analysis, carcinogenicity, metabolism and mutagenicity reviewed (12,27).

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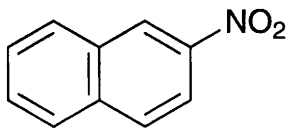
N129 2-nitronaphthalene



$C_{10}H_7NO_2$ **Mol. Wt.** 173.17 **CAS Registry No.** 581-89-5

Synonyms β-nitronaphthalene

EINECS No. 209-474-5 **RTECS No.** QJ 9760000

Physical properties

M. Pt. 79°C **B. Pt.** 165°C **Partition coefficient** log P_{ow} 3.24 (1)
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2538 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid
Supply classification toxic
Risk phrases May cause cancer (R45)
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, rabbit 2700, 4400 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal mouse 1300 mg kg^{-1} (3).
Intraperitoneal rat, single injection of 87 mg kg^{-1} caused lesions throughout the lung epithelium similar to those caused by toxic gases such as methyl isocyanate (4).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (5).
Oral ♀ monkey administered 244 mg l^{-1} day^{-1} 6 days wk^{-1} for 54 months. Numerous papillomas were found in the urinary bladder. The neoplasms were composed of papillae of transitional epithelium with metaplastic changes, but without malignancy (6).

Bladder implantation mouse, (490 day) single pellet (dose unspecified). The incidence of carcinomas and benign tumours of the bladder was not significantly different between treated and control animals (7).

Metabolism and toxicokinetics

Following intraperitoneal administration to ♂ rats, 2-naphthylamine was identified in the urine (8).
Following oral administration to rats 2-amino-1-naphthyl sulfate, 2-amino-1-naphthol and *N*-hydroxy-2-naphthylamine, which is tumorigenic, were excreted in the urine over the subsequent 32 hr (9).
Under *in vitro* anaerobic conditions, metabolised to 2-naphthylamine by rat liver postmitochondrial supernatant fraction (10).
In monkeys given oral doses of 2-nitronaphthalene, urinary metabolites included 2-amino-1-naphthyl sulfate.
Following oral administration to rats, 2-nitronaphthalene was found to be covalently bound to haemoglobin (11).

Irritancy

Reported to be irritating to the lungs and skin (12).

Genotoxicity

Salmonella typhimurium TA98 (metabolic activation unspecified) negative (13).
Escherichia coli PQ37, SOS-chromotest negative (13).
Saccharomyces cerevisiae D3 recombination assay positive (14).
In vitro rat and mouse hepatocytes, unscheduled DNA synthesis negative (15).
In vitro Syrian hamster embryo cells, morphological transformation positive (16).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (17).

Other comments

Occurs in vehicle exhausts and in some batches of carbon black (5).
Physical properties, occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (5,12,18).

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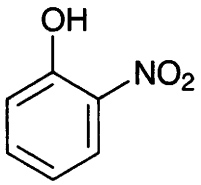
N130 2-nitrophenol



$C_6H_5NO_3$ **Mol. Wt.** 139.11 **CAS Registry No.** 88-75-5

Synonyms 2-hydroxynitrobenzene; *o*-nitrophenol

EINECS No. 201-857-5 **RTECS No.** SM 2100000

Uses Organic synthesis. pH indicator.

Occurrence Photooxidation product of aromatic hydrocarbons including benzene, toluene, phenanthrene and nitrobenzene. Occurs in vehicles exhaust emissions (1).

Physical properties

M. Pt. 45°C **B. Pt.** 214.5°C **Specific gravity** 1.495 at 20°C **Partition coefficient** log P_{ow} 2.24 (2)

Volatility v.p. 1 mmHg at 49.3°C

Solubility Water: 2.1 g l^{-1} at 20°C. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1663 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 100 mg l^{-1} flow-through bioassay (3).

LC_{50} (48 hr) bluegill sunfish 46 mg l^{-1} (4).

LC_{50} (6 hr) *Vairon* 14-130 mg l^{-1} (5).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 35 ppm, Microtox test (6).

IC_{50} (24 hr) *Daphnia magna* 42 mg l^{-1} (7).

LC_{50} (24 hr) *Daphnia magna* 210 mg l^{-1} (8).

Bioaccumulation

The calculated bioconcentration factor is 14 (9).

Environmental fate

Nitrification inhibition

IC_{50} (25 days) *Nitrosomonas* 11 mg l^{-1} (3).

Carbonaceous inhibition

IC_{50} (5 days) aerobic heterotrophic bacteria isolated from activated sludge 11 mg l^{-1} (3).

Anaerobic effects

IC_{50} (50 days) methanogenic bacterial culture 12 mg l^{-1} (3).

46% inhibition of anaerobic digestion, bench scale, at 50 mg l^{-1} for 5 hr (10).

Degradation studies

Completely degraded in anaerobic serum bottle assay in 2 months at an initial concentration of 100 mg l^{-1} (11).

Completely degraded by activated sludge process in 13 hr at concentrations of up to 400 mg l^{-1}. Degradation intermediates identified were pyrocatechol, pyroracemic acid and acetaldehyde (12).
Utilised as a sole nitrogen source by *Pseudomonas* sp. N31 isolated from soil (13).

Abiotic removal

11% photodegradation in 3 days at >290 nm when adsorbed onto silica gel (14).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 14 hr (15).
Estimated volatilisation $t_{1/2}$ 296 hr in model river water (16).

Adsorption and retention

Estimated K_{oc} of 65 indicates that adsorption to soil and sediments would not be significant (16).
K_{oc} for Brookston clay loam soil 114 (17).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 330, 1297 mg kg^{-1}, respectively (18,19).
LD_{50} intraperitoneal mouse 380 mg kg^{-1} (20).
LD_{Lo} subcutaneous cat, rabbit 600, 1700 mg kg^{-1}, respectively (21).
LD_{Lo} intramuscular mouse 600 mg kg^{-1} (21).

Carcinogenicity and chronic effects

A CASE study predicted it to be non-carcinogenic (22).

Metabolism and toxicokinetics

Absorbed through human skin (23).

Irritancy

Irritating to the skin: vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species, dose unspecified) (24).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (22,25,26).
Bacillus subtilis H17, M45 *rec* assay negative (26).
Allium cepa induction of nitrosis positive (27).

Other effects

Other adverse effects (human)

Causes central nervous system depression and dyspnoea. Headache, cyanosis and nausea may also occur (24).
Leads to the formation of methaemoglobin, which in sufficient concentration causes cyanosis (23,24).

Other comments

Environmental fate reviewed (1).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (28).

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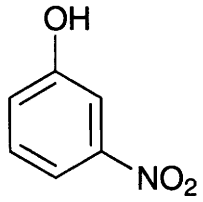
N131 3-nitrophenol



$C_6H_5NO_3$ **Mol. Wt.** 139.11 **CAS Registry No.** 554-84-7

Synonyms 3-hydroxynitrobenzene; *m*-nitrophenol

EINECS No. 209-073-5 **RTECS No.** SM 1925000

Uses Organic synthesis. pH indicator. Fungicide.

Physical properties

M. Pt. 96-98°C **B. Pt.** 194°C at 70 mmHg **Specific gravity** 1.485 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.00 (1) **Volatility** v.p. 0.75 mmHg at 20°C
Solubility Water: 13.5 g l^{-1} at 25°C. Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1663 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (6 hr) *Vairon* 9-22 mg l^{-1} (2).
LC_{50} (8 hr) goldfish 24 mg l^{-1} (3).

Invertebrate toxicity

IC_{50} (24 hr) *Daphnia magna* 22 mg l^{-1} (4).

Bioaccumulation

Calculated bioconcentration factor of 19 indicates that environmental pollution is unlikely (5).

Environmental fate

Anaerobic effects

IC_{50} (50 days) methanogenic bacterial culture 18 mg l^{-1} (6).

Degradation studies

Completely degraded in anaerobic serum bottle assay in 2 months of an initial concentration of 100 mg l^{-1} (7).
Utilised as a sole nitrogen source by *Pseudomonas* species N32 isolated from soil (8).

Abiotic removal

Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 14 hr (9).
Estimated volatilisation $t_{1/2}$ 101 hr in model river water (5).

Adsorption and retention

Estimated K_{oc} of 23 indicates that adsorption to soil and sediments would not be significant (5).
K_{oc} for Brookston clay loam soil 53 (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 330, 1070 mg kg^{-1}, respectively (11,12).
LD_{50} dermal mammal (species not specified) 540 mg kg^{-1} (13).
LD_{50} intraperitoneal mouse 70 mg kg^{-1} (14).

Metabolism and toxicokinetics

May be absorbed through human skin, giving rise to the same symptoms as inhalation exposure (15).

Irritancy

Dermal rabbit, 500 mg caused moderate irritation, 5 mg instilled into rabbit eye for 24 hr caused severe irritation (16).

Sensitisation

Reported to cause dermatitis (17).

Genotoxicity

Salmonella typhimurium TA97, TA100, TA1535 with and without metabolic activation negative; TA98 without metabolic activation weakly positive, with metabolic activation negative (18).
Bacillus subtilis H17, M45 *rec* assay positive (19).
Allium cepa induction of nitrosis positive (11).

Other effects

Other adverse effects (human)

May be absorbed through human skin giving rise to the same symptoms as inhalation exposure (15).
Symptoms include headache, drowsiness, central nervous system depression and methaemoglobin which in sufficient concentration causes cyanosis (17,20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (21).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (22).

Other comments

Environmental fate reviewed (23).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (24).

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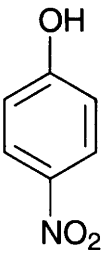
N132 4-nitrophenol



$C_6H_5NO_3$ **Mol. Wt.** 139.11 **CAS Registry No.** 100-02-7

Synonyms 4-hydroxynitrobenzene; *p*-nitrophenol

EINECS No. 202-811-7 **RTECS No.** SM 2275000

Uses Fungicide. Organic synthesis. pH indicator.

Physical properties

M. Pt. 113-115°C **B. Pt.** 279°C (decomp.) **Specific gravity** 1.270 at 120°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.87 (1) **Volatility** v.p. 1×10^{-3} mmHg at 25°C
Solubility Water: 16 g l^{-1} at 25°C. Organic solvents: acetone, chloroform, diethyl ether, ethanol, toluene, pyridine

Occupational exposure

UN No. 1663 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful by inhalation, in contact with skin and if swallowed – Danger of cumulative effects (R20/21/22, R33)
Safety phrases Keep out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water (S2, S28)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 27 mg l^{-1} – flow-through bioassay (2).
LC_{50} (6 hr) *Vairon* 4-33 mg l^{-1} (3).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 13 ppm, Microtox test (4).
IC_{50} (24 hr) *Daphnia magna* 11 mg l^{-1} (5).
LC_{50} (24 hr) *Daphnia magna* 35 mg l^{-1} (6).
Toxic to *Chlorella vulgaris* when applied to soil at 0.5 kg ha^{-1} (7).

Bioaccumulation
Bioconcentration factor 11 in *Chlorella fusca*, 58 in golden orfe and 79 in fathead minnow (8,9).

Environmental fate

Nitrification inhibition
IC_{50} (25 days) *Nitrosomonas* 2.6 mg l^{-1} (2).

Carbonaceous inhibition
IC_{50} (5 days) aerobic heterotrophic bacteria isolated from activated sludge 160 mg l^{-1} (2).

Anaerobic effects
IC_{50} (50 days) methanogenic bacterial culture 4.0 mg l^{-1} (2).
63% inhibition of anaerobic digestion, bench scale, at 50 mg l^{-1} for 5 hr (10).

Degradation studies
Completely degraded in anaerobic serum bottle assay in 2 months at an initial concentration of 100 mg l^{-1} (11).
Following adsorption onto granular activated carbon, significant biodegradation of the sorbed substrate occurred. Investigations were carried out over the concentration range 1-25 μg l^{-1} (12).

Abiotic removal
Photodegradation in sunlight $t_{1/2}$ 5.7, 6.7 and 14 days at pH 5, 7 and 9, respectively (13).

Adsorption and retention
Estimated K_{oc} of 21 indicates that adsorption to soil and sediments would not be significant (14).
K_{oc} for Brookston clay loam soil 55 (15).
4-Nitrophenol is reported to form strong complexes with montmorillonite clays (16).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 250, 300 mg kg^{-1}, respectively (17,18).
LD_{50} dermal mammal 920 mg kg^{-1} (species unspecified) (19).
LD_{50} intraperitoneal mouse 75 mg kg^{-1} (20).
LD_{Lo} intravenous dog 10 mg kg^{-1} (21).

Carcinogenicity and chronic effects
A CASE study predicted it to be non-carcinogenic (22).
National Toxicology Program tested mice via dermal administration. No evidence of carcinogenicity in ♂ and ♀ mice (23).

Metabolism and toxicokinetics
Absorbed through rabbit skin and metabolised to the glucuronide and sulfate conjugates (24).

Irritancy
Irritating to the skin. Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species dose unspecified) (25).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (26-28).
Bacillus subtilis H17, M45 *rec* assay positive (28).
In vitro Chinese hamster ovary cells, HGPRT assay negative (29).
In vitro mouse lymphoma L5178Y tk^+/tk^- assay negative (29).
In vitro primary rat hepatocytes, unscheduled DNA synthesis negative (29).
Allium cepa induction of mitosis and chromosome fragmentation positive (30).

Other effects

Other adverse effects (human)
Symptoms of exposure include headache, drowsiness and nausea. Leads to the formation of methaemoglobin, which in sufficient concentration causes cyanosis (18,31).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (32).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (33).

Other comments

Metabolite of parathion. Photooxidation product of aromatic hydrocarbons including benzene, toluene, phenanthrene and nitrobenzene. Occurs in vehicle exhaust emissions (34).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (35).

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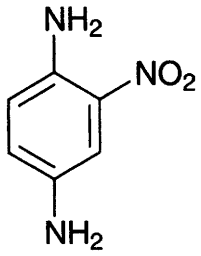
N133 2-nitro-*p*-phenylenediamine



$C_6H_7N_3O_2$ **Mol. Wt.** 153.14 **CAS Registry No.** 5307-14-2

Synonyms C.I. 76070; 4-amino-2-nitroaniline; 1,4-diamino-2-nitrobenzene; 2-nitro-1,4-benzenediamine; 2-nitro-1,4-phenylenediamine; 2-NP; 2-NPPD

EINECS No. 226-164-5 **RTECS No.** ST 3000000

Uses In fur dyes and intermediate in brown hair dyes.

Physical properties

M. Pt. 137-140°C
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3080 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 348 mg kg^{-1} (1).

Sub-acute and sub-chronic data
No histological, blood or urine changes were reported in rats fed 500 mg kg^{-1} diet for 13 wk (2).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (3).
NTP tested rats and mice via feed. Clear evidence of carcinogenicity in mice, causing lung tumours; no evidence of carcinogenicity in rats (4).

Teratogenicity and reproductive effects
A dye formulation including 1.1% 2-nitro-*p*-phenylenediamine, 3% *p*-phenylenediamine and 2% 2,4-diaminoanisole sulfate was neither teratogenic nor embryotoxic in rats when applied dermally at 2 ml kg^{-1} on day 1, 4, 7, 10, 13, 16 and 19 of pregnancy (2).
A significantly increased incidence of malformation occurred in mice subcutaneously injected with 160-256 mg kg^{-1} day^{-1} on days 6-15 of pregnancy, a maternally toxic dose (5).

Irritancy
100 µl of 5 or 2.5% (w/v) solution was not irritating to the eye of guinea pigs in the Draize test (6).

Genotoxicity

Salmonella typhimurium TA1538 with and without metabolic activation positive; metabolic activation reduced mutagenicity (2).
Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation positive (7), TA1537 without metabolic activation weakly positive (8).
Mouse lymphoma cell L51178Y forward mutation assay positive (2).

Induced chromatid breaks and chromosomal aberrations in hamster cells, and chromatid breaks and gaps in human peripheral lymphocytes *in vitro* (2,8).
Did not induce micronuclei in rat bone marrow after oral administration of 2000 mg kg^{-1} (2).
Did not induce dominant lethal effect in rats after intraperitoneal injection of 20 mg kg^{-1} 3 × wk^{-1} for 8 wk (2).
Urine of rats treated intraperitoneally was not mutagenic to *Salmonella typhimurium* TA98 with and without metabolic activation (9).

Other comments

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

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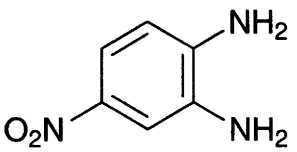
N134 4-nitro-o-phenylenediamine



$C_6H_7N_3O_2$ **Mol. Wt.** 153.14 **CAS Registry No.** 99-56-9

Synonyms 4-nitro-1,2-phenylenediamine; 4-nitro-1,2-diaminobenzene; C.I. 76020; 2-amino-4-nitroaniline; 1,2-diamino-4-nitrobenzene; 4NDB; 4-nitro-1,2-benzenediamine

EINECS No. 202-766-3 **RTECS No.** ST 2975000

Uses Reagent for keto acids; in hair dyes.

Physical properties

M. Pt. 201°C
Solubility Water: sparingly soluble. Organic solvents: acetone

Ecotoxicity

Invertebrate toxicity
EC_{50} (60 hr) *Tetrahymena pyriformis* 46 mg l^{-1} (1).
EC_{50} (5-30 min) *Photobacterium phosphoreum* 21.6 ppm Microtox test (2).

Mammalian & avian toxicity

Acute data

LD_{50} rat, mouse 680 mg kg^{-1} (3).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (4).
NTP tested rats and mice via feed. No evidence of carcinogenicity in rats or mice (5).

Teratogenicity and reproductive effects

No significant changes in foetal soft tissue or skeleton reported in rats after topical administration of 2 ml kg^{-1} of a composite hair dye containing 0.25% 4-nitro-*o*-phenylenediamine and 6% 2,4-diaminotoluene sulfate on days 1, 4, 7, 10, 13, 16 and 19 of pregnancy (6).
Teratogenic effects in mice following subcutaneous injection of ≥256 mg kg^{-1} day^{-1} on days 6-15 of pregnancy (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 with and without metabolic activation positive (8,9).
Aspergillus nidulans forward mutation assay negative (10).
Salmonella typhimurium TA1538 with and without metabolic activation positive; metabolic activation reduced mutagenicity (6).
Salmonella typhimurium TA98, TA100, SOS Chromotest and *umu* test with and without metabolic activation positive (11).
Induced chromosome aberrations in hamster cells but not in human peripheral lymphocytes *in vitro* (6).
Induced sister chromatid exchanges in Chinese hamster cells with and without metabolic activation (9).
Negative results reported for gene mutation and micronucleus induction with and without metabolic activation in the CHO/HGPRT mutation and CHO micronucleus assay (12).
Mouse lymphoma cell L51178Y forward mutation assay with and without metabolic activation positive (13).
Did not induce micronuclei in rat bone marrow after oral administration of 5000 mg kg^{-1} (6).
Induced sex-linked recessives in *Drosophila melanogaster* (6).
Did not induce micronuclei in bone marrow cells of mice after intraperitoneal injection (14).
Did not induce chromosomal aberrations or sister chromatid exchanges in bone marrow cells in B6C3F1 mice after injection; the micronucleus test was negative at two sampling times (48 and 72 hr), but showed a statistically significant response at 24 hr (15).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).
Mutagenicity reviewed (17).

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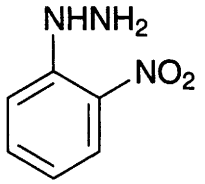
N135 2-nitrophenylhydrazine



$C_6H_7N_3O_2$ **Mol. Wt.** 153.14 **CAS Registry No.** 3034-19-3

Synonyms *o*-nitrophenylhydrazine; *o*-hydrazinonitrobenzene

EINECS No. 221-222-6 **RTECS No.** MV 8210000

Uses Organic synthesis. Analytical reagent.

Physical properties

M. Pt. 90-92°C (decomp.)
Solubility Water: miscible. Organic solvents: benzene

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 180 mg kg^{-1} (1).

Irritancy
Irritating to the skin, eyes, mucous membranes and upper respiratory tract (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (hydrochloride) (3).
Photobacterium leiognathi BE8 (SD-18) bioluminescence mutagenicity assay positive (4).

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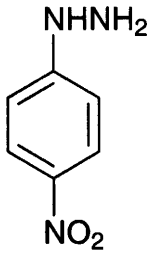
N136 4-nitrophenylhydrazine



$C_6H_7N_3O_2$ **Mol. Wt.** 153.14 **CAS Registry No.** 100-16-3

Synonyms *p*-nitrophenylhydrazine; *p*-hydrazinonitrobenzene

EINECS No. 202-824-8 **RTECS No.** MV 8225000

Uses Organic synthesis. Analytical reagent for ketones and aliphatic aldehydes.

Physical properties

M. Pt. 156°C (decomp.) **Partition coefficient** log P_{ow} -2.35 (1)

Solubility Water: slightly soluble in cold water, soluble in hot water. Organic solvents: benzene, chloroform, diethyl ether, ethanol, ethyl acetate

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 1.22 ppm, Microtox test (2).

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 250 mg kg^{-1} (3).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (species, dose, duration unspecified) (4).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation positive; TA100 with and without metabolic activation equivocal (5).

Photobacterium leiognathi BE8 (SD-18) bioluminescence mutagenicity assay positive (6).

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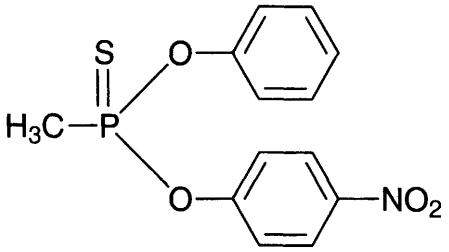
N137 *O*-(4-nitrophenyl) *O*-phenyl methylphosphonothioate



$C_{13}H_{12}NO_4PS$ **Mol. Wt.** 309.28 **CAS Registry No.** 2665-30-7

Synonyms methylphosphonothioic acid, *O*-(*p*-nitrophenyl) *O*-phenyl ester; Colep; CP40294

RTECS No. TB 1680000

Physical properties

M. Pt. 78.5-80°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 8 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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N138 1-nitropropane

$$CH_3CH_2CH_2NO_2$$

$C_3H_7NO_2$ **Mol. Wt.** 89.09 **CAS Registry No.** 108-03-2

Synonyms 1-NP

EINECS No. 203-544-9 **RTECS No.** TZ 5075000

Uses Organic synthesis. Solvent. Fuel additive.

Physical properties

M. Pt. -108°C **B. Pt.** 132°C **Flash point** 33°C **Specific gravity** 0.9934 at 20°C

Partition coefficient log P_{ow} 0.87 **Volatility** v.p. 7.5 mmHg at 20°C ; v.den. 3.06

Solubility Water: 15 g l^{-1}. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 25 ppm (92 mg m^{-3})
FR-VME 25 ppm (90 mg m^{-3})
SE-LEVL 5 ppm (18 mg m^{-3}) **SE-CEIL** 10 ppm (35 mg m^{-3})
UK-LTEL 25 ppm (93 mg m^{-3})
US-TWA 25 ppm (91 mg m^{-3})

UN No. 2608 **HAZCHEM Code** 2[illegible] **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation, in contact with skin and if swallowed (R10, R20/21/22)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place (S2, S9)

Environmental fate

Abiotic removal
Low pressure gas phase photolysis at ~ 282 mm leads to hydroxyl radical formation via a 5-membered ring transition state (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 460, 800 mg kg^{-1}, respectively (2,3).
LC_{50} (8 hr) inhalation rat 3100 ppm (3).
LD_{50} intraperitoneal 250 mg kg^{-1} (4).

Carcinogenicity and chronic effects
Gavage ♂ rat (77 wk) 89 mg kg^{-1} 3 × wk^{-1} for 16 wk, then wkly for 10 wk. No treatment-related tumours occurred (5).
Gavage rat (52 wk) 0, 0.03, 3 or 10 mg $animal^{-1}$ 5 days wk^{-1} for 52 wk. The only outstanding observation compared with controls was the occurrence of a papilloma of the oesophagus in 1 ♂ rat in the 3 mg dose group (6).
Inhalation rat (22 month) 100 ppm 7 hr day^{-1} 5 days wk^{-1} for up to 21.5 months produced no gross or microscopic effects in any tissues or organs (7).

Metabolism and toxicokinetics
Metabolised by the liver microsomal cytochrome P_{450}-dependent mixed-function oxidase system, undergoing oxidative denitrification to yield nitrite (8).

Irritancy
Inhalation human (15 min) 150 ppm was irritating to the eyes (9).
Irritating to the skin, eyes and mucous membranes (species unspecified) (10).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (11).
In vitro human lymphocytes, sister chromatid exchanges with and without metabolic activation negative (11).
In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (12).
In vitro Chinese hamster V79 lung fibroblasts, DNA repair negative (13).
In vitro rat hepatoma cell lines 2s Fou, H4IIEC3/G–, and C2Rev 7, DNA PA repair, induction of micronuclei, 6-thioguanine resistance negative (13).
In vivo rat bone marrow, induction of micronuclei negative (14).
In vivo rat liver, unscheduled DNA synthesis negative (14).

Other effects

Other adverse effects (human)
Symptoms of exposure include headache, dizziness, nausea, vomiting, diarrhoea, restlessness and muscular uncoordination (10).

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). Autoignition temperature 421°C.

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N139 2-nitropropane

$$CH_3CH(NO_2)CH_3$$

$C_3H_7NO_2$ **Mol. Wt.** 89.09 **CAS Registry No.** 79-46-9

Synonyms dimethylnitromethane; isonitropropane; nitroisopropane; β-nitropropane; 2-NP; NiPan S-20 Solvent

EINECS No. 201-209-1 **RTECS No.** TZ 5250000

Uses Organic synthesis. Solvent. Fuel additive.

Physical properties

M. Pt. –93°C **B. Pt.** 120°C **Flash point** 37°C **Specific gravity** 0.9934 at 20°C
Partition coefficient log P_{ow} 0.554 (1) **Volatility** v.p. 13 mmHg at 20°C ; v.den. 3.06
Solubility Water: 170 g l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Occupational exposure

SE-LEVL 2 ppm (7 mg m^{-3}) **SE-CEIL** 6 ppm (20 mg m^{-3})
UK-LTEL MEL 5 ppm (19 mg m^{-3})
US-TWA 10 ppm (36 mg m^{-3})

UN No. 2608 **HAZCHEM Code** 2[illegible] **Conveyance classification** flammable liquid

Supply classification toxic
Risk phrases May cause cancer – Flammable – Harmful by inhalation and if swallowed (R45, R10, R20/22)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 4.7 mg l^{-1} (2).

Bioaccumulation
In a three-day experiment performed with ^{14}C-2-nitropropane, no bioconcentration was observed in fish (3).

Environmental fate

Degradation studies
Aerobic and anaerobic microbial degradation, 3.0% and 1.3% conversion into carbon dioxide, respectively, in 35 days (3).

Abiotic removal
Low-pressure gas-phase photolysis at ~282 nm leads to hydroxyl radical formation via a 5-membered ring transition state (4).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 3.3 hr (5).
Removal from wastewater by pilot steam stripping and batch distribution process (6).
Estimated volatilisation $t_{1/2}$ 9.5 hr in model river water (7).

Adsorption and retention
Estimated K_{oc} of 5.0 indicates that adsorption to soil and sediments would not be significant (7).

Mammalian & avian toxicity

Acute data
LC_{50} oral rabbit, rat 500, 720 mg kg^{-1}, respectively (8,9).
LC_{50} (6 hr) inhalation rat 400 ppm (10).
LD_{50} intraperitoneal mouse 75 mg kg^{-1} (11).

Sub-acute and sub-chronic data
Inhalation cat, rat, rabbit, guinea pig (4.5 hr) maximum tolerated dose 1200-8700 mg m^{-3}. Rats, rabbits and guinea pigs survived 130 × 7 hr exposures of 1200 mg m^{-3}. Liver damage, pulmonary oedema and haemorrhage, selective disintegration of brain neurones and general vascular endothelial damage in all tissues were observed. Cats developed dose-dependent methaemoglobinaemia and Heinz-body formation. These changes were observed to a lesser degree in rabbits, and were not seen in rats or guinea pigs (12).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (13).
Inhalation rat and rabbit (9 month) 100 or 750 mg m^{-3} 7 hr day^{-1} 5 days wk^{-1} for 6 months. All animals survived the period of treatment. No neoplastic lesions or toxic effects were observed in rabbits. In rats, 10/10 animals exposed to the high dose exhibited multiple hepatocellular carcinomas and considerable liver damage. Mild pulmonary oedema and haemorrhagic foci in the lungs were also reported. No significant neoplastic lesion or other toxic effect was observed in the lower dose group (10).
Gavage ♂ rat (77 wk) 89 mg kg^{-1} 3 × wk^{-1} for 16 wk, then weekly for 10 wk induced benign and malignant liver tumours in all treated animals (14).
Inhalation rat 91 mg m^{-3} 7 hr day^{-1} 5 days wk^{-1} for 22 months. No increase in the incidence of malignancies was observed in the livers or other organs in treated animals compared with controls. However, focal areas of hepatocellular nodules were noted in 3/250 controls and in 13/249 treated animals (15).

Teratogenicity and reproductive effects
Intraperitoneal rat, lowest toxic dose 2550 mg kg^{-1} day^{-1} on days 1-15 of gestation (foetal mortality) (16).

Metabolism and toxicokinetics
Metabolised by rat liver microsomes *in vitro* to yield nitrite. This was dependent upon the presence of NADPH. Acetone was also identified as a metabolite (17).
Acetone oxime was identified as an intermediate in the reductive metabolism. Acetone and nitrite are oxidative metabolites which may be responsible for the genotoxicity and carcinogenicity of 2-nitropropane (18).
Metabolised in rats and other mammals *in vivo* to nitrous acid and acetone (19,20).

Irritancy
Irritating to the skin. Vapour or mist irritating to the eyes, mucous membranes and upper respiratory tract (21).

Sensitisation
Reported not to cause allergic sensitisation (22).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (23).
In vitro human lymphocytes, sister chromatid exchanges with metabolic activation positive (23).
In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (24).
In vitro Chinese hamster ovary cells with and without metabolic activation chromosomal aberrations and sister chromatid exchanges negative (25).
In vitro Chinese hamster V79 lung fibroblasts without metabolic activation, DNA repair negative (26).
In vitro rat hepatoma cell lines 2s Fou, H4IIEC3/G-, and C2 Rev 7, DNA repair, induction of micronuclei and 6-thioguanine resistance positive (26).
In vivo rat bone marrow, induction of micronuclei negative (27).
In vivo rat liver, unscheduled DNA synthesis and induction of micronuclei positive (27).
In vivo rat liver DNA and RNA damage positive (28).
In vivo rat bone marrow cells, DNA damage positive (comet assay)(29).

Other effects

Other adverse effects (human)
In man, no symptoms were observed at 10-30 ppm, 4 hr day^{-1} 3 days wk^{-1}, but headache, anorexia, dizziness, nausea, vomiting, diarrhoea and respiratory tract irritation may occur at 30-300 ppm (22).
Four fatal and 1 non-fatal case of acute intoxication were reported in workers exposed after 6-16 hr in confined or inadequately ventilated spaces. Toxic hepatitis and gastro-intestinal bleeding developed, leading to typical hepatorenal syndrome, with severe metabolic acidosis. Death occurred 6-10 days after exposure. Post-mortem findings were ascites and pulmonary oedema, but there was no overt liver enlargement. Histological examination indicated centrilobular necrosis, proliferation of bile ducts and fatty degeneration of parenchymal cells in the liver, and severe degenerative changes in the tubular epithelia of the kidney. In other organs, the typical signs secondary to hepatic and renal insufficiency were seen (30).
An epidemiological study of mortality in 1481 exposed workers in the USA is reported in an abstract. No excess in mortality from all cancers was evident in ♂ workers. Seven deaths from sarcomatous cancer were observed, of which 4 were classified histologically as lymphatic cancer; only 1 case of lymphatic cancer was expected (31).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (32).

Other comments

Physical properties, use, mutagenicity, mammalian toxicity metabolism and mutagenicity reviewed (22,33-36).
Environmental fate reviewed (37).
Autoignition temperature 425°C.

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N140 3-nitropropionic acid

$$NO_2CH_2CH_2CO_2H$$

$C_3H_5NO_4$ **Mol. Wt.** 119.08 **CAS Registry No.** 504-88-1

Synonyms hiptagenic acid; 3-nitropropanoic acid; β-nitropropionic acid

EINECS No. 208-003-0 **RTECS No.** UF 6220000

Occurrence In *Astragalus* spp.

Physical properties

M. Pt. 68-70°C **Partition coefficient** log P_{ow} 0.1229 (1)

Solubility Water: >100 g l^{-1} at 20°C. Organic solvents: acetone, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 2811

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 68 mg kg^{-1} (2).

LD_{50} subcutaneous rat 22 mg kg^{-1} (3).

LD_{50} intraperitoneal rat 67 mg kg^{-1} (4).

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

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via gavage. Negative results were reported for ♀ rats, ♀ mice and ♂ mice. Equivocal results were reported for ♂ rats (6).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (7).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive; TA98 with and without metabolic activation negative (8).

In vitro Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations negative (metabolic activation unspecified) (9).

In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (10).

In vitro mouse lymphoma L5178Y cells (metabolic activation unspecified) tk^+/tk^- positive (11).

In vitro human lymphoblast TK6 cells (metabolic activation unspecified) gene-locus assay positive (11).

Other effects

Any other adverse effects

Oral dog 1.0, 3.1 or 10 mg kg^{-1} produced an anti-hypertensive effect in renal hypertensive animals. This effect was attributed mainly to vasodilatory action, although the presence of bradycardia suggested that a modest cardiac depressor component may be involved (12).

3-Nitropropionic acid irreversibly inhibits the tricarboxylic acid cycle enzyme succinate dehydrogenase, causing severe neurological disease and morphological brain damage when given subcutaneously to rats (13).

Signs of intoxication following oral administration to sheep and cattle were emphysema and difficulty in locomotion. The lungs had varying degrees of alveolar emphysema and there was Wallerian degeneration of the spinal chord (14).

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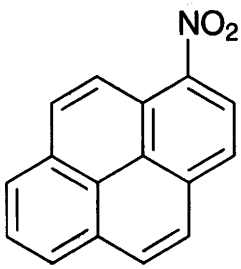
N141 1-nitropyrene



$C_{16}H_9NO_2$ **Mol. Wt.** 247.25 **CAS Registry No.** 5522-43-0

Synonyms 3-nitropyrene

EINECS No. 226-868-2 **RTECS No.** UR 2480000

Uses Photosensitiser.

Physical properties

M. Pt. 153-154°C **Partition coefficient** log P_{ow} 4.69 (1)

Solubility Organic solvents: acetone, benzene, diethyl ether, dimethyl sulfoxide, ethanol

Environmental fate

Degradation studies

Degraded by a Gram-positive rod-shaped bacterium isolated from sediment below an oil field (2).

Abiotic removal

Photodegradation to 2-propanol at ≥310 nm $t_{1/2}$ 1.2 days in dimethyl sulfoxide, 6 days when coated onto silica gel. Degradation was associated with concomitant loss of mutagenicity to *Salmonella typhimurium* TA98 (3,4).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Oral rat, single doses of up to 5000 mg kg^{-1} caused no observable toxicity or histological damage (5).

Carcinogenicity and chronic effects

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

National Toxicology Program classification: reasonably anticipated to be a human carcinogen (7).

Subcutaneous rat (1 yr) 2 mg $animal^{-1}$ 2 × wk^{-1} for 10 wk. The first tumour in treated animals was seen after 162 days. 8/17 animals surviving beyond this time developed tumours, described as 1 extra skeletal osteosarcoma and 7 malignant fibrous histiocytomas at the site of injection. No tumour was observed in controls (8).

Intraperitoneal or subcutaneous ♀ rat (61 wk) 250 mg kg^{-1} wk^{-1} for 4 wk induced mammary gland tumours in 59% of all treated rats compared with 37% in controls. The incidences of adenocarcinomas in the intraperitoneally administered group was 28%, and fibroadenoma in the subcutaneously administered group was 52%, compared with 7 and 27%, respectively, in controls. When 0.5 mg was injected into the mammary glands under each of the 6 left nipples, mammary tumour incidence was 21% compared to similar incidence in controls and ~67% in animals treated with 4-nitropyrene (9).

Intratracheal ♂ hamster (92 wk) 1 or 2 mg $animal^{-1}$ wk^{-1}, with or without concomitant exposure to 0.25 mg benzo[*a*]pyrene. Treatment with 1-nitropyrene alone showed a dose-related decrease in survival and body weight gain and a small but significant increase in the incidence of tumours of the lungs and trachea. Evaluation of the carcinogenic effect revealed that the combined effect, although enhanced, was statistically no greater than could be expected from the addition of individual effects (10).

Oral ♀ rat (78 wk) 2.5 mg kg^{-1} 3 × wk^{-1} for 4 wk. The number of mammary tumours in treated rats (16/35) was not significantly different from controls (12/35) (11).

Intraperitoneal rat (93 wk) 25 mg kg^{-1} wk^{-1} for 5 wk induced mammary adenocarcinomas and fibroadenomas in 17/29 treated rats compared with 11/30 in controls (11).

Gavage ♀ rat (2 yr) 0, 5, 10 or 20 mg kg^{-1} wk^{-1} for 55 wk. The first tumour was observed at 46 wk. Mammary adenocarcinomas were induced in a dose-dependent manner, in 0/28, 2/36 and 14/45, respectively. The incidence of clitoral gland tumours was 1/28, 0/36, 11/39 and 12/45, respectively. The incidence of mononuclear cell leukaemia was 9/28, 23/36, 22/39 and 27/45, respectively (12).

Dermal mouse, study of initiating activity (31 wk) single or double dose of 0-3.0 mg. As a positive control, a group was given a single dose of 0.05 mg benzo[*a*]pyrene. One wk after initiation all mice received dermal applications of 12-*O*-tetradecanoylphorbol-13-acetate 2× wk^{-1} for 30 wk. No significant increase in the number of mice with skin papillomas was observed in the 1-nitropyrene-treated group, while all positive control animals developed skin papillomas (13).

Metabolism and toxicokinetics

Following administration in rats of 5000 mg kg^{-1} by gavage, ~70% was excreted unchanged in the faeces over 4 days, 80% of which was excreted in 24 hr. Free 1-aminopyrene constituted 2% of the administered dose. Sulfate and glucuronide esters of 1-aminopyrene (<1%), but little or no free 1-nitropyrene and 1-aminopyrene were detected in the urine. ~28% of the administered dose was unaccounted for (5).

In rats by 'nose only' inhalation of radiolabelled substance, 75% of the radioactivity was excreted in the urine (14).

Metabolised *in vitro* by an Aroclor-induced rat liver supernatant yielding: 1-nitropyren-3-ol; 1-nitropyren-6-ol; 1-nitropyren-8-ol, *trans*-4,5-dihydro-4,5-dihydroxy-1-nitropyrene, and a small amount of 1-aminopyrene. When incubated under reduced oxygen tension (4% in nitrogen) 1-aminopyrene was the major metabolite (15).

Following oral, intravenous or intraperitoneal administration in rats, >60% of the dose was excreted in the bile over 24 hr, and most of this in the faeces within 96 hr (16,17).

Biliary metabolites have been characterised mainly as glucuronide and glutathione conjugates of oxidised nitropyrene metabolites. Urinary metabolites are excreted in conjugated form, mainly as glucuronides (17,18).

Genotoxicity

Salmonella typhimurium TA98 without metabolic activation positive (19).

Saccharomyces cerevisiae D4 negative (20,21).

In vitro rat and mouse hepatocytes, DNA repair assay positive (22).
In vitro mouse lymphoma L5178Y cells, tk^+/tk^- with metabolic activation, positive (23).
In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges positive (24).
In vitro Chinese hamster ovary cells (metabolic activation unspecified) DNA adduct formation positive (25).
In vitro Syrian hamster embryo cells (metabolic activation unspecified) induction of morphological transformation positive (26).
In vivo rat bone marrow, sister chromatid exchanges positive (27).
In vivo mouse lung, DNA damage positive (28).

Other effects

Any other adverse effects
Oral rat, single doses of up to 5000 mg kg^{-1} caused no observable toxicity or histological damage (5).
Intraperitoneal ♀ rat, 26 mg kg^{-1} induced the formation of an oncofoetal protein (29).
ED_{50} *in vitro* rat tracheal epithelial cells 2.3 mg l^{-1} (decrease in relative colony forming efficiency) (30).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (31).

Other comments

In emissions from stationary combustion sources and in vehicle exhausts. Reported to be one of the most abundant nitroarenes in ambient particulate matter. Occurs in carbon black (6,32).
Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (6,32-34).

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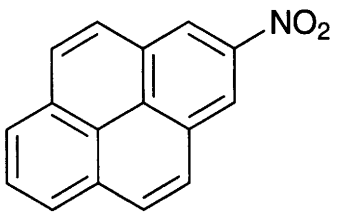
N142 2-nitropyrene



$C_{16}H_9NO_2$ **Mol. Wt.** 247.25 **CAS Registry No.** 789-07-1

Synonyms **RTECS No.** UR 2481000

Occurrence Reported to be one of the most abundant nitroarenes in ambient particulate matter, formed by reaction with nitrogen dioxide in the atmosphere. Occurs in carbon black (1).

Physical properties

M. Pt. 197-199°C **Partition coefficient** log P_{ow} 4.69 (2)

Solubility Organic solvents: benzene, toluene

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

Intraperitoneal ♀ rat (62 wk) 17 mg kg^{-1} 3 × wk^{-1} for 4 wk induced a significant increase in leukaemia compared with controls. When 0.5 mg was injected into the mammary glands under each of the left nipples, mammary tumour incidence was 21% compared with similar incidence in controls and ~67% in animals treated with 4-nitropyrene (3).

Metabolism and toxicokinetics

Metabolised by rat liver supernatant fraction *in vitro* under aerobic conditions to 6-hydroxy-2-nitropyrene and 2-aminopyrene. Under anaerobic conditions only 2-aminopyrene was formed. Two DNA adducts catalysed by xanthine oxidase were characterised as *N*-(deoxyguanosin-8-yl)-2-aminopyrene and *N*-(deoxyadenosin-8-yl)-2-aminopyrene which may be responsible for the mutagenicity of 2-nitropyrene (4).

Genotoxicity

Salmonella typhimurium TA96, TA97, TA100, TA102, TA104, TA1538 without metabolic activation positive (2,5,6).

Legislation

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

Other comments

Physical properties, occurrence, carcinogenicity and mutagenicity reviewed (1,8,9).

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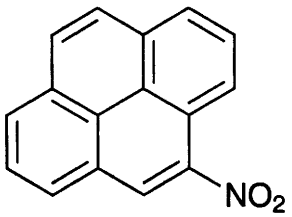
N143 4-nitropyrene



$C_{16}H_9NO_2$ **Mol. Wt.** 247.25 **CAS Registry No.** 57835-92-4

RTECS No. UR 2482000

Physical properties

M. Pt. 190-192°C **Partition coefficient** log P_{ow} 4.69 (1)
Solubility Organic solvents: dimethyl sulfoxide

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

National Toxicology Program classification: reasonably anticipated to be a human carcinogen (3).

Intraperitoneal ♀ rat (61 wk) 17 mg kg^{-1} 3× wk^{-1} for 4 wk induced a significant increase in the incidence of mammary tumours. When 0.5 mg was injected into the mammary glands under each of the left nipples, mammary tumour incidence was 67% compared to ~21% in controls and animals treated with 1- or 2-nitropyrene (4).

Intraperitoneal mouse (1 yr) total dose of 700 μg and/or 140 μg benzo[*a*]pyrene $animal^{-1}$ administered on days 1, 8 and 15 of age. Liver-cell tumours occurred in 24/29 ♂ and 2/29 ♀ mice. Lung tumours occurred in 11/29 ♂ and 9/29 ♀ mice. Benzo[*a*]pyrene alone induced liver-cell tumours in 18/37 ♂ and 0/27 ♀ mice, and lung tumours in

13/37 ♂ and 13/27 ♀ mice. Of vehicle controls 7/73 ♂ and 0/65 ♀ had liver tumours, and 5/73 ♂ and 2/65 ♀ had lung tumours (5).
Subcutaneous ♀ rat (86 wk) 2 mg kg^{-1} $animal^{-1}$ wk^{-1} for 8 wk induced mammary tumours in 20/27 treated rats with an induction period of 263 days, compared with 17/47 controls with an induction period of 502 days. Ten treated rats developed other malignant tumours (fibrous histiocytomas, leukaemias and ear-duct tumours) that were not observed in controls (6).

Metabolism and toxicokinetics
Rat liver microsomes catalysed the conversion of 4-nitropyrene into 4-nitropyrene-9,10-dione, 8-hydroxy-4-nitropyrene, and 4-nitropyrene-1,6-hydroquinone (7).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (1,8).
Bacillus subtilis H17, M45 *rec* assay positive (9).

Other effects

Any other adverse effects
ED_{50} *in vitro* rat tracheal epithelial cells 2.2 mg l^{-1} (decrease in relative colony forming efficiency) (10).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (11).

Other comments

Detected in ambient airborne particulate samples. Occurs in some samples of carbon black (2).
Physical properties, occurrence, carcinogenicity and mutagenicity reviewed (2,12,13).

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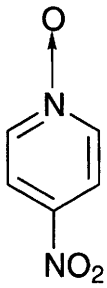
N144 4-nitropyridine 1-oxide



$C_5H_4N_2O_3$ **Mol. Wt.** 140.10 **CAS Registry No.** 1124-33-0

Synonyms 4-nitropyridine *N*-oxide; Amitrol-100

EINECS No. 214-395-4 **RTECS No.** UT 6380000

Uses Catalyst.

Physical properties

M. Pt. 159-162°C

Solubility Organic solvents: polypropylene glycol

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 0.93 ppm, Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat, chicken, dog 8, 23, 34 mg kg^{-1}, respectively (2).

LD_{50} dermal rabbit 360 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Subcutaneous mouse (450 days) 1.5 mg $animal^{-1}$ wk^{-1} for 16 wk induced sarcomas at the site of injection in 3/10 mice. No sarcomas were observed in controls (3).

Irritancy

Irritating to the skin, eyes, mucous membranes and upper respiratory tract (species unspecified) (4).

Genotoxicity

Salmonella typhimurium TA98, TA100 without metabolic activation postive (3).

In vitro mouse fibroblasts, L.P3 DNA damage postive (5).

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N145 *N*-nitrosobis(2,2,2-trifluoroethyl)amine

$$(CF_3CH_2)_2NNO$$

$C_4H_4F_6N_2O$ **Mol. Wt.** 210.08 **CAS Registry No.** 625-89-8

Synonyms 2,2,2-trifluoro-*N*-nitroso-*N*-(2,2,2-trifluoroethyl)ethanamine; hexafluorodiethylnitrosamine; 6-F-DEW

RTECS No. IA 3522000

Physical properties

B. Pt. 114-115°C

Mammalian & avian toxicity

Acute data

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

Genotoxicity

In vitro primary rat, hamster and pig cells, DNA damage negative (2).

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N146 *N*-nitrosodibutylamine

$$CH_3(CH_2)_3N(NO)(CH_2)_3CH_3$$

$C_8H_{18}N_2O$ **Mol. Wt.** 158.24 **CAS Registry No.** 924-16-3

Synonyms DBNA; *N*-butyl-*N*-nitroso-1-butanamine; dibutylnitrosamine; NDBA

EINECS No. 213-101-1 **RTECS No.** EJ 4025000

Physical properties

B. Pt. 235°C **Specific gravity** 0.9009 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.920 (1) **Volatility** v.p. 3×10^{-2} mmHg at 20°C

Solubility Water: 0.12%. Organic solvents: acetic acid, vegetable oils

Ecotoxicity

Bioaccumulation

Calculated bioconcentration factor of 17 indicates that environmental accumulation is unlikely (2).

Environmental fate

Abiotic removal

90% photodegradation at a concentration of 0.65 mg l^{-1} in lake water after 8 hr exposure to sunlight (3).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 2.8 days (4).

Adsorption and retention

Estimated K_{oc} of 263 indicates that nitrosodibutylamine will not adsorb significantly to soil and sediments (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, hamster 1200, 2200 mg kg^{-1}, respectively (5,6).
LD_{50} subcutaneous rat, hamster 1200, 2500 mg kg^{-1}, respectively (5-7).
LD_{50} intraperitoneal hamster 1200 mg kg^{-1} (6).

Sub-acute and sub-chronic data

Subcutaneous ♂ mice (40 wk) 9 mg $animal^{-1}$ every 2 wk. Haematuria was observed after 28 wk (8).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (9)
Intraperitoneal hamster, single dose of 200, 400 or 800 mg kg^{-1} produced tumours of the respiratory tract in 4/10, 6/10 and 7/10 animals, respectively. The first tumour appeared after wk-17 (6).
Oral mouse continuous administration of 8 or 30 mg kg^{-1} day^{-1} in drinking water led to the development of squamous cell carcinomas and papillomas of the oesophagus of almost all treated animals, together with some tumours of the tongue and soft palate. With the lower dose, carcinomas of the forestomach also occurred in 5/89 mice. 44/90 mice given the high dose and 19/89 given the lower dose developed papillomas and multifocal squamous cell carcinomas of the urinary bladder. ♂ mice were more susceptible to bladder carcinogenesis than ♀ mice (10).
Gavage Syrian and Chinese hamsters, 300 mg kg^{-1} wk^{-1} for life. In Syrian hamsters the incidence of papillomas and carcinomas of the trachea was 41/100 and of the lungs 14/100. In Chinese hamsters 39/66 developed papillomas and 21/66 carcinomas of the forestomach. Both groups developed a low incidence of papillomas and carcinomas of the bladder (11-14%) (11).
Subcutaneous mouse, 5 mg $animal^{-1}$ every 2 wk for 26 wk induced bladder carcinomas in 12/44, lung carcinomas in 19/44, lung adenomas in 21/44 and mammary carcinomas in 19/44 treated animals. Mammary carcinomas were also observed in 13/40 controls (12).
Intravenous mouse, 0.6 μg $animal^{-1}$ 2 × wk^{-1} for 25-30 wk resulted in acute leukaemia of the reticulum-cell type in 13/39 ♂ and 17/37 ♀ mice within 218 days. No leukaemia occurred in 51 controls (13).
Prenatal hamster, 30 mg kg^{-1} administered subcutaneously 1-8 × on days 8-15 of gestation. Postnatal mortality was 212/357 and 202/282 for the multiple-and single-dose groups, respectively. Single-dose administration induced no respiratory tract neoplasms in the parental generation, but 7% incidence in the F_1 generation. Multiple administrations led to 22% incidence of respiratory tract tumours in the parental generation and 6% in the F_1 generation (14).
Oral rat (1 yr) 0.06, 0.125 or 0.25% in drinking water for 2 wk induced preneoplastic lesions in the liver, oesophagus, forestomach and urinary bladder. Carcinomas were found only in the liver (15).

Teratogenicity and reproductive effects

Intraperitoneal rat, single dose of 1000 mg kg^{-1}, or single oral dose of 1200 mg kg^{-1} (maximum tolerated doses) caused an increase in foetal mortality, with peaks of susceptibility on days 3 and 9, and of high susceptibility on days 10 and 12 of gestation (16).

Metabolism and toxicokinetics

In rats, mice, hamsters, guinea pigs and dogs the major urinary metabolites were: *N*-nitroso-*N*-(*n*-butyl)-*N*-(4-hydroxybutyl) amine and *N*-nitroso-*N*-(*n*-butyl)-*N*-(3-carboxypropyl) amine. Other metabolites included: *N*-nitroso-*N*-(*n*-butyl)-*N*-(2-hydroxy-3- carboxypropyl)amine *N*-nitroso-*N*-(*n*-butyl)-*N*-(carboxymethyl) amine,

N-nitroso-*N*-(*n*-butyl)-*N*-(2-hydroxypropyl) amine, *N*-nitroso-*N*-(*n*-butyl)-*N*-(2-oxopropyl) amine, *N*-nitroso-*N*-(*n*-butyl)-*N*-(3-hydroxypropyl) amine, *N*-nitroso-*N*-(*n*-butyl)-*N*-(3-isopropyl) amine, *N*-nitroso-*N*-(*n*-butyl)-*N*-(2-carboxyethyl) amine, and the glucuronamides of the hydroxy compounds (17-20).
Undergoes oxidation to form *n*-butyraldehyde and small amounts of acetaldehyde in rat liver microsomal fractions *in vitro* (21).
Urinary metabolites identified in the rat included: *N*-acetyl-*S*-butyl-L-cysteine, *N*-acetyl-*O*-(3-oxobutyl)-L-cysteine and *N*-acetyl-*S*-(3-hydroxybutyl)-L-cysteine and their methyl esters (22).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 positive response in one of these strains (metabolic activation unspecified) (23).
Drosophila melanogaster wing spot assay positive (24).
In vitro primary rat and human hepatocytes, DNA damage negative (25).
In vivo rat liver DNA damage positive (26).
In vivo mouse 500 mg kg^{-1} (route unspecified) induced a 50% reduction of thymidine incorporation into DNA of mouse testes (27).

Other effects

Any other adverse effects
ED_{50} (7 days) *in vivo* suppression of the day 4 IgM antibody response in mice 250 mg kg^{-1} (28).

Other comments

Residues have been isolated from nitrite treated cooked meats, dairy products, and in cigarette smoke (29).
Physical properties, use, occurrence, carcinogenicity, mammalian toxicity, metabolism, teratogenicity and mutagenicity reviewed (29,30).
It has been suggested that the induction of bladder tumours may be due to the major urinary metabolite *N*-nitroso-*N*-(*n*-butyl)-*N*-(3-carboxypropyl) amine (19).

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N147 *N*-nitrosodi-*sec*-butylamine

$$CH_3CH_2CH(CH_3)N(NO)CH(CH_3)CH_2CH_3$$

$C_8H_{18}N_2O$ **Mol. Wt.** 158.24 **CAS Registry No.** 5350-17-4

Synonyms *N*-(1-methylpropyl)-*N*-nitroso-2-butanamine; *N*-(1-methylpropyl)-*N*-nitroso-*sec*-butylamine; *N*-nitroso-*N*-(1-methylpropyl)-2-butanamine

RTECS No. HR 8401500

Physical properties

M. Pt. –20°C

Solubility Water: miscible. Organic solvents: diethyl ether

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Oral (130 wk) ♀ rat 110 mg l^{-1} in drinking water for 50 wk (total dose 500 mg $animal^{-1}$) did not induce a statistically significant increase in tumours compared with controls (1).

Genotoxicity

Salmonella typhimurium Ames mutagenicity assay negative (details unspecified) (1).

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N148 *N*-nitrosodiethanolamine

$$HOCH_2CH_2N(NO)CH_2CH_2OH$$

$C_4H_{10}N_2O_3$ **Mol. Wt.** 134.14 **CAS Registry No.** 1116-54-7

Synonyms diethanolnitrosamine; 2,2'-dihydroxy-*N*-nitrosodiethylamine; *N*-nitrosobis(2-hydroxyethyl)amine; 2,2'-(nitrosoimino)bisethanol; nitrosoiminodiethanol; NDELA

EINECS No. 214-237-4 **RTECS No.** KL 9550000

Uses Antioxidant.

Physical properties

B. Pt. 114°C at 1.5 mmHg **Flash point** 11°C **Specific gravity** 1.484 at 20°C **Partition coefficient** log P_{ow} −1.583 (1) **Volatility** v.p. 5×10^{-4} mmHg at 20°C
Solubility Water: 1 g l^{-1}. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

Supply classification toxic
Risk phrases May cause cancer (R45)
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

Degradation studies
Slowly biodegraded in lake water and sewage sludge. 1.0 μg l^{-1} was completely degraded in 9 days in lake water in the summer, however no degradation occurred in 32 days during the winter (2).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals, estimated $t_{1/2}$ 1.4 days (3).

Adsorption and retention
Estimated K_{oc} of 3 indicates that adsorption to soil and sediments is unlikely (4).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat >7500 mg kg^{-1} (5).
LD_{50} subcutaneous hamster 11 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).
Oral rat, 600-1000 mg kg^{-1} day^{-1} in drinking water. All 20 treated animals developed hepatocellular carcinomas in 242-325 days. Renal adenomas also occurred in 4/20 treated rats (5).
Subcutaneous hamster (78 wk) 7×2260 mg kg^{-1} $2 \times wk^{-1}$, or 27×565 mg kg^{-1} over 45 wk. In the first group 28/30 animals were still alive at the appearance of the first tumour at wk-33. Twenty developed tumours, including 10 adenocarcinomas of the nasal cavity, 8 papillary tumours of the trachea and 3 hepatocellular adenomas. In the second group 27/30 animals survived at 33 wk. Nineteen developed tumours including 12 adenocarcinomas of the nasal cavity, 7 papillary tumours of the trachea and 3 fibrosarcomas at the site of injection. Of 27 controls, 3 developed 1 thyroid carcinoma, 1 haemangioendothelioma of the spleen and 2 adenomas of the adrenal gland (8).
Oral mouse (120 wk) total dose of 750 mg $animal^{-1}$ via drinking water for 50 wk induced hepatocellular tumours in 70% treated mice (9).

Metabolism and toxicokinetics
Metabolised in rat, hamster, mice and rabbit *in vivo* and *in vitro* with metabolic activation through the β-oxidation pathway to yield the urinary metabolites *N*-(2-hydroxyethyl)-*N*-(formylmethyl)nitrosamine and *N*-(2-hydroxyethyl)-*N*-(carboxymethyl)nitrosamine (10).
Absorbed through the skin and via the gastro-intestinal tract in mammals (11).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 with and without metabolic activation positive (12).
Drosophila melanogaster DNA-repair host mediated assay positive (13).
In vitro primary rat, hamster and pig hepatocytes, DNA damage positive (14).
In vivo mouse micronucleus assay negative (15).

In vivo mouse bone marrow, chromosomal aberrations negative (15).
In vivo rat liver DNA damage positive (16).

Other comments

Residues have been isolated from cigarette smoke, in cosmetics, in an atrazine formulation emulsified with triethanolamine, and in cutting fluids incorporating nitrite and triethanolamine (8).
Physical properties, occurrence, analysis, carcinogenicity and mammalian toxicity reviewed (8,11,17).

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N149 *N*-nitrosodiethylamine

$$(CH_3CH_2)_2NNO$$

$C_4H_{10}N_2O$ **Mol. Wt.** 102.14 **CAS Registry No.** 55-18-5

Synonyms diethylnitrosamine; *N*-ethyl-*N*-nitrosoethanamine; DEN; DENA; NDEA

EINECS No. 200-226-1 **RTECS No.** IA 3500000

Uses Formerly used as fuel and lubricant additive; antioxidant and stabiliser.

Physical properties

B. Pt. 175-177°C **Specific gravity** 0.9422 at 20°C with respect to water at 4°C
Solubility Water: ~10%. Organic solvents: acetone, benzene, diethyl ether, ethanol, freons

Ecotoxicity

Fish toxicity
Guppy, exposed to 26-100 mg l^{-1} for 4-8 wk, 60/224 fish developed liver tumours, with an average latent period of 18 wk (1).
LC_{50} (56 day) guppy ~100 mg l^{-1} (1).

Oryzias latipes exposed to 10 ppm in ambient water had liver DNA-adduct concentrations at or only slightly higher than background levels. Fish exposed to 100 ppm averaged 34 and 53 pmol O^6-ethylguanine μmol^{-1}, 15 and 41 pmol O^2-ethylthymidine μmol^{-1} thymidine, and 2 and 6 pmol O^4-ethylthymidine μmol^{-1} thymidine at 0 and 24 hr post-exposure, respectively. Ethyl-DNA adducts appear to accumulate in liver tissue in a non-linear fashion after exposure to diethylnitrosamine. The authors propose that DNA repair enzymes such as O^6-alkylguanine DNA alkyltransferase, which are relatively efficient at lower carcinogen levels, are probably saturated at 100 ppm concentration level of diethylnitrosamine (2).

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 141 ppm Microtox test (3).

Environmental fate

Degradation studies

Degradation of *Pseudomonas aeruginosa* culture 18-31% in 24 hr. Degradation by other enteric bacteria 4-6% in 24 hr (4).

Abiotic removal

Degraded by UV irradiation by 1st order kinetics, rate constant of 3.3×10^{-4}. Enthalpy of activation was 191 kJ mol^{-1} and entropy of activation was 340 J mol^{-1}, which is consistent with disruption of the N-N bond (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, rat 250, 280 mg kg^{-1}, respectively (6).

LD_{50} intraperitoneal mouse, rat 132, 216 mg kg^{-1}, respectively (7,8).

LD_{50} intravenous rat 280 mg kg^{-1} (6).

LD_{50} subcutaneous rat, hamster 195, 250 mg kg^{-1}, respectively (9-11).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (12).

Single injection mouse of 1.25, 2.5 or 5.0 mg kg^{-1} induced hepatocellular adenomas composed predominantly of basophilic cells, with excessive amounts of stored fat and glycogen. The authors concluded that progression from adenomas to hepatocellular carcinomas was associated with a change in the activity of several enzymes associated with cell membrane function, glycogen metabolism, the oxidative pentose phosphate pathway and glycolysis (13).

Oral rat (20 wk) 1 mg day^{-1} in drinking water induced liver tumours, including hepatocellular carcinomas, 9 haemangiosarcomas and 1 blastoma in 23/25 rats (14).

Oral rat 0.0114% in diet for 26 wk induced carcinomas of the oesophagus. Animals survived an average of 28 wk (15).

Dermal mouse (10 months) application of 2 drops of 0.2% solution $2 \times wk^{-1}$ induced squamous-cell carcinomas of the nasal cavity in 17/24 animals. No local skin tumours were observed (16).

Intratracheal hamster (6 months) 0.05 ml of 7% solution $1 \times wk^{-1}$ induced tumours of the trachea and bronchi, but no liver tumours (17).

Teratogenicity and reproductive effects

Intraperitoneal rat, single doses of 180 mg kg^{-1} and oral rat single doses of 200 mg kg^{-1} caused no teratogenic effects. Foetal mortality was increased when the substance was administered on day 3, 9, 10, or 12 of gestation (18,19).

Metabolism and toxicokinetics

Undergoes oxidative deethylation at similar rates in human respiratory nasal mucosa and human liver (20).

In goats, 1 hr after oral administration of 30 mg kg^{-1}, 11.4 mg kg^{-1} was detected in the milk and 11.9 mg kg^{-1} in the blood. Only traces were found in the milk and none in the blood after 24 hr (21).

After administration to rats or hamsters, several ethylated derivatives were produced in the liver and kidney

nucleic acids. These included 7-ethylguanine, O^5-ethylguanine and 3-ethyladenine. Oxidative *N*-deethylation accounts for the production of carbon dioxide and alkylating species (22).
N-Nitrosoethyl-*N*-(2-hydroxyethyl)amine and *N*-nitrosoethyl-*N*-(carboxymethyl)amine have been detected in the urine of rats administered diethylnitrosamine (23).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (24).
Drosophila melanogaster sex-linked recessive lethal assay positive (25).
In vitro Chinese hamster V79 ovary cells, division arrest assay and sister chromatid exchanges with metabolic activation positive (26,27).
In vitro human hepatocytes, DNA repair induction positive (28).

Other comments

Present in tobacco smoke condensate. Residues have been found in cheeses, fish and meat products treated with nitrite, and in water (29).
Physical properties, occurrence, carcinogenicity, genotoxicity, mammalian toxicity, teratogenicity and metabolism of diethylnitrosamine reviewed (29,30).

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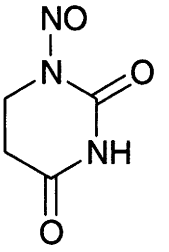
N150 1-nitroso-5,6-dihydrouracil



$C_4H_5N_3O_3$ **Mol. Wt.** 143.10 **CAS Registry No.** 16813-36-8

Synonyms dihydro-1-nitroso-2,4(1*H*,3*H*)-pyrimidinedione; 5,6-dihydro-1-nitrosouracil; NDHU; NO-DHU

RTECS No. MX 9280000

Physical properties

Solubility Water: 11 g l^{-1} at 25°C

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 850 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral rat 90 mg l^{-1} in drinking water for 8 wk following a single intraperitoneal dose of 200 mg kg^{-1} diethylnitrosamine, induced a significant increase in the incidence of hypoplastic liver nodules compared with animals given diethylnitrosamine alone (2).

Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation positive (3).
In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (4).
In vivo rat liver, DNA damage positive (5).

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N151 *N*-nitrosodiisopropanolamine

$$CH_3CH(OH)CH_2N(NO)CH_2CH(OH)CH_3$$

$C_6H_{14}N_2O_3$ **Mol. Wt.** 162.19 **CAS Registry No.** 53609-64-6

Synonyms *N*-nitrosobis(2-hydroxypropyl)amine; 1,1'-nitrosoiminobis(2-propanol); diisopropanolnitrosamine; di(2-hydroxypropyl)nitrosamine; 2,2'-dihydroxydipropylnitrosamine

RTECS No. JL 9650000

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous rat, mouse, guinea pig 4900-5200 mg kg^{-1} (1-3).

Carcinogenicity and chronic effects

Oral rat (94 wk) 1% diet induced tumours of the nasal cavity, lung, oesophagus, liver and urinary bladder. The incidence of nasal cavity and lung tumours was 74 and 58%, respectively (4).

Intraperitoneal rat (30 wk) 0, 2100, 4200, 6300 or 8400 mg kg^{-1} wk^{-1} induced thyroid tumours at incidences of 0, 4, 24, 80 and 76% in ♂ rats, and 0, 0, 4, 20 and 17% in ♀ rats, respectively. No relationship between *N*-nitrosobis-(2-hydroxypropyl)amine dose, tumour incidence and serum thyroid stimulating hormone levels was evident (5).

Subcutaneous hamster, lowest toxic dose, 100 mg kg^{-1} on day-14 of gestation. Placentally induced tumours of the nasal cavity, lungs and liver were seen in the F_1 generation (6).

Genotoxicity

Salmonella typhimurium TA100, TA104, TA1535, TA1975 *Uvr* repair, error-prone repair and critical site for mutation assay positive (metabolic activation unspecified) (7).

In vitro primary rat hepatocytes, DNA repair assay positive (8).

In vitro Chinese hamster V79 lung cells, gene mutation with and without metabolic activation positive (9).

Other comments

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

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N152 *N*-nitrosodiisopropylamine

$$[(CH_3)_2CH]_2NNO$$

$C_6H_{14}N_2O$ **Mol. Wt.** 130.19 **CAS Registry No.** 601-77-4

Synonyms *N*-(1-methylethyl)-*N*-nitroso-2-propanamine; 1,1'-dimethyl-*N*-nitrosodiethylamine

RTECS No. IM 4360000

Physical properties

M. Pt. 48°C **B. Pt.** 194-195°C **Specific gravity** 0.9422 at 20°C with respect to water at 4°C

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

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 850 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral (80 wk) ♂ rat 90 mg l^{-1} or 600 mg l^{-1} in drinking water for up to 50 wk (total dose 450 and 2400 mg $animal^{-1}$, respectively). The first fatalities occurred after 40 wk in both groups. All low-dose animals died within 80 wk and high-dose animals within 60 wk. Tumours of the nasal turbinate were observed in 8/15 of the low-dose and 10/15 of the high-dose group. Hepatocellular carcinomas were also observed in 3/15 of the high-dose group (2).

Genotoxicity

Salmonella typhimurium mutagenicity assay weakly positive (details unspecified) (3).

Escherichia coli WP2S(λ) Microscreen assay positive (3).

Other comments

Detected in nitrite-treated smoked fish (4).

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

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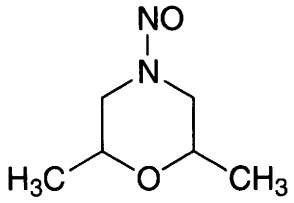
N153 *N*-nitroso-2,6-dimethylmorpholine



$C_6H_{12}N_2O_2$ **Mol. Wt.** 144.17 **CAS Registry No.** 1456-28-6

Synonyms 2,6-dimethyl-4-nitrosomorpholine; 2,6-dimethyl-*N*-nitrosomorpholine; 2,6-dimethylnitrosomorpholine; DMNM; nitroso-2,6-dimethylmorpholine

RTECS No. QE 2150000

Physical properties

B. Pt. 65-68°C at 1 mmHg; 112-114°C at 23 mmHg

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, hamster 280, 370 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous hamster, rat 320, 390 mg kg^{-1}, respectively (3,4).
LD_{50} intraperitoneal rat 290 mg kg^{-1} (5).

Carcinogenicity and chronic effects

Intraperitoneal rat (55 wk) single administration of 38, 75 or 150 mg kg^{-1} induced dose-related incidence of lung tumours compared with none in controls. Thyroid tumours were also induced in treated animals compared with none in controls (5).
Oral hamster (2 yr) 37 or 110 mg kg^{-1} induced tumours of the nasal cavity in 33-77% treated animals. Tumours of the lung, larynx and trachea were also observed . None of these tumours occurred in controls (6).
Subcutaneous ♂ and ♀ hamster (2 yr) 85 mg kg^{-1} induced tumours of the nasal cavity in 80% trreated animals, tumours of the larynx in 13%, tumours of the trachea in 20% and lung tumours in 57%. In controls 13% ♂ hamsters developed tumours of the nasal cavity (6).

Genotoxicity

Salmonella typhimurium positive (strain and metabolic activation unspecified) (7).
In vivo rat and hamster pancreas, DNA damage positive (8).

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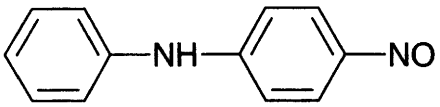
N154 4-nitrosodiphenylamine



$C_{12}H_{10}N_2O$ **Mol. Wt.** 198.22 **CAS Registry No.** 156-10-5

Synonyms *p*-nitrosodiphenylamine; 4-nitroso-*N*-phenylbenzenamine; 4-nitroso-*N*-phenylaniline; *N*-phenyl-*p*-nitrosoaniline; TKB

EINECS No. 205-848-7 **RTECS No.** JK 0175000

Uses Antioxidant in rubbers. Vulcanisation accelerator. Organic synthesis. Manufacture of dyes.

Physical properties

M. Pt. 144°C (decomp.)

Solubility Water: <1 g l^{-1} at 19°C. Organic solvents: benzene, chloroform, diethyl ether, ethanol, petroleum ether

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2100 mg kg^{-1} (1).

LD_{50} intravenous mouse 180 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rat and mouse (4 wk) up to 3.2 and 2.6% diet, respectively. There was a dose-dependent mortality in mice but not in rats. The rats showed dose-dependent depression of mean body weight of up to 53% (3).

Carcinogenicity and chronic effects

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

Oral rat (2 yr) 2500 or 5000 mg kg^{-1} diet for 78 wk. A statistically significant increase in the incidence of hepatocellular carcinomas or neoplastic nodules was observed in ♂ rats only (3).

Oral mouse (92 wk) 5000 mg kg^{-1} diet for 40 wk, then 2500 mg kg^{-1} diet for 17 wk, or 10,000 mg kg^{-1} diet for 40 wk, then after a 7 wk interval 5000 mg kg^{-1} diet for 10 wk. Of the high-dose group 19/50 ♂ mice died before wk-52 due to toxicity. By the end of the study, 85, 88 and 60% of ♂, and 90, 84 and 52% of ♀ were still alive in the control, low-dose and high-dose groups, respectively. A statistically significant increase in the incidence of liver tumours was observed in ♂ mice only (3).

Irritancy

100 mg instilled into rabbit eye for 24 hr caused moderate irritation (1).

Sensitisation

Strongly allergenic in guinea pig skin tests (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6).

In vitro mouse lymphoma L5178Y cells, tk^+/tk^- assay positive (7).

In vivo mouse embryo cells, cell transformation negative (8).

Other effects

Other adverse effects (human)

Exposure has been reported to cause damage to the liver and kidneys (9).

Other comments

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

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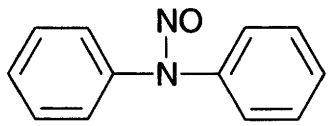
N155 *N*-nitrosodiphenylamine



$C_{12}H_{10}N_2O$ **Mol. Wt.** 198.22 **CAS Registry No.** 86-30-6

Synonyms diphenylnitrosamine; diphenyl-*N*-nitrosamine; *N*,*N*-diphenylnitrosamine; NDPA; *N*-nitroso-*N*-phenylbenzenamine; Curetard; Delac J; Redax; Vulcalent A; Vultrol

EINECS No. 201-663-0 **RTECS No.** JJ 9800000

Uses Organic intermediate. Vulcanisation accelerator.

Occurrence Formed during the ageing of explosives in which diphenylamine is incorporated as a stabiliser for cellulose nitrate (1).

Physical properties

M. Pt. 66.5°C **Specific gravity** 1.23 **Partition coefficient** log P_{ow} 3.1303 (2) **Volatility** v.p. 0.1 mmHg at 25°C

Solubility Water: <1 g l^{-1} at 19°C. Organic solvents: acetone, benzene, diethyl ether, ethanol, ethylene dichloride

Ecotoxicity

Bioaccumulation

Bioconcentration factor for bluegill sunfish 220 (3).

Environmental fate

Degradation studies

Degradation (24 hr) by enteric bacteria isolated from the guinea pig was 66%, and by *Pseudomonas aeruginosa* 85% (4).

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 7 hr (5).

Adsorption and retention
Estimated K_{oc} of 1200 indicates that *N*-nitrosodiphenylamine will adsorb to soil and sediments (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 1650, 3850 mg kg^{-1}, respectively (7-9).
LD_{50} intraperitoneal mouse 1000 mg kg^{-1} (10).

Sub-acute and sub-chronic data
Oral rat, mouse ≤46 g kg^{-1} diet for 7 or 11 wk. ♀ rats did not survive doses >16 g kg^{-1} diet. ♂ rats and mice survived the highest doses tested (10 and 22 g kg^{-1} diet, respectively). Reductions in weight gain ranged from 37% in ♀ rats fed 16 g kg^{-1} diet to 14% in ♀ mice fed 46 g kg^{-1} diet (11).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (12).
Oral mouse (2 yr) ♂ received 10,000 or 20,000 mg kg^{-1} diet for 101 wk, ♀ received 5000 or 10,000 mg kg^{-1} diet for 38 wk, none for 3 wk, then 1000 or 4000 mg kg^{-1} diet for 60 wk. Survival was reduced in the high-dose groups of both sexes. There was no statistically significant increase in tumour incidence compared with controls. Epithelial hyperplasia of urinary bladder mucosa occurred in 2/49 low-dose ♂, 7/46 high-dose ♂, 3/47 low-dose ♀ and 6/38 high-dose ♀ mice. These lesions were not observed in controls (11).
Oral rat 1000 or 4000 mg kg^{-1} diet for 100 wk. No dose-related trend in mortality was observed in ♂ rats. In ♂ rats 70% survival was observed for the high-dose group compared with 90% for controls and 88% for the low-dose group. Significantly increased incidences were observed for the following neoplasms: transitional cell carcinomas of the urinary bladder, among ♂ 0/19 in controls, 0/46 low dose, 16/45 high dose, and among ♀ 0/18 in controls, 0/48 low dose, 40/49 high dose; fibromas of the subcutis and skin among ♂, 1/20 in controls, 1/50 low dose, 10/50 high dose (11).
Dermal mouse (80 wk) 0.1 ml $animal^{-1}$ day^{-1}. Among 14/16 surviving ♂ and 21/24 surviving ♀ mice 3 ♂ mice had lung adenomas. No control data reported (13).
Intraperitoneal rat (2 yr) 25 mg $animal^{-1}$ wk^{-1}. Survival rates were 5/24 treated rats and 10/24 controls. Neoplasms were found in 2 treated rats, 1 hepatoma and 1 pituitary adenoma. One control rat had a hepatoma (14).

Irritancy
500 mg instilled into rabbit eye for 24 hr caused mild irritation (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (15).
Drosophila melanogaster wing spot assay marginally positive (16).
In vitro Chinese hamster ovary cells, chromosomal aberrations marginally positive, sister chromatid exchanges positive (metabolic activation unspecified) (17).
In vitro primary rat hepatocytes, DNA damage equivocal results (18).
In vitro Chinese hamster V79 lung fibroblasts DNA damage with metabolic activation positive. The *N*-hydroxy derivative was identified as the active metabolite (19).
In vivo rat liver DNA damage negative (20).

Legislation

The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (21).

Other comments

Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity and mutagenicity reviewed (1,22-24).

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N156 *N*-nitrosodipropylamine

$$CH_3CH_2CH_2N(NO)CH_2CH_2CH_3$$

$C_6H_{14}N_2O$ **Mol. Wt.** 130.19 **CAS Registry No.** 621-64-7

Synonyms dipropylnitrosamine; DPNA; *N*-nitroso-*N*-propyl-1-propanamine; NDPA

EINECS No. 210-698-0 **RTECS No.** JL 9700000

Physical properties

B. Pt. 77-78°C **Flash point** 98°C **Specific gravity** 0.9160 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.360 (1) **Volatility** v.p. 8.6×10^{-2} mmHg at 20°C
Solubility Water: ~1%. Organic solvents: diethyl ether, ethanol

Occupational exposure

Supply classification toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer – Harmful if swallowed – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R22, R51/53)
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) – Avoid release to the environment. Refer to special instructions/safety data sheet – Restricted to professional users (S53, S45, S61)

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor of 6 indicates that environmental accumulation is not likely (2).

Environmental fate

Degradation studies
Biodegradation using settled domestic wastewater inoculum after 7 days, in original culture and 1st, 2nd and 3rd subcultures was 27, 37, 47 and 50%, respectively, at an initial concentration of 5 mg l^{-1} and 0, 8, 40 and 40%, respectively, at an initial concentration of 10 mg l^{-1} (3).

Abiotic removal
90% photolysis occurred in water in 8 hr. The major products were *n*-propylamine and di-*n*-propylamine (4,5).
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 4.03 days (3).
47% volatilisation from soil in 2 hr following application of 570 μg m^{-2} soil (6).

Adsorption and retention
Estimated K_{oc} of 131 indicates that adsorption to soil and sediment will not be significant (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 480 mg kg^{-1} (7).
LD_{50} subcutaneous rat, hamster, mouse 480, 600, 690 mg kg^{-1}, respectively (8-11).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (12).
Oral rat, 4, 8, 15 or 30 mg kg^{-1} day^{-1} in drinking water induced liver carcinomas in 45/48 treated animals, with mean induction times of 300, 202, 155 or 120 days, respectively. In addition, 8 animals which received doses of 8 or 15 mg kg^{-1} day^{-1} developed papillomas or carcinomas of the oesophagus, and 6 carcinomas of the tongue (7).
Subcutaneous rat 25, 50 or 100 mg kg^{-1} wk^{-1} for life. Tumours of nasal and/or paranasal cavities occurred in 45/58 treated animals (48 tumours, 19 of which were malignant). In addition, 13 liver tumours (mainly liver-cell carcinomas), 11 adenomas or carcinomas of the lung, and 11 squamous-cell papillomas of the oesophagus were observed. Two adenomas and 1 adenocarcinoma of the kidney developed in 3/20 animals treated with 50 mg kg^{-1}. No tumours were reported among controls (8,9).
Intraperitoneal hamster 3.75, 7.5, 15, 30 or 60 mg kg^{-1} wk^{-1} for life. A total of 591 tumours of the nasal and paranasal cavities occurred in 134/185 treated animals, 163/185 developed 1224 tumours of the laryngobronchial tract, and 56/185 developed 112 tumours of the lung. A few tumours also occurred in a variety of other organs. The first neoplasms were seen after 16 wk. Two thyroid adenomas, 1 cortical adenoma of the adrenal gland and 1 papilloma of the vagina were observed among 40 controls (10,13).
Gavage mouse 10 or 30 μg $animal^{-1}$ 2 × wk^{-1} for 50 wk. Both doses induced tumours of the oesophagus, forestomach, lung and lymphomas. Pulmonary adenomas and forestomach papillomas were more frequent in the high-dose group (14).

Metabolism and toxicokinetics

In goats, 1 hr after oral administration of 30 mg kg^{-1}, 4.9 mg kg^{-1} was found in the milk and 1.6 mg kg^{-1} in the blood. Only traces were found in the milk after 24 hr (15).

Following oral administration to rats, *N*-nitroso-3-hydroxy-*N*-propyl-*n*-propylamine; *N*-nitroso-2-(carboxyethyl)-*n*-propylamine and, to a lesser extent, *N*-nitroso-2-hydroxy-*N*-propyl-*n*-propylamine and *N*-nitrosocarboxymethyl-*n*-propylamine, were identified in the urine during 48 hr (16).

Administration of 1-[^{14}C]-labelled substance to rats produced 7-[^{14}C]-*n*-propylguanine together with 7-[^{14}C]methylguanine in the liver RNA. In contrast, administration of 2-[^{14}C]-labelled substance led to the formation of only 7-[^{14}C]-*n*-propylguanine in rat liver RNA (17).

Genotoxicity

Salmonella typhimurium positive (strain and metabolic activation unspecified) (18).

In vitro primary rat and human hepatocytes, DNA damage positive (19).

In vitro Chinese hamster V79 lung fibroblasts, induction of 8-azaguanine resistant mutants, with metabolic activation positive (20).

In vivo rat liver DNA damage positive (11).

Other effects

Any other adverse effects

Reversible competitive inhibition of acetylcholinesterase activity (species unspecified) (21).

ED_{50} (7 days) *in vivo* suppression on day-4 of IgM antibody response in mice 61 mg kg^{-1} (22).

Other comments

Residues have been isolated from cheese and alcoholic beverages, in trade wastes, and as a contaminant in the herbicide trifluralin (23).

Physical properties, occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (23,24,25).

Carcinogenicity of metabolites reviewed (23).

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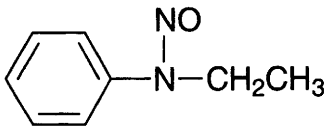
N157 *N*-nitroso-*N*-ethylaniline



$C_8H_{10}N_2O$ **Mol. Wt.** 150.18 **CAS Registry No.** 612-64-6

Synonyms *N*-ethyl-*N*-nitrosobenzenamine; *N*-nitroso-*N*-ethylphenylamine; ethylnitrosoaniline; NEA

RTECS No. BY 0480000

Physical properties

B. Pt. 119-120°C at 15 mmHg **Specific gravity** 1.087 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 180 mg kg^{-1} (1).

Teratogenicity and reproductive effects

Pregnant rats administered 180 mg kg^{-1} intraperitoneally on selected days showed an increase in foetal mortality. The effect was most marked on days 9 and 12-15 with effects including hydrocephaly being produced by treatment on day-9 (2).

Other comments

Occurs as an atmospheric pollutant during manufacture of rubber and metals, and in the leather industry (3). Reviews on human health effects, experimental toxicology, physico-chemical properties listed (4).

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N158 1-nitroso-1-ethylurea

$$H_2NC(O)N(NO)CH_2CH_3$$

$C_3H_7N_3O_2$ **Mol. Wt.** 117.11 **CAS Registry No.** 759-73-9

Synonyms ENU; *N*-nitroso-*N*-ethylurea; 1-ethyl-1-nitrosourea

EINECS No. 212-072-2 **RTECS No.** YT 3150000

Uses Experimental mutagen. Organic synthesis. Ethylating agent.

Physical properties

M. Pt. 103-104°C (decomp.) **Partition coefficient** log P_{ow} 0.23 (1)
Solubility Water: ~1.3%. Organic solvents: acetone, ethanol

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor of 0.88 indicates that environmental accumulation is unlikely (2).

Environmental fate

Abiotic removal
Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 14.7 days (3).
Undergoes hydrolysis to diazoethane in water. $t_{1/2}$ 31 hr at pH 6.0; 1.5 hr at pH 7.0; 0.1 hr at pH 8.0; and 0.05 hr at pH 9.0 (20°C) (4).

Adsorption and retention
Estimated K_{oc} of 9.45 indicates that adsorption to soil and sediments is unlikely (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 300, 960 mg kg^{-1}, respectively (5,6).
LD_{50} subcutaneous rat 240 mg kg^{-1} (5,7).
LD_{50} intravenous rat 240 mg kg^{-1} (5,7).
LD_{50} intraperitoneal mouse 490-640 mg kg^{-1} (6).

Sub-acute and sub-chronic data
Intraperitoneal mouse, 0, 2, 8 or 32 mg kg^{-1} 2 × wk^{-1} for 3 wk. Primary antibody production by splenic lymphocytes from animals challenged with a T-dependent antigen (sheep red blood cells), was stimulated at low doses, but depressed in the highest dose group compared with controls. T-dependent cell response showed no significant change (8).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (9).
Oral rat, single dose of 10, 20, 40 or 80 mg kg^{-1} induced malignant neurogenic tumours in the brain, spinal chord and peripheral nervous system in 75/80 treated animals. Even at the lowest dose 23/26 animals died with neurogenic tumours. At the highest dose, 9/16 rats had nephroblastomas (10).
Oral rat, 60 mg l^{-1} in drinking water 5 day wk^{-1} for 52 wk induced 7 stomach tumours, 9 tumours of the large intestine, 9 adenocarcinomas of the mammary gland (8 in ♀ and 1 in ♂ rats), and 12 myeloytic leukaemias among 39 treated animals (11).
Intraperitoneal mouse, single dose of 10-160 mg kg^{-1} induced liver tumours in 48/119, lung tumours in 74/235, and tumours of the nervous system in 9/119 treated animals (11).

Intraperitoneal mouse single injection of 60 or 120 mg kg^{-1} at 1, 15 or 42 days of age. Most animals had died by wk-90 of age due to the development of benign and malignant tumours at multiple sites. Newborn animals were more susceptible to liver, kidney and ovarian tumours. Young adults were more susceptible to tumours of the lung, Harderian gland, stomach and lymphoreticular system. The sex of the animals influences the development of tumours. Tumours of the liver and Harderian gland were more common in ♂ mice, whereas tumours of the lymphoreticular system were more common in ♀ mice (12).
Intravenous monkey (30 month) 12 mg kg^{-1} every 2 wk for 2 yr induced malignant tumours (mainly of the ovary, uterus, vascular endothelium, bone, bone marrow and skin) in 2/4 ♂ and 5/9 ♀ monkeys 700-900 days after the start of treatment (13).
Intracerebral rat, 1.25-6.25 mg kg^{-1} to 1, 3 and 10 day old animals resulted in 70 neurogenic tumours, 37 of which occurred in the brain, in 85 animals. Malignant neurinomas of the trigeminal nerve appeared only as a result of treatment on day-1 of life (14).
Transplacental mouse, single injection of 56 mg kg^{-1} on day 12, 14, 16 or 18 of gestation. The most common tumours were single or multiple pulmonary adenomas and leukaemias, which appeared in the offspring of dams treated on day 16 and 18, respectively. Hepatomas, Harderian gland adenomas, tumours of the endocrine glands, and neurogenic tumours were also found. Hepatomas occurred preferentially in ♂ mice (15).

Teratogenicity and reproductive effects
Intravenous rat, single dose of 20 mg kg^{-1}. Peaks of embryonic mortality were noted for administration on days 4 (40%) and 9 (25%) of gestation. Teratogenic effects, which included hydrocephaly and exencephaly, were observed in ~60% of the surviving foetuses that had been exposed on days 9 and 10 of gestation (16).
Intraperitoneal rat, single injection (dose unspecified) on day-9, 10 or 12 caused several types of craniofacial malformations. Treatment on day-9 induced significantly more malformations than on days 10 and 12 (17).
Intraperitoneal ♂ A/J mice 5 × 50 mg kg^{-1}. On day 64-82 post-treatment, the males were mated with untreated virgin females of the same strain. On day-18 of gestation, viable foetuses were inspected for external malformation. Cleft palate or cleft lip was the predominant malformation both in controls (8%) and the treated group (15%). Based on these and other data the authors propose that a large fraction of external malformation in foetuses from mutagenised paternal germ cells are a result of increased yields of spontaneously occurring malformations (18).

Metabolism and toxicokinetics
N-Nitroso-*N*-ethylurea is a direct alkylating agent *in vitro* and *in vivo*. 7-Ethylguanine, O^6-ethylguanine, 3-ethyladenine, 7-ethyladenine and ethyl phosphate triesters have been detected in rat tissues (1).
Decomposes *in vivo* to yield cyanate which reacts with proteins. This carbamoylation has been found to be important in *in vitro* toxicity studies (19).

Genotoxicity

CASE structure-activity methodology predicted positive mutagenicity to *Salmonella typhimurium* (20).
Drosophila melanogaster sex-linked recessive lethal assay positive (21).
In vitro Chinese hamster ovary cells without metabolic activation chromosomal aberrations positive (22).
In vitro primary rat and human hepatocytes DNA damage postive (23).
In vivo mouse lung cells without metabolic activation chromosomal aberrations and mutations positive (24).
In vivo mouse erythrocytes micronucleus test positive (7).
In vivo rat liver DNA damage positive (25).
In vivo rat spermatocytes unscheduled DNA synthesis positive (26).
Allium sativum chromosomal aberrations positive (27).

Other effects

Any other adverse effects
The major toxic effects result from severe damage to haematopoietic, lymphoid and other tissues with a rapid rate of cell turnover (28).

Intraperitoneal rat, single dose of 50 mg kg^{-1} on day-14 after birth caused incomplete differentiation and development of the cerebellum. The cell in the exterior granule layer was damaged at an early stage and [^{3}H]thymidine autoradiography indicated inhibition of DNA synthesis in the granule layer (29).

Other comments

Physical properties, use, analysis, carcinogenicity, mammalian toxicity, metabolism, teratogenicity and mutagenicity reviewed (4,30).

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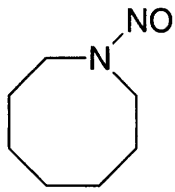
N159 *N*-nitrosoheptamethyleneimine



$C_7H_{14}N_2O$ **Mol. Wt.** 142.20 **CAS Registry No.** 20917-49-1

Synonyms octahydro-1-nitrosoazocine; *N*-nitrosoazacyclooctane; NHMI

RTECS No. CN 4900000

Physical properties

M. Pt. 22°C **B. Pt.** 102-103°C at 4 mmHg

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 283 mg kg^{-1} (1).

LD_{50} subcutaneous hamster 220 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Apparent synergy with chrysotile asbestos in induction of pulmonary tumours in rats has been demonstrated (3).

Genotoxicity

Escherichia coli WU3610 (Tyr^-,Leu^-) negative without metabolic activation, positive with metabolic activation (4).

Salmonella typhimurium TA100, TA1530 without metabolic activation negative, positive with metabolic activation by isolated rabbit lung cells (5).

Unscheduled DNA synthesis *in vitro* rabbit lung cells positive (5).

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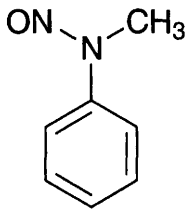
N160 *N*-nitroso-*N*-methylaniline



$C_7H_8N_2O$ **Mol. Wt.** 136.15 **CAS Registry No.** 614-00-6

Synonyms *N*-methyl-*N*-nitrosobenzenamine; *N*-methyl-*N*-nitrosoaniline; methylphenylnitrosamine; *N*-nitrosomethylphenylamine; MNA; nitrosomethylaniline

EINECS No. 210-366-5 **RTECS No.** BY 5775000

Occurrence As a contaminant and atmospheric pollutant in rubber manufacture.

Physical properties

M. Pt. 12-15°C **B. Pt.** 120-121.5°C at 13 mmHg **Specific gravity** 1.1266 at 20°C

Mammalian & avian toxicity

Acute data

LD_{50} oral ♀ and ♂ rat 225 and 336 mg kg^{-1}, respectively (1).

LD_{50} oral ♂ hamster 150 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Rats receiving 2 mg day^{-1} 5 days wk^{-1} for a year via drinking water developed tumours. Rats receiving 7.5 mg day^{-1} 2 days wk^{-1} orally for the same period also developed tumours at many sites including in particular squamous epithelium of the mouth and upper gastro-intestinal tract. Other sites included skin, lung and pituitary gland (1).

Teratogenicity and reproductive effects

Pregnant rats receiving 140 mg kg^{-1} intraperitoneally on selected days showed an increase in foetal mortality. The effect was most marked when the compound was administered on day-9 or days 12-15 (2).

Metabolism and toxicokinetics

The compound can be metabolised by several tissues, but particularly by liver and oesophagus. Products of metabolism include aniline and *N*-methylaniline, but different metabolites may be produced by use of different inducers of metabolism (3,4).

Rats pretreated with phenobarbitone produced phenol as a metabolite with benzenediazonium ion as an intermediate. This ion can react with DNA *in vitro* to form an adduct seen in *in vivo* by treatment of rats with nitrosomethylaniline (4,5).

Genotoxicity

Salmonella typhimurium TA1537 without metabolic activation negative; with activation by phenobarbitone pretreated rat hepatic tissue negative; with activation by pyrazole pretreated rat hepatic tissue positive (4).

In vitro initiator tRNA acceptance assay with metabolic activation, positive (6).

Host-mediated assay using *Drosophila melanogaster*, *Escherichia coli* uvr+/rec+ and uvrB/recA strains positive differential killing effects (7).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (8).

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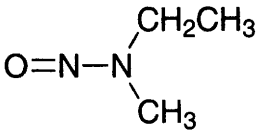
N161 *N*-nitroso-*N*-methylethylamine



$C_3H_8N_2O$ **Mol. Wt.** 88.11 **CAS Registry No.** 10595-95-6

Synonyms *N,N*-methylethylnitrosamine; ethylmethylnitrosamine; methylethylnitrosamine; *N*-methyl-*N*-nitrosoethylamine; NEMA; NMEA

RTECS No. KR 9200000

Physical properties

B. Pt. 156°C **Flash point** 80°C **Specific gravity** 0.96

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 90 mg 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).

Oral rat TD_{Lo} 600 mg kg^{-1}, administered intermittently over 15 weeks. Carcinogenic effects (3).

Oral rat TD 2250 mg kg^{-1}, administered continuously over 30 weeks. Equivalent tumorigenic agent (4).

A strong liver carcinogen in Fischer 344 rats (5).

More effective as a liver carcinogen by gavage than in drinking water and gave rise to tumours of the lung and nasal mucosa by the former route, but not the latter (6).

In rats, induced hemangiosarcomas and hepatocellular carcinomas, together with some oesophageal tumours (4).

Teratogenicity and reproductive effects

Oral rat TD 420 mg kg^{-1}, administered continuously over 71 weeks. Equivocal tumorigenic agent. Reproductive effects (1).

Genotoxicity

Salmonella typhimurium, 500 μg plate^{-1}, microsomal mutagenicity assay positive (7).
Escherichia coli, 100 mg l^{-1}, phase inhibition capacity positive (8).
Liver post-mitochondrial supernatants (S-9 mix) from five species were tested for activating activity with *N*-nitroso-*N*-methylethylamine in the Ames test. Mouse and hamster S-9 mix activated the compound, but human, rat, and pig S-9 mix did not (9).

Other comments

When heated to decomposition it emits toxic fumes of NO_x.

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N162 *N*-nitroso-*N*-methylundecylamine

$$CH_3(CH_2)_{10}N(NO)CH_3$$

$C_{12}H_{26}N_2O$ **Mol. Wt.** 214.35 **CAS Registry No.** 68107-26-6

Synonyms *N*-methyl-*N*-nitroso-1-undecanamine; nitrosomethylundecylamine

RTECS No. YQ 3158000

Genotoxicity

A single oral dose to rats of 0.02 g kg^{-1} resulted in DNA methylation of tissue within 6 hr (1).
In vitro initiator tRNA acceptance assay with metabolic activation positive (2).

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N163 1-nitroso-1-methylurea

$H_2NC(O)N(NO)CH_3$

$C_2H_5N_3O_2$ **Mol. Wt.** 103.08 **CAS Registry No.** 684-93-5

Synonyms *N*-nitroso-*N*-methylurea; 1-methyl-1-nitrosourea; *N*-nitroso-*N*-methylcarbamide; MNU; NMU

EINECS No. 211-678-4 **RTECS No.** YT 7875000

Uses Experimental mutagen. Organic synthesis. Has been studied for use as a cancer therapy agent (1).

Physical properties

M. Pt. 124°C (decomp.) **Partition coefficient** log P_{ow} –0.03 (2)

Solubility Water: ~1.4%. Organic solvents: acetone, benzene, chloroform, ethanol

Ecotoxicity

Bioaccumulation

Calculated bioconcentration factor of 0.56-2.8 indicates that environmental accumulation is unlikely (3).

Environmental fate

Abiotic removal

Hydrolysis $t_{1/2}$ 24 hr at pH 6.0; 1.2 hr at pH 7.0; 0.1 hr at pH 8.0; 0.03 hr at pH 9.0 (20°C) (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 110 mg kg^{-1} (4).

LD_{50} intravenous rat, hamster 50, 110 mg kg^{-1}, respectively (4,5).

LD_{50} subcutaneous hamster 50-110 mg kg^{-1} (6-8).

LD_{50} intraperitoneal rat, mouse 110, 140 mg kg^{-1}, respectively (9,10).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (11).

Oral rat (2 yr) 4 or 8 mg kg^{-1} day^{-1} for life induced squamous cell carcinomas of the forestomach (4).

Gavage guinea pig 10 mg kg^{-1} wk^{-1}, of 34/74 survivors at 27 wk, 10 had adenocarcinomas of the pancreas, 2 adenocarcinomas of the stomach, 1 of the colon, 3 lymphomas of the mesenteric lymph nodes and 1 hepatocellular carcinoma (12).

Dermal rat, hamster, 0.5% solution 3 × wk^{-1} for 30 wk in rats, for 13 wk in hamster. Multiple squamous and basal cell carcinomas of the skin occurred in 9/9 rats, the first appearing at 20 wk. Squamous cell carcinomas of the skin occurred in 18/18 hamsters, the first appearing at 8 wk (13).

Intravenous hamster 2.5 or 10 mg kg^{-1} wk^{-1} for 18 wk resulted in tumour incidences of 20-93%. The main tumour types were sarcomas of the heart and squamous cell carcinomas of the stomach (5).

Intratracheal hamster 0.5 mg $animal^{-1}$ 2 × wk^{-1} for 2.5 month produced epidermoid carcinomas in the nasopharyngeal tube, pharynx, larynx, trachea, bronchi, oesophagus and forestomach (14).

Intraperitoneal guinea pig, 10 mg kg^{-1} wk^{-1} for 18 wk induced tumours in 11/22 treated animals that survived beyond 22 wk. Tumours included 2 adenocarcinomas of the pancreas, 2 fibrosarcomas and 2 angiosarcomas of the mesentery, 1 mesothelioma of the peritoneum, 2 tumours of the small intestine and 1 haemangiosarcoma of the liver (15).

Intravenous ♀ rat 3 × 50 mg kg^{-1} at 4 wk intervals induced mammary carcinomas in 89% treated rats, with a mean latent period of 86 days (16).

Intraperitoneal rat, single dose of 20 mg kg^{-1} during pregnancy induced mammary gland tumours in 5/8 and a lymphoma in 1/8 treated dams. A variety of tumours were seen in the F_1 generation including 5 tumours of

nervous tissue in 5/54 animals, and 5 mesenchymal tumours and 1 carcinoma of the kidney in 6/54 animals. Kidney tumours were seen in 2/120 and a nervous tissue tumour in 1/120 of F_2 descendants. Nervous tissue tumours were observed in 2/88 of the F_3 descendants. No kidney or nervous tissue tumours were seen in 64 controls (17).

Bladder instillation ♀ rat 4 × 1.5 mg animal^{-1} on alternate wk induced papillomas and transition cell carcinomas of the bladder in all 100 treated animals within 30 wk (18).

Intracerebral newborn rat, mouse 0.05-0.8 mg animal^{-1} did not induce brain tumours in either species, but produced some kidney fibrosarcomas and 1 mammary gland carcinoma in rats, and leukaemias and pulmonary tumours in mice (19).

Intraperitoneal rat, single dose of 12.5, 25, 38 or 50 mg kg^{-1} at 50 days of age induced benign and malignant mammary tumours. The incidence of tumours decreased with dosage, whereas the induction time increased with dosage (20).

♀ Sprague-Dawley rats (50-day-old) were injected intraperitoneally with 30 or 60 mg kg^{-1} 7,12-dimethyl[*a*]anthracene (DMBA) alone, 30 or 60 mg kg^{-1} *N*-nitro-*N*-nitrosourea (MNU) alone, or 30 mg kg^{-1} MNU followed by 30 mg kg^{-1} DMBA. At 30 wk of age the animals were killed. Intraperitoneal MNU alone caused no deaths. All tumours caused by MNU were mammary adenocarcinomas, whereas DMBA produced tumours of other than mammary origin. Combined treatment with DMBA and MNU increased the mammary carcinogenic effect significantly (21).

Teratogenicity and reproductive effects

Intraperitoneal rat, single dose of 10 mg kg^{-1} surviving foetuses of dams treated on day-9 of gestation developed brain abnormalities. Treatment on days 11, 12 or 13 of gestation caused limb malformations, treatment on days 13 or 14 of gestation caused micrognathia, and treatment on day-12 of gestation caused hydrocephaly. Microcephaly was induced in offspring of rats treated on days 11-16 of gestation. Surviving foetuses showed significantly retarded growth (22,23).

Intraperitoneal mouse, single dose, 10, 20 or 30 mg kg^{-1} on days 0, 1, 2 or 3 of gestation. No significant differences were observed between the number of implantation sites of the treated groups and controls. Treatment on day 2 or 3 of gestation caused a significant dose-dependent increase in the incidence of foetal abnormalities. Cleft palate, exencephalus and malformed vertebrae were the most common types of abnormalities (24).

Metabolism and toxicokinetics

N-Nitroso-*N*-methylurea alkylates nucleic acids *in vitro* and *in vivo*. Alkylation has been observed in the brain, lung, kidney, liver, intestine, thymus, and spleen in several mammals. The major methylation product is 7-methylguanine (1).

Decomposes *in vivo* to yield cyanate which reacts with proteins. This carbamoylation has been found to be important in *in vitro* toxicity studies (25).

Genotoxicity

CASE structure-activity methodology predicted postive mutagenicity to *Salmonella typhimurium* (26).

In vitro Chinese hamster ovary cells, DNA damage positive (27).

In vitro primary rat and human hepatocytes, DNA damage positive (28).

In vivo mouse bone marrow, sister chromatid exchanges positive (29).

In vivo rat spermatocytes, unscheduled DNA synthesis positive (30).

In vivo rat liver DNA damage positive (31).

Allium sativum L. chromosomal aberrations positive (32).

Other effects

Any other adverse effects

The major toxic effects of *N*-nitroso-*N*-methylurea result from severe damage to haemopoietic, lymphoid and other tissues that have rapid cell turnover. Acute administration inhibits protein and nucleic acid synthesis (33,34).

Other comments

Physical properties, use, carcinogenicity, mammalian toxicity, teratogenicity, metabolism and mutagenicity reviewed (1,35).

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N164 *N*-nitroso-*N*-methylurethane

$$CH_3N(NO)CO_2CH_2CH_3$$

$C_4H_8N_2O_3$ **Mol. Wt.** 132.12 **CAS Registry No.** 615-53-2

Synonyms ethyl methylnitrosocarbamate; *N*-methyl-*N*-nitroso(ethyl carbamate); *N*-methyl-*N*-nitroso-urethane; MNUM; NMUT

EINECS No. 210-432-3 **RTECS No.** FC 6300000

Physical properties

B. Pt. 62-64°C at 12 mmHg **Specific gravity** 1.133 at 20°C with respect to water at 4°C
Solubility Water: miscible Organic solvents: benzene, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 180 mg kg^{-1} (1).
LC_{Lo} (10 min) inhalation mouse 600 mg m^{-3} (2).
LD_{50} intraperitoneal mouse 37 mg kg^{-1} (3).
LD_{50} intravenous rat 4 mg kg^{-1} (4).
LD_{Lo} subcutaneous mouse, hamster 7, 21 mg kg^{-1}, respectively (5,6).
LD_{Lo} subcutaneous rat 125 mg kg^{-1} (7).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (8).
Oral rat, 4 mg kg^{-1} day^{-1} in drinking water for 330 days. Squamous cell carcinomas of the forestomach developed in 10/20 animals (4).
Oral guinea pig, 2.5 mg kg^{-1} day in drinking water, 5 days wk^{-1} for life, induced tumours in 27/38 animals. Adenocarcinomas were found in the stomach and pancreas. Some tumours were also found in the lungs and larynx. Many of the tumours had metastasised (9).
Gavage hamster, 0.8 mg $animal^{-1}$ wk^{-1} for 2 months, then 2 × wk for 4-5 months induced epidermoid carcinomas of the oesophagus in 13/16 and epidermoid carcinomas of the forestomach in all treated animals (10).
Subcutaneous mouse, 3.3 mg kg^{-1} $month^{-1}$ for life. No tumours were found at the site of injection. Pulmonary adenomas occurred in all animals surviving more than 80 days, and in 26/32 mice which survived the same period. Adenomas occurred in 15/69 controls (5).
Intraperitoneal newborn mouse (1 yr) single dose of 10.5 mg kg^{-1} induced lung adenomas in all treated mice, compared with 3/50 in controls. One lymphoma and 1 lung carcinoma were also observed in treated animals. Lung tumorigenesis was more evident in newborn mice than in adult mice in which a single dose of 25 mg kg^{-1} produced only 0.86 lung adenomas $mouse^{-1}$ (3).
Pre-natal exposure in rats, intravenous administration of 40 mg kg^{-1} at various days of gestation induced an increased incidence of tumours in the offspring, including tumours of the nervous system. The highest incidence occurred when *N*-nitroso-*N*-methylurethane was administered between days 14-18 of gestation. An increased incidence of tumours was also reported in the second generation of untreated descendants of the treated mothers (11).

Teratogenicity and reproductive effects

Intravenous rat, lowest toxic dose 80 mg kg^{-1} on day-13 of gestation (musculoskeletal and central nervous system effects) (12).

Genotoxicity

CASE structure-activity methodology predicted positive mutagenicity to *Salmonella typhimurium* (13).
Escherichia coli SOS-chromotest positive (14).
In vivo rat brain, DNA fragmentation positive (15).
Methylation of nucleic acids has been demonstrated *in vitro* and *in vivo*. The major reaction products are 7-methylguanine and 3-methyladenine. Methylation also occurs in organs that do not usually develop cancers (16-18).

Other comments

Can be formed from *N*-methylurethane and nitrosating agents, such as nitrite, under conditions prevalent in the stomach (19).
Physical properties, occurrence, carcinogenicity and metabolism reviewed (19,20).

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N165 *N*-nitroso-*N*-methylvinylamine

$$CH_2=CHN(NO)CH_3$$

$C_3H_6N_2O$ **Mol. Wt.** 86.09 **CAS Registry No.** 4549-40-0

Synonyms methylvinylnitrosamine; *N*-methyl-*N*-nitrosovinylamine

RTECS No. YZ 0875000

Physical properties

B. Pt. 47-48°C at 30 mmHg
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 24 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).

Rats receiving 0.3 or 0.6 mg kg^{-1} day^{-1} developed papillomas and squamous cell carcinomas of the oesophagus. Abnormalities of tongue, pharynx, bile duct, and liver cysts were also observed. Rats exposed to a single inhalation exposure of 18 mg kg^{-1}, or repeated exposures of 25-50 ppm for 30 min twice wkly, developed inflammation of respiratory tract, squamous cell carcinomas and cholesteatomas in the nasal canal (1,3,4)

Genotoxicity

Drosophila melanogaster sex-linked recessive lethal mutation positive (5).
Initiator tRNA acceptance assay positive (6).

Other comments

Environmental pollutant. May be present in apple brandy.
Carcinogenicity and adverse health effects reviewed (7).

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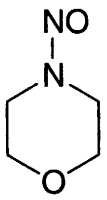
N166 *N*-nitrosomorpholine



$C_4H_8N_2O_2$ **Mol. Wt.** 116.12 **CAS Registry No.** 59-89-2

Synonyms 4-nitrosomorpholine; NMOR

RTECS No. QE 7525000

Occurrence An atmospheric pollutant in metal industries (1).
May be formed *in situ* in human stomach by the interaction of nitrile with morpholine (2).

Physical properties

M. Pt. 29°C **B. Pt.** 224-224.5°C
Solubility Water: miscible Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 282 mg kg^{-1} (3).
Can cause acute liver injury and induce kidney tumours after a single dose (4).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (5).
Rats receiving 8 mg kg^{-1} each day via drinking water developed a high incidence of hepatocellular hepatomas by 165 days (3).

Light and electron microscopy of hepatocellular foci produced in rats given drinking water containing 60-200 mg l^{-1} showed that such foci consistently preceded hepatocellular carcinomas (6).
Hamsters receiving 0.5 ml of a 1 in 125 solution of *N*-nitrosomorpholine subcutaneously twice wkly for more than 2 months developed papillary tumours of the trachea (7).
Mice receiving 16 mg day^{-1} via drinking water in a lifetime study developed benign hepatic tumours, lung adenomas and squamous cell carcinomas (8).

Metabolism and toxicokinetics

After intraperitoneal injection into rats of [^{14}C]nitrosomorpholine, <5% ^{14}C was exhaled within 32 hr while 80% was eliminated in urine. The same dose inhibited incorporation of [^{14}C]orotate and [^{14}C]leucine into hepatic but not kidney RNA within 2-4 hr (4).

Genotoxicity

Salmonella typhimurium TA1530 with metabolic activation by hepatic tissue weakly positive (9).
Salmonella typhimurium TA100, TA1530 with and without metabolic activation negative, with activation by isolated rabbit lung cells positive (10).
Escherichia coli WU3610 (Tyr$^-$,Leu$^-$) without metabolic activation negative, with metabolic activation positive (11).
In vitro initiator tRNA acceptance assay with metabolic activation, positive (12).
Drosophila melanogaster host mediated assay, *Escherichia coli* avr$^+$/rec$^+$ and uvrB/recA strains positive differential killing effects (13).
Unscheduled DNA synthesis *in vitro* rabbit lung cells positive (10).
Drosophila melanogaster wing spot test and lethal assay positive (14).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (15).
Carcinogenicity and toxicology reviewed (16).

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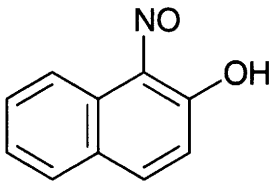
N167 1-nitroso-2-naphthol



$C_{10}H_7NO_2$ **Mol. Wt.** 173.17 **CAS Registry No.** 131-91-9

Synonyms 1-nitroso-2-naphthalenol; α-nitroso-β–naphthol

EINECS No. 205-043-0 **RTECS No.** QL 4725000

Uses Organic synthesis. Polymerisation inhibitor. Analytical reagent. Fuel additive.

Occurrence In vehicle exhaust (1).

Physical properties

M. Pt. 106°C (decomp.)

Solubility Water: 1 mg l^{-1} Organic solvents: benzene, carbon disulfide, ethanol, diethyl ether, glacial acetic acid, petroleum ether

Ecotoxicity

Fish toxicity

Caused death of stickleback and rainbow trout in 1-2 hr at 10 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 500 mg kg^{-1} (3).

Irritancy

Causes skin irritation (species unspecified) (4).

Genotoxicity

Salmonella typhimurium TA98, TA100 (metabolic activation unspecified) marginally positive (5).

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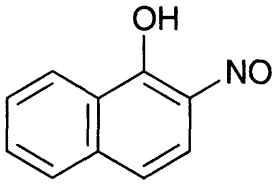
N168 2-nitroso-1-naphthol



$C_{10}H_7NO_2$ **Mol. Wt.** 173.17 **CAS Registry No.** 132-53-6

Synonyms 2-nitroso-1-naphthalenol

EINECS No. 205-064-5 **RTECS No.** QL 4550000

Uses Chemical intermediate.

Physical properties

M. Pt. 106°C

Ecotoxicity

Invertebrate toxicity

Inhibited photosynthetic function in *Chlorella vulgaris* (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Rats administered by gavage 0.1-30 mg day^{-1} for 5 days wk^{-1}. At the highest dose there was one hepatoma with metastases in a rat after a survival period of 463 days (2).

Other comments

Included in QSAR study using developing chick embryo and developing mouse model (3).

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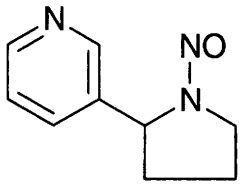
N169 *N*-nitrosonornicotine



$C_9H_{11}N_3O$ **Mol. Wt.** 177.21 **CAS Registry No.** 16543-55-8

Synonyms 1′-nitroso-1′-demethylnicotine; 1-nitroso-2-(3-pyridyl)pyrrolidine; 3-(1-nitroso-2-pyrrolidinyl)pyridine; NNN

RTECS No. QS 6550000

Occurrence In tobacco and tobacco smoke.

Physical properties

B. Pt. 154°C

Mammalian & avian toxicity

Sub-acute and sub-chronic data

LD_{50} (8 day) subcutaneous rat >1 g kg^{-1}, haemorrhage occurred in lungs and abdominal organs (1).

Carcinogenicity and chronic effects

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

♂ rats given 0.02% in drinking water 5 days wk^{-1} for 30 wk developed a high incidence of papillomas, carcinomas and tumours of the pharynx and nasal cavity (1).

♂ and ♀ mice administered 0.1 ml of the compound intraperitoneally for 6 wk developed multiple tumours (3).

Rats given 10 mg kg^{-1} subcutaneously 3 × wk^{-1} or in liquid diet at 17.5 mg l^{-1} for 4 wk developed tumours of the nasal mucosa and oesophagus (4).

Metabolism and toxicokinetics

Human liver microsomes and expressed human cytochrome P450s metabolise *N*′-nitrosonornicotine to 4-hydroxy-1-(3-pyridyl)-1-butanone and 5-(3-pyridyl)-2-hydroxytetrahydrofuran (5).

Metabolism can be effected by many cells including those of the nasal and oral mucosa (4).

Metabolism by rat oral tissue is thought to be by the same enzymes that metabolise nicotine. There is mutual inhibition with all metabolites of *N*-nitrosonornicotine being reduced in the presence of nicotine (6).

N-Nitrosonornicotine crosses the placenta of hamsters and mice and can be metabolised by late-phase foetal tissue and by neonate tissues (7).

Hydroxylation of the 2′ and 5′ carbons is thought to yield electrophilic species which can damage DNA. Intermediates in metabolism include 2′-hydroxy-*N*-nitrosonornicotine and diazohydroxy-*N*-nitrosonornicotine (4).

Extensively hydroxylated by rat nasal mucosa microsomes with low K_Ms in the range 2-5 μM. The authors suggest that *N*′-nitrosonornicotine, *N*-nitrosobenzylmethylamine, coumarin, and ethoxycoumarin are hydroxylated in this system by closely related P450 enzymes, and that a coumarin hydroxylase metabolises both *N*′-nitrosonornicotine and *N*-nitrosobenzylmelthylamine (8).

Genotoxicity

In vitro initiator tRNA acceptance assay with metabolic activation positive (9).

Other comments

Carcinogenicity reviewed (10).

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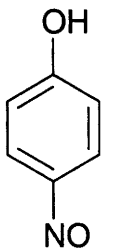
N170 4-nitrosophenol



$C_6H_5NO_2$ **Mol. Wt.** 123.11 **CAS Registry No.** 104-91-6

Synonyms *p*-nitrosophenol; quinone oxime; quinone monoxime

EINECS No. 203-251-6 **RTECS No.** SM 4725000

Uses Chemical intermediate.

Occurrence Metabolite of acetaminophen and phenacetin.

Physical properties

M. Pt. 144°C (decomp.)

Solubility Organic solvents: acetone, ethanol, ether

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 250 mg kg^{-1} (1).

Genotoxicity

Salmonella typhimurium TA98, TA100 without metabolic activation positive, with metabolic activation negative (2).

Saccharomyces cerevisiae JDI with and without metabolic activation mutotic gene conversion negative (2).

Incubation with λ phage DNA induced strand breaks (3).

Morphological transformation assay in mouse embryo cells negative (4).

In vitro rat liver cell structural chromosome damage positive (2).

Other comments

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

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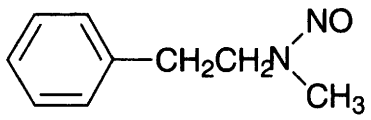
N171 *N*-nitroso-*N*-(2-phenylethyl)methylamine



$C_9H_{12}N_2O$ **Mol. Wt.** 164.21 **CAS Registry No.** 13256-11-6

Synonyms *N*-methyl-*N*-nitrosobenzeneethanamine; methylphenylethylnitrosamine

RTECS No. SI 0770000

Physical properties

B. Pt. 100°C at 0.10 mmHg

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 48 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Oral rat (2 yr) 0.4, 1.1, 3.2, 9.5, 28 or 115 mg l^{-1} in drinking water for 33 wk (21 wk for highest dose in which toxicity caused early death in some animals). In all groups, except the lowest dose and those in the high dose that died early, ≥50% animals had tumours of the oesophagus or forestomach (2).

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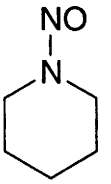
N172 nitrosopiperidine



$C_5H_{10}N_2O$ **Mol. Wt.** 114.15 **CAS Registry No.** 100-75-4

Synonyms 1-nitrosopiperidine; hexahydro-*N*-nitrosopyridine; *N*-nitrosopiperidine; NO-PIP; NPIP

EINECS No. 202-886-6 **RTECS No.** TN 2100000

Physical properties

B. Pt. 217-218°C **Specific gravity** 1.063 at 18.5°C with respect to water at 4°C

Solubility Water: 77 g l^{-1}. Organic solvents: acetone, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 200 mg kg^{-1} (1).

LD_{50} oral hamster 617 mg kg^{-1} (2).

LD_{50} subcutaneous rat 100 mg kg^{-1} (1).

LD_{50} intravenous rat 60 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 (3).

♂ mice administered the compound at a concentration of 50 mg kg^{-1} diet for up to 1 yr developed a high incidence of tumours particularly of lung, liver and forestomach (4).

Rats that received the compound via drinking water at doses of 5 or 20 mg kg^{-1} day^{-1} developed tumours with an average induction time of 280 days. Tumour types included hepatocellular and oesophageal carcinomas (1).

Hepatocellular carcinomas have also been observed in monkeys given oral doses (5).

Hamsters given wkly subcutaneous injections for life of 14-65 mg kg^{-1} developed large numbers of papillomas and carcinomas of the respiratory tract (6).

Offspring of Syrian golden hamsters that had been treated on day 8, 10, 12 or 14 of gestation with a single dose of 100 mg kg^{-1} showed a low incidence of respiratory tract tumours whereas the mothers showed a high (54%) incidence (7).

Metabolism and toxicokinetics

[^{3}H]-*N*-nitrosopiperidine injected into the bladder of rats or hamsters has been shown to be absorbed and radioactivity found in most soft tissues of the body (8).

Tritiated or deuterated compound administered to rats bound to the DNA and RNA of the liver (9).

N-Nitrosopiperidine is oxidised by rat liver microsomes to 4-hydroxynitrosopiperidine (10).

Rats given 70 mg kg^{-1} doses yielded hydroxy derivatives in urine within 24 hr (11).

Oesophageal epithelial cells can metabolise the compound to cytotoxic metabolites in a dose-dependent manner (12).

Genotoxicity

In vitro Chinese hamster V79 cells positive in presence of hepatocytes, negative in absence of hepatocytes (13).

In vitro initiator tRNA acceptance assay with metabolic activation positive (14).

Escherichia coli WU3610 (Tyr$^-$,Leu$^-$) without metabolic activation negative, with metabolic activation positive (15).

Drosophila melanogaster wing spot test and lethal assay positive (16).
Salmonella typhimurium TA100, TA1530, TA1535 with metabolic activation positive (17).

Other comments

In tobacco smoke, some foods and animal feeds (18).
In some rubber products (19).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (20).
Carcinogenicity and toxicology reviewed (21).

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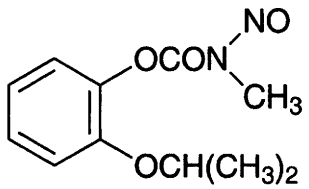
N173 nitrosopropoxur



$C_{11}H_{14}N_2O_4$ **Mol. Wt.** 238.24 **CAS Registry No.** 38777-13-8

Synonyms 2-(1-methylethoxy)phenyl methylnitrosocarbamate; *N*-nitroso-2-isopropoxyphenyl methylcarbamate; nitrosobaygon; *N*-nitrosopropoxur; NO-propoxur

RTECS No. FC 6480000

Uses Formerly used as insecticide.

Physical properties

M. Pt. –20°C
Solubility Organic solvents: acetic acid, diethyl ether

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Gavage rat (100 wk) 16 mg kg^{-1} wk^{-1} for 40 wk induced stomach tumours in 24/31 animals compared with 0/40 in controls (1).

Genotoxicity

CASE structure-activity methodology predicted positive mutagenicity to *Salmonella typhimurium* (2).
In vitro human lymphocytes, sister chromatid exchanges and induction of micronuclei positive (3).
Mutagenic in seeds of *Arabidopsis thaliana* (4).

References

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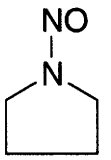
N174 *N*-nitrosopyrrolidine



$C_4H_8N_2O$ **Mol. Wt.** 100.12 **CAS Registry No.** 930-55-2
Synonyms tetrahydro-*N*-nitrosopyrrole; 1-nitrosopyrrolidine; NO-PYR; NPYR
EINECS No. 213-218-8 **RTECS No.** UY 1575000

Physical properties

B. Pt. 214°C
Solubility Water: miscible. Organic solvents: acetone, diethyl ether; ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 900 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 6 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 administered 0.01% 5 days wk^{-1} via drinking water developed sub-acute hepatic injury and lung adenomas (4).

Rats receiving 5-10 mg kg^{-1} via drinking water with a doubling of dose at 150 days developed hepatocellular carcinomas, papillary mesotheliomas and other tumours (1,5).

Metabolism and toxicokinetics

Intraperitoneal injection of 6 mg kg^{-1} into rats of ^{14}C-*N*-nitrosopyrrolidine labelled in the 2,5-positions or 3,4-positions resulted in 18-25% of ^{14}C being eliminated as CO_2 within 6 hr with 7% in urine and 1-2% in faeces (6).

When the 2,5 ^{14}C-compound was administered orally, ^{14}C-CO_2 production was dose dependent over 24 hr (7).

After intraperitoneal injection in rats, less than 1% of dose was converted into *N*-nitroso-3-hydroxypyrrolidine (8).

The DNA adduct 1,N^2-propanodeoxyguanosine was identified in rat liver after administration of 88 mg l^{-1} via drinking water (9).

Genotoxicity

Salmonella typhimurium TA1530 weakly positive with metabolic activation (10).

Using hamster liver microsomal fraction for activation ^{14}C-*N*-nitrosopyrrolidine labelled in the 2,5-positions bound to DNA in *Salmonella typhimurium* to yield 3 times as much in TA1535 as TA1975. Positive mutagenicity was seen with both strains (11).

Drosophila melanogaster wing spot test and lethal assay positive (12).

Host mediated assay using *Drosophila melanogaster* and *Escherichia coli* uvr^+/rec^+ and uvr B/rec A strains gave a positive result (13).

In vitro tRNA acceptance assay positive (14).

Escherichia coli WU3610 (Try^-,Leu^-) without metabolic activation negative, with metabolic activation positive (15).

Other comments

Formed in some nitrite treated processed foods, feeds and in tobacco smoke (16).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (17).

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N175 *N*-nitrososarcosine

$$CH_3N(NO)CH_2CO_2H$$

$C_3H_6N_2O_3$ **Mol. Wt.** 118.09 **CAS Registry No.** 13256-22-9

Synonyms *N*-methyl-*N*-nitrosoglycine; *N*-methyl-*N*-nitrosoglycine; *N*-nitrosomethylglycine

RTECS No. VQ 3150000

Physical properties

M. Pt. 66-67°C

Solubility Water: miscible. Organic solvents: polar organic solvents

Environmental fate

Abiotic removal

Conditions necessary for denitrosation have been reported (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat >5 g kg^{-1} (2).

LD_{50} intraperitoneal mouse 184 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).

Mice given 0.25% in diet for 3 months developed squamous cell carcinomas of the nasal region, lung and small intestine (5). Rats given 100 or 200 mg kg^{-1} day^{-1} via drinking water for up to 286 days developed oesophageal carcinomas and papillomas (2,6).

Newborn mice given intraperitoneal injections of 75 mg kg^{-1} on days 1, 4 and 7 after birth developed carcinomas of liver cells and liver hyperplasia (3).

Genotoxicity

Host mediated assay using mice, *Salmonella typhimurium* 9-46 negative (7).

In vitro tRNA acceptance assay positive (8).

Other effects

Any other adverse effects

Administration of 1 g kg^{-1} of the compound to mice inhibited hepatic aminopyrine demethylase and aniline hydroxylase activities (9).

Doses of 100-500 mg kg^{-1} inhibited hepatic *N*-nitrosodimethylamine *N*-demethylase activity (10).

Other comments

Detected in some nitrite-treated foods and in tobacco smoke (11).

Can be detected in urine after high nitrite intake by humans (12), and may be formed in the upper gastro-intestinal tract (13).

The toxicology of the compound has been reviewed (11).

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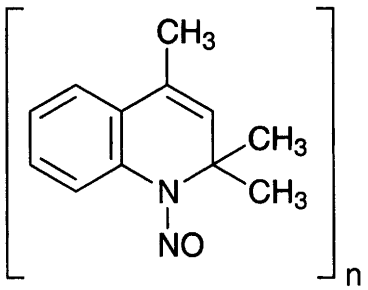
N176 *N*-nitroso-2,2,4-trimethyl-1,2-dihydroquinoline, polymers



$(C_{12}H_{14}N_2O)_n$ **CAS Registry No.** 29929-77-9

Synonyms 1-nitroso-2,2,4-trimethyl-1(2*H*)-quinoline, polymers; Curetard

RTECS No. VC 2300000

Uses Rubber additive.

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Subcutaneous rat (100 wk) 25 mg animal^{-1} wk^{-1} for 20 wk induced local sarcomas. No such tumours occurred, rats administered the same dosages by gavage (1).

References

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N177 nitrosyl chloride

NOCl

ClNO **Mol. Wt.** 65.46 **CAS Registry No.** 2696-92-6

EINECS No. 220-273-1 **RTECS No.** QZ 7883000

Occurrence Chemical intermediate.

Physical properties

M. Pt. –61.5°C **B. Pt.** –5.5°C **Specific gravity** 1.250 at 30°C **Volatility** v.p. 76 mmHg at 50°C ; v.den. 2.3

Occupational exposure

UN No. 1069 **Conveyance classification** toxic gas, corrosive

Mammalian & avian toxicity

Irritancy

Irritant to human eyes, skin and mucous membranes (1).

Other effects

Other adverse effects (human)

Inhalation may cause pulmonary oedema (1).

Other comments

May be formed as a result of faulty air – hydrocarbon equilibria during waste incineration (2).

Decomposes in water.

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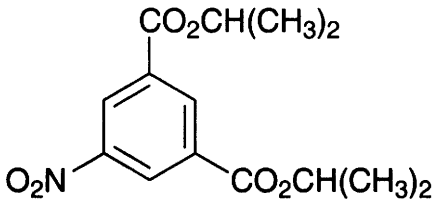
N178 nitrothal-isopropyl



$C_{14}H_{17}NO_6$ **Mol. Wt.** 295.29 **CAS Registry No.** 10552-74-6

Synonyms bis(1-methylethyl) 5-nitro-1,3-benzenedicarboxylate; nitrothale-isopropyl; di-isopropyl 5-nitroisophthalate

EINECS No. 234-139-5 **RTECS No.** CZ 4330000

Uses Fungicide, especially for mildews.

Physical properties

M. Pt. 65°C **Flash point** 400°C **Partition coefficient** log P_{ow} 2.041 (1) **Volatility** v.p. 7.52×10^{-8} at 20°C
Solubility Water: 2.7 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform

Ecotoxicity

Fish toxicity
Non-toxic to fish (1).

Invertebrate toxicity
LD_{50} (oral) >100 μg bee^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >6.4 g kg^{-1} (2).
LD_{50} dermal rat >2.5 g kg^{-1} (1).
LD_{50} dermal rabbit >4 g kg^{-1} (1).

Sub-acute and sub-chronic data
A 90-day feeding trial in rats established a NOEL of 500 mg kg^{-1} diet (1).
A 90-day feeding trial in dogs established a NOEL of 20 g kg^{-1} diet (1).

Metabolism and toxicokinetics
Rats receiving the compound daily for 7 days eliminated 85% in urine and 12.5% in faeces within 6 days of the last dose being administered (1).

Irritancy
Slightly irritant to eyes and mucous membranes of rabbit (dose and duration unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (4).
WHO Class Table 5 (5).
EPA Toxicity Class IV (formulation) (2).

Other comments

Non-toxic to bees (1).

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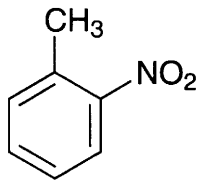
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

N179 2-nitrotoluene



$C_7H_7NO_2$ **Mol. Wt.** 137.14 **CAS Registry No.** 88-72-2

Synonyms *o*-nitrotoluene; 1-methyl-2-nitro-benzene; 2-methylnitrobenzene; ONT

EINECS No. 201-853-3 **RTECS No.** XT 3150000

Uses In manufacture of dyes and rubber. Chemical intermediate.

Occurrence Environmental pollutant, particularly in water (1,2).

Physical properties

M. Pt. –4 to –3°C **B. Pt.** 222°C **Flash point** 106°C (closed cup) **Specific gravity** 1.1622 at 19°C with respect to water at 15°C **Partition coefficient** log P_{ow} 2.30 **Volatility** v.p. 1 mmHg at 50°C ; v.den. 4.72

Solubility Water: 0.498 g l^{-1} at 30°C. Organic solvents: benzene, ethanol, petroleum ether

Occupational exposure

SE-LEVL 1 ppm (6 mg m^{-3}) **SE-STEL** 2 ppm (11 mg m^{-3})

UK-LTEL 5 ppm (29 mg m^{-3}) **UK-STEL** 10 ppm (57 mg m^{-3})

US-TWA 2 ppm (11 mg m^{-3})

UN No. 1664 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification toxic, dangerous for the environment

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R33, R51/53)

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 gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S37, S45, S61)

Ecotoxicity

Invertebrate toxicity

Cell multiplication inhibition test *Pseudomonas putida* 18 mg l^{-1}, *Entosiphon sulcatum* 48 mg l^{-1} (3).

EC_{50} (15 min) *Photobacterium phosphoreum* 1.85 ppm Microtox test (4).

Environmental fate

Degradation studies

Decomposition by soil microflora takes >64 days (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 891 mg kg^{-1} (6).

LD_{50} oral mouse 970 mg kg^{-1} (7).

Carcinogenicity and chronic effects

National Toxicology Program feeding study in progress (8).

Confirmed as a carcinogen causing mesotheliomas and cholangiocarcinomas in rats after 13 or 26 wk exposure (9).

Metabolism and toxicokinetics

Metabolites include 2-nitrobenzyl alcohol conjugates, which may be responsible for the genotoxicity observed (10).

Intestinal flora have an obligatory role in metabolism by rats. Such metabolism may be sex dependent, being seen most readily in ♂ (10).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (11,12).

In vitro Chinese hamster ovary cells sister chromatid exchange without metabolic activation weakly positive, with metabolic activation positive (13).

Cultured hepatocytes taken from ♂ rats given oral doses of 2-nitrotoluene showed unscheduled DNA repair. Negative results were obtained *in vitro* (10).

Other comments

Removal from river water studied (1,2).

Metabolism and excretion reviewed (14).

Uptake and clearance by carp studied (15).

Included in a QSAR study of toxicity in fathead minnow (16).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (17).

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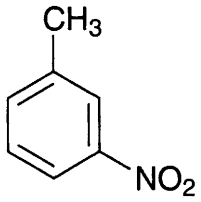
N180 3-nitrotoluene



$C_7H_7NO_2$ **Mol. Wt.** 137.14 **CAS Registry No.** 99-08-1

Synonyms *m*-nitrotoluene; 1-methyl-3-nitrobenzene

EINECS No. 202-728-6 **RTECS No.** XT 2975000

Uses In manufacture of dyes. Chemical intermediate. Explosive component.

Physical properties

M. Pt. 15.5°C **B. Pt.** 156.9°C at 100 mmHg **Flash point** 106°C **Specific gravity** 1.1581 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.45 **Volatility** v.p. 1 mmHg at 50.2°C ; v.den. 4.72
Solubility Water: 0.5 g l^{-1} at 30°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (28 mg m^{-3})
FR-VME 2 ppm (11 mg m^{-3})
SE-LEVL 1 ppm (6 mg m^{-3}) **SE-STEL** 2 ppm (11 mg m^{-3})
UK-LTEL 5 ppm (29 mg m^{-3}) **UK-STEL** 10 ppm (57 mg m^{-3})
US-TWA 2 ppm (11 mg m^{-3})

UN No. 1664 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (1 hr) fathead minnow 43 mg l^{-1}, 30 mg l^{-1} (24-96 hr) static bioassay at 18-22°C (1).

Invertebrate toxicity

Cell multiplication inhibition test *Pseudomonas putida* 10 mg l^{-1}, *Entosiphon sulcatum* 12 mg l^{-1} (2).
EC_{50} (15 min) *Photobacterium phosphoreum* 3.96 ppm Microtox test (3).
IC_{50} (48 hr) *Daphnia magna* 7.54 mg l^{-1} (4).
IC_{50} (21 day) *Daphnia magna* 8.26 mg l^{-1} (4).

Environmental fate

Degradation studies

Decomposition by soil microflora takes >64 days (5).

Abiotic removal

The use of freezing techniques for removal from soil contaminated by explosives residues assessed. Concentration was reduced by 37% compared with control (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1.07 g kg^{-1} (7).
LD_{50} oral mouse 330 mg kg^{-1} (8).
LD_{50} oral rabbit 2.4 g kg^{-1} (8).
LD_{50} oral guinea pig 3.6 g kg^{-1} (8).

Carcinogenicity and chronic effects

National Toxicology Programme feeding study in progress (9).

Metabolism and toxicokinetics

Metabolized to nitrobenzyl alcohols in a cytochrome P_{450}-dependent process in isolated Fischer 344 rat hepatocytes (10).
In a ^{14}C-radiolabel study using Fischer 344 rats 40% of the label was excreted via the urine. Biliary excretion was greater in ♂ than ♀. The major metabolites were the acetamidobenzoic acid, nitrobenzoic acid, *S*-(nitrobenzyl)glutathione, *S*-(nitrobenzyl)-*N*-acetylcysteine and nitrobenzyl glucuronide. Enterohepatic recycling was involved in activating the compound making it capable of covalently binding to hepatic macromolecules (11).

Genotoxicity

Cultured hepatocytes taken from ♂ rats dosed orally with 3-nitrotoluene showed no unscheduled DNA repair. Negative results were also obtained *in vitro* (12).

Other comments

Environmental pollutant, particularly of water (13,14).
Removal from river water studied (13).
The effectiveness of ozone hydrogen peroxide treatment for removal from groundwater studied (14).
Uptake and clearance by carp studied (15).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (16).

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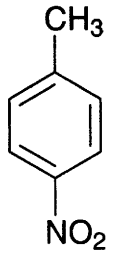
16. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

N181 4-nitrotoluene



$C_7H_7NO_2$ **Mol. Wt.** 137.14 **CAS Registry No.** 99-99-0

Synonyms *p*-nitrotoluene; 1-methyl-4-nitrobenzene; 4-methylnitrobenzene; 4-nitrotoluol

EINECS No. 202-808-0 **RTECS No.** XT 3325000

Uses Manufacture of fuchsin dyes. Synthesis of intermediates and explosives.

Physical properties

M. Pt. 53-54°C **B. Pt.** 238°C **Flash point** 106°C (closed cup) **Specific gravity** 1.392
Partition coefficient log P_{ow} 2.42 **Volatility** v.p. 1 mmHg at 53.7°C ; v.den. 4.72
Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (28 mg m^{-3})
SE-LEVL 1 ppm (6 mg m^{-3}) **SE-STEL** 2 ppm (11 mg m^{-3})
UK-LTEL 5 ppm (29 mg m^{-3}) **UK-STEL** 10 ppm (57 mg m^{-3})
US-TWA 2 ppm (11 mg m^{-3})

UN No. 1664 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic, dangerous for the environment
Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23/24/25, R33, R51/53)
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 gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S37, S45, S61)

Ecotoxicity

Invertebrate toxicity
Cell multiplication inhibition test *Pseudomonas putida* 26 mg l^{-1}, *Entosiphon sulcatum* 8.6 mg l^{-1} (1).
EC_{50} (30 min) *Photobacterium phosphoreum* 12.5 ppm Microtox test (2).

Environmental fate

Degradation studies
Decomposition by soil microflora takes >64 days (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1960 mg kg^{-1} (4).
LD_{50} oral mouse 1230 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Oral rats, mice (13 wk) 0, 625, 1250, 2500, 5000, 10,000 ppm in feed toxic to kidney, spleen, reproductive system. Histopathological lesions were not observed in the liver (6).

In 90-day histopathological studies ♂ rats showed: kidney damage (nephropathy, hyaline droplets), degeneration in testes, kidney damage (karyomegaly, pigmentation) and spleen damage (congestion, haematopoiesis, haemosiderin) (6).

Carcinogenicity and chronic effects

National Toxicology Program feeding study in progress (6).

Genotoxicity

In vitro Chinese hamster ovary cells sister chromatid exchanges with and without metabolic activation positive (7).

In vitro hamster lung, chromosomal aberrations negative (8).

Cultured hepatocytes taken from ♂ rats dosed orally with 4-nitrotoluene showed no unscheduled DNA repair. Negative results were also obtained *in vitro* (9).

Unscheduled DNA synthesis rat, mouse hepatocytes negative (10).

In vivo cytogenic assays mice, micronuclei equivocal (11).

Other effects

Other adverse effects (human)

Symptoms of poisoning include headache, dizziness, nausea and vomiting leading to increased irritability and convulsions. Poisoning can be cumulative (12).

Other comments

Environmental pollutant particularly in water (13).

Removal from river water studied (13).

Uptake and clearance by carp studied (14).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (15).

Metabolism and excretion have been reviewed (16).

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15. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
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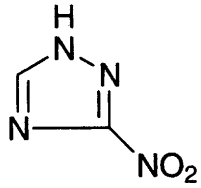
N182 3-nitro-1,2,4-triazole



$C_2H_2N_4O_2$ **Mol. Wt.** 114.06 **CAS Registry No.** 24807-55-4

Synonyms nitrotriazole; 3-nitro-1*H*-1,2,4-triazole; 3-nitro-*s*-triazole

EINECS No. 236-468-1

Uses Chemical intermediate.

Physical properties

M. Pt. 210°C (decomp.)

Other comments

Can bind to DNA when included in oligopeptide lexitropsins related to the natural anti-tumour agent distamycin (1).

Active portion of a number of derivatives with hypoxic-cell radiosensitising properties (2,3).

References

1. Rao, K. E. et al *Chem. Res. Toxicol.* 1991, **4**(2), 241-252.
2. Sugita, T. et al *Anti-Cancer Drug Des.* 1992, **7**(3), 277-284.
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N183 nitrous oxide

N_2O

N_2O **Mol. Wt.** 44.01 **CAS Registry No.** 10024-97-2

Synonyms nitrogen oxide; dinitrogen monoxide; hyponitrous acid anhydride; laughing gas

EINECS No. 233-032-0 **RTECS No.** QX 1350000

Uses Oxidant in chemical synthesis. In medicine as an adjunct to other anaesthetics or with oxygen to provide analgesia.

Physical properties

M. Pt. –90.81°C **B. Pt.** –88.46°C **Specific gravity** 1.978

Solubility Water: 0.67 g ml^{-1} at 761 mmHg. Organic solvents: chloroform, ethanol

Occupational exposure

DE-MAK 100 ppm (180 mg m^{-3})

SE-LEVL 100 ppm (180 mg m^{-3}) **SE-STEL** 500 ppm (900 mg m^{-3})

UK-LTEL 100 ppm (183 mg m^{-3})
US-TWA 50 ppm (90 mg m^{-3})

UN No. 1070 (compressed); 2201 (refrigerated liquid) **HAZCHEM Code** 2R (compressed); 2PE (refrigerated liquid) **Conveyance classification** non-flammable non-toxic gas, fire intensifying hazard

Environmental fate

Nitrification inhibition
The role of nitrous oxide in denitrification has been reviewed (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 505 mg kg^{-1} (2).
LC_{50} (1 hr) inhalation rat 1274 ppm (2).
LC_{Lo} (2 hr) inhalation man 24 mg kg^{-1} (3).
LD_{50} intravenous dog 167 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Rats exposed to 60 mg m^{-3} for 6 days developed lesions of the alveolar epithelium and infiltration into the perivascular lung tissue (5).
Rats exposed to 50% nitrous oxide for 3 or 7 days showed some abnormalities of blood and bone marrow cells. In those exposed for 7 days, effects on haematopoiesis and chromosomal aberrations were observed (6).

Teratogenicity and reproductive effects
Foetotoxic in rats (6).
Lack of evidence of foetotoxicity in man (7,8).
Pregnant rats exposed to a variety of regimes for 8 or 24 hr demonstrated effects on growth pre- and post-birth. No effect was observed on brain or liver levels of protein or DNA (9).

Metabolism and toxicokinetics
In humans nitrous oxide is rapidly absorbed on inhalation and rapidly eliminated through the lungs. A small amount escapes through skin (10,11).

Genotoxicity

Drosophila melanogaster sex linked recessive lethal assay, no potentiation of mutagenicity induced by other anaesthetics (12).
In vitro Chinese hamster lung cells chromosome aberration positive (13).

Other effects

Other adverse effects (human)
A mixture of 2-3% v/v diethyl ether and 75% nitrous oxide completely suppressed the reflex response of the musculus soleus and musculus gastrocnemius in humans to a single stimulus of the tibial nerve (14).
Cumulative toxicity can result from repeated exposure leading to effects on DNA synthesis and to megaloblastic marrow changes (15,16).
Neurological deficit is seen in chronic abusers of nitrous oxide (10).
There is evidence of cross tolerance and dependence with ethanol in mice and humans which can be of use for management of alcohol withdrawal in humans (17,18).
Nitrous oxide used as a 1:1 mixture with oxygen as an anaesthetic for child birth did not suppress labour activity and elevated the freqency, duration and amplitude of labour pains during childbirth (19,20).

Any other adverse effects
Mild anaesthetic when mixed with oxygen; suffocating at high concentrations as expels from the lungs. ≤20% nitrous oxide/air caused no specific changes to functions in the rat (5,21).

The gas interacts with vitamin B_{12} which is a coenzyme. The result is a depletion of methionine and tetrahydrofolate which may lead to a variety of consequences including interference with DNA synthesis and neurological problems (10,15,16).

Other comments

Formation in soil, release and techniques for controlling these have been reviewed (22).
Formed in soil ecosystems. Atmospheric pollutant (22,23).
When administered to man and a variety of mammals, analgesia and reduced anxiety are observed. Opiate reception of the κ and δ but not μ types are thought to be involved in these effects (24).
Reviews on human health effects, experimental toxicology, physico-chemical properties listed (25).
Environmental health criteria reviewed (26).
The effects of nitrous oxide as a 'greenhouse gas' and its influence on climate reviewed (23).

References

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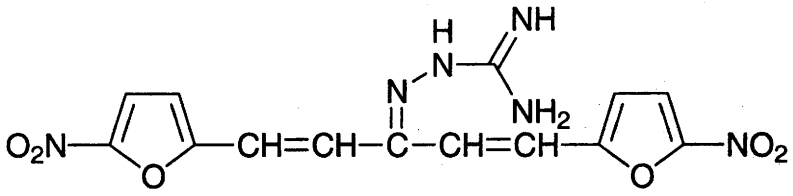
N184 nitrovin



$C_{14}H_{12}N_6O_6$ **Mol. Wt.** 360.29 **CAS Registry No.** 804-36-4

Synonyms 2-[3-(5-nitro-2-furanyl)-1-[2-(5-nitro-2-furanyl)ethenyl]-2-propenylidene]hydrazinecarboximidamide; [[3-(5-nitro-2-furyl)-1-[2-(5-nitro-2-furyl)vinyl]allylidene]amino]guanidine; *sym*-bis(5-nitro-2-furfurylidene)-acetone guanylhydrazone; 1,5-bis(5-nitro-2-furyl)-3-pentadienone guanylhydrazone; 1,5-bis(5-nitro-2-furyl)-3-pentadienone amidinohydrazone; Panazone; Payzone

EINECS No. 212-358-7

Uses In veterinary medicine as a growth promoter and antibacterial.

Physical properties

M. Pt. 217°C (dec.)
Solubility Organic solvents: dimethylformamide

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 5330 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 300 mg kg^{-1} (1).
LD_{50} subcutaneous mouse 3750 mg kg^{-1} (1).
No observed effect in mice after oral administration of 9 g kg^{-1} (2).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (3).
Oral ♀ Sprague-Dawley rats (3 weeks old) 1000 mg nitrovin hydrochloride kg^{-1} diet for 46 weeks (total cumulative dose 5 g rat^{-1}). No significant difference in survival or weight was seen between treated and control rats, and no statistically significant increase in incidence of tumours occurred in treated rats. Of control rats and treated rats 6/37 and 3/26, respectively, developed solitary mammary adenoma (4).
No toxic effect reported after long-term administration to rats of 0.001-0.004% in the diet (2).

Metabolism and toxicokinetics

In rats, of orally administered ^{14}C-nitrovin, 0.6% was absorbed through the intestine, and the highest amount was found in the liver and kidneys. About 90% of the dose was recovered via the faeces within 48 hours. Only 1% of the dose was found in the urine and a trace was detected in exhaled carbon dioxide. A small amount of radioactivity was detected in the bodies of rats 12 days after administration (5).
Some metabolites of nitrovin undergo enterohepatic circulation (6).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation negative, without metabolic activation positive (7).
Bacillus subtilis rec assay positive (7).
Escherichia coli WP2 *hcr* assay positive (7).
Escherichia coli PQ37 (SOS chromotest) without metabolic activation positive (8).

References

1. *Prog. Med. Chem.* 1967, **5**, 320.
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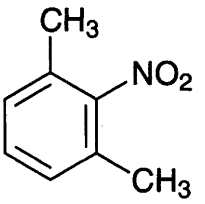
N185 2-nitro-*m*-xylene



$C_8H_9NO_2$ **Mol. Wt.** 151.16 **CAS Registry No.** 81-20-9

Synonyms 1,3-dimethyl-2-nitrobenzene; 2,6-dimethylnitrobenzene; 2-nitro-1,3-dimethylbenzene; 2-nitro-1,3-xylene

EINECS No. 201-333-6 **RTECS No.** ZE 4686000

Physical properties

M. Pt. 14-16°C **B. Pt.** 225°C at 744 mmHg **Specific gravity** 1.147

Environmental fate

Abiotic removal

Sunlight induced photodegradation (1).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (2).

Other comments

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

Genotoxicity, biological properties and human exposure limits reported (4).

References

1. Simmons, M. S. et al *Water Res.* 1986, **20**(7), 899.
2. Maynard, A. T. et al *Mol. Pharmacol.* 1986, **29**(6), 629.
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.
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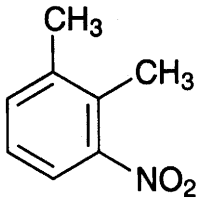
N186 3-nitro-*o*-xylene



$C_8H_9NO_2$ **Mol. Wt.** 151.16 **CAS Registry No.** 83-41-0

Synonyms 1,2-dimethyl-3-nitrobenzene; 2,3-dimethylnitrobenzene

EINECS No. 201-474-3

Uses Chemical intermediate. Used in the manufacture of plasticisers.

Physical properties

M. Pt. 7-9°C **B. Pt.** 245°C **Flash point** 107°C **Specific gravity** 1.147 at 15 °C

Solubility Organic solvents: ethanol

Ecotoxicity

Fish toxicity

LC_{50} guppy 40.74 µmol l^{-1} (1).

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 0.536 mg l^{-1} Microtox test (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (3).

Other comments

Classified as a Class 2, less inert chemical in a guppy LC_{50} QSAR (4).

Reviews on human health effects and experimental toxicology listed (5).

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2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Canada* 1991, **26**(3), 361-431.
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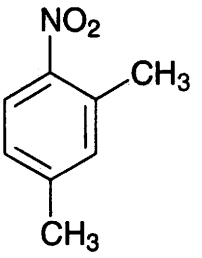
N187 4-nitro-*m*-xylene



$C_8H_9NO_2$ **Mol. Wt.** 151.16 **CAS Registry No.** 89-87-2

Synonyms 2,4-dimethyl-1-nitrobenzene; 1,3-dimethyl-4-nitrobenzene; 1-nitro-2,4-dimethylbenzene; 4-nitro-1,3-dimethylbenzene; 4-nitro-1,3-xylene

EINECS No. 201-947-4

Physical properties

M. Pt. 2°C **B. Pt.** 244°C

Solubility Organic solvents: diethyl ether, acetone

Environmental fate

Abiotic removal

Sunlight induces photodegradation (1).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 45 mg kg^{-1} (2).

Other comments

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

References

1. Simmons, M. S. et al *Water Res.* 1986, 20(7), 899.
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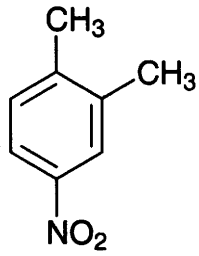
N188 4-nitro-o-xylene



$C_8H_9NO_2$ **Mol. Wt.** 151.16 **CAS Registry No.** 99-51-4

Synonyms 1,2-dimethyl-4-nitrobenzene; 3,4-dimethyl-1-nitrobenzene; 4-nitro-1,2-dimethylbenzene

EINECS No. 202-761-6

Physical properties

M. Pt. 29-31°C **B. Pt.** 143°C at 20 mmHg

Solubility Organic solvents: ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (15 min) *Photobacterium phosphoreum* 2.14 mg l^{-1} Microtox test (1).

Environmental fate

Abiotic removal

Sunlight induced photodegradation (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (3).

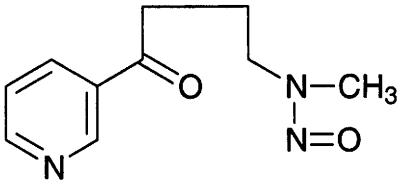
Other comments

Reviews on human health effects, experimental toxicology listed (4).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Canada* 1991, 26(3), 361-431.
2. Simmons, M. S. et al *Water Res.* 1986, 20(7), 899.
3. Maynard, A. T. et al *Mol. Pharmacol.* 1986, 29(6), 629.
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

N189 NNK



$C_{10}H_{13}N_3O_2$ **Mol. Wt.** 207.23 **CAS Registry No.** 64091-91-4

Synonyms 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; 4-(*N*-methyl-*N*-nitrosoamino)-1-(3-pyridyl)-1-butanone

Physical properties

M. Pt. 63-65°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification Group 2B (1).

Subcutaneous Fischer 344 rats (52 wk) administered 11.7 mg 3 × wk^{-1} for 20 wk. 6/12 ♂s and 4/12 ♀s developed malignant tumours of the nasal cavity, 5/12 ♂s malignant tumours of the lung, 7/12 ♂s and 12/12 ♀s malignant tumours of the liver. No such malignant tumours developed in 12 control rats (2).

Intraperitoneal ♀ A/J mice (261 days) 0.1 ml 1% solution NNK 3 × wk^{-1} for 7.3 wk (23 mg total dose). All surviving treated mice (23/25) had lung tumours of which 412/865 were carcinomas. In a group of vehicle controls (0.9 & trioctanoin) 4/25 had lung tumours with a total of 5 adenomas and 0 carcinomas. In a group of untreated controls 10/25 had lung tumours including 16 adenomas and 2 carcinomas (3).

Metabolism and toxicokinetics

Human tissues obtained at immediate autopsy cultured with [carbonyl-^{14}C]NNK for 24 hr metabolised NNK to 4-(methylnitrosoamino)-1-(3-pyridyl)butan-1-ol, 4-hydroxy-4-(3-pyridyl)butyric acid and an unidentified metabolite (4).

Investigations using cultured human placental microsomes established that in this system, cytochromes P450 are likely to be involved in the metabolism of NNK and that the metabolism of NNK to 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanol is catalysed by an NADPH-dependent carbonyl reductase(s) and an NADH-dependent carbonyl reductase(s) (5).

[4-^{3}H]NNK administered intravenously to patas monkeys was metabolised by two major pathways. α-Hydroxylation was rapid and extensive and led to 4-hydroxy-4-(3-pyridyl)butyric acid and 4-oxo-4-(3-pyridyl)butyric acid which accounted for a relatively large proportion of serum and urinary metabolites. The formation of these metabolites is associated with modification of DNA by NNK. The other major pathway was carbonyl reduction of NNK to 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), unconjugated and as two glucuronides. The two glucuronides accounted for 15-20% of urinary metabolites (6).

♂ Fischer 344 rats administered 7.1 μg kg^{-1} [carbonyl-^{14}C]NNK orally excreted 88% of the dose in 48-hr urine, 3% in faeces, and <0.5% in expired air. 5.1 μg kg^{-1} [$^{14}CH_3$]NNK administered orally was excreted in 48-hr urine (39% of the dose), faeces (8%), and in expired air as $^{14}CO_2$ (47%) (7).

Intraperitoneal ♀ Sprague-Dawley rats 0.7 μmol kg^{-1} [carbonyl-^{14}C]NNK. The concentration of radioactivity in the bile peaked at 30 min after administration and then decreased exponentially. 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butyl. β-D-glucopyranosiduronic acid (NNAL Glu) was the major metabolite accounting for 34% of the total radioactivity in bile at 30 min and 58% at 5 hr. Other metabolites detected in the bile were 4-hydroxy-4-(3-pyridyl)butyric acid (hydroxy acid), 4-oxo-4-(3-pyridyl)butyric acid (keto acid), 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanol (NNAL) and unchanged NNK. A one-compartment model fitted the elimination kinetics of

NNK and its metabolites with half-lifes for NNK of 37 min, NNAL 52 min, and NNAL Glu and acidic metabolites 110 min (8).

Enzymes in rat lung micrsomes catalysed the α-hydroxylation, pyridine *N*-oxidation and carbonyl reduction of NNK. Apparent K_ms for the formation of the NNK-derived ketoaldehyde, NNK *N*-oxide, NNK-derived keto alcohol, and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanol were 28.8, 10.4, 7.0, and 178.1 μM, respectively. Apparent K_ms for the formation by enzymes of rat nasal microsomes of keto aldehyde and keto alcohol were 9.6 and 10.1 μM, respectively. α-Hydroxylation was the predominant pathwayin nasal microsomes and the rate was *c.* 200 × higher than in lung microsomes. Cytochrome P450s are involved in the metabolic activation of NNK in rat lung and nasal microsomes (9).

NNK injected intraperitoneally into pregnant hamsters can cross the placental barrier and may be a transplacental carcinogen (10).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with metabolic activation positive (11).

Induces sister chromatid exchanges and DNA single-strand breaks in V-79 cells (12).

Intraperitoneal hamster 0-200 mg kg^{-1} on day-14 of gestation, chromosome aberrations (mostly of chromatid type) were observed in epithelial cells established from lung and tracheal explant outgrowths. A high frequency of chromatid exchange was seen in tracheal cells (10).

Other comments

Oxidation and nitrosation product of nicotine formed during curing, ageing, processing and smoking of tobacco. Found at the following levels: tobacco 0.1-35 mg kg^{-1}, snuff 0.2-8.3 mg kg^{-1}, cigarette smoke 0.1-0.5 μg $cigarette^{-1}$ (1).

The biological half-life of NNK in the Syrian golden hamster, CD-1 mouse, Fischer rat and baboon ranged from 0.21-0.43 hr (13).

Results from feeding studies suggest that vitamin E inhibits the development of lung tumours in NNK-treated mice (14).

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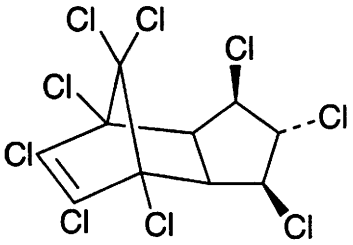
N190 *trans*-nonachlor



$C_{10}H_5Cl_9$ Mol. Wt. 444.22 CAS Registry No. 39765-80-5

Synonyms 4,7-methano-1*H*-indene, 1,2,3,4,5,6,7,8,8-nonachloro-2,3,3*a*,4,7,7*a*-hexahydro-, (1α,2β,3α,3*a*α,4β,7β,7*a*α)-; *trans*-nonachlordane

Mammalian & avian toxicity

Metabolism and toxicokinetics

Rats *in vivo* and *in vitro* (liver microsomal preparations) metabolise *trans*-nonachlor to transchlordane which is further metabolised to 1,2-dichlorochlordene and oxychlordane. From the latter metabolite, two major stable products are formed, 1-hydroxy-2-chlorochlordene and 1-hydroxy-2-chloro-2,3-epoxychlordene. Chlordene chlorohydrin is formed directly from *trans*-nonachlor and is a precursor for 1,2-*trans*-dihydroxydihydrochlorodene (1).

Other effects

Other adverse effects (human)

Human breast adipose tissues examined for metabolites of technical chlordane contained a geometric mean concentration of *trans*-nonachlor of 120 ng g^{-1} of fat. The concentration increased with subject's age but overall the results were similar to 1970-80 values. Nonachloro- and pentachlorocyclopentene compounds are the most highly retained compounds in people, when compared to their abundances in technical chlordane. The authors concluded that exposure to chlordane in indoor air was an important source of these components to the US population (2).

Any other adverse effects

Rats were fed 10 ppm technical chlordane in their diets for 28 days. The depuration of the various chlordane compounds was then followed for 32 days. The half-life of *trans*-nonachlor in the adipose tissue was 54.1 days (3). Adult ♀ big brown bats (*Eptesicus fuscus*) collected in Laurel, Maryland contained < 0.5 ppm *trans*-nonachlor (4). In birds fed chlordane followed by untreated feed the order of persistence of metabolites was oxychlordane, *trans*-nonachlor, heptachlor epoxide (5).

Other comments

trans-Nonachlor, at the concentration found in alligator eggs from Lake Apopka, Florida, has been shown to compete with [3H]17β-estradiol for binding to the oestrogen-binding receptor of alligator oviduct. Similar findings for other environmental chemicals support the hypothesis that the reported reproductive abnormalities found in American alligators from Lake Apopka are related to the modulation of endocrine-related responses by these chemicals (6).

Endocrine disruptor causing sex reversal in alligator embryos (7).

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N191 nonadecanenitrile

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

$C_{19}H_{37}N$ **Mol. Wt.** 279.51 **CAS Registry No.** 28623-46-3

EINECS No. 249-107-6

Uses Chemical intermediate.

Occurrence

In shale oil (1).

In flowers such as Karo-Karounde (2).

Physical properties

M. Pt. 42-43°C **Specific gravity** 0.84 at 20°C

Ecotoxicity

Invertebrate toxicity

Can be lethal to *Schistosoma mansoni* cercariae and can affect penetration behaviour (3).

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N192 nonanal

$$CH_3(CH_2)_7CHO$$

$C_9H_{18}O$ **Mol. Wt.** 142.24 **CAS Registry No.** 124-19-6

Synonyms aldehyde C-9; 1-nonanal; 1-nonaldehyde; nonanoic aldehyde; nonyl aldehyde; pelargonic aldehyde; pelargonaldehyde

EINECS No. 204-688-5 **RTECS No.** RA 5700000

Uses Flavour agent. In perfumery.

Occurrence Aroma component in plant oils, cooked meat, fish and dairy products. Sex pheromone in some insects.

Physical properties

M. Pt. 63°C **B. Pt.** 190-192°C **Flash point** 63°C **Specific gravity** 0.8264 at 22°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol, propylene glycol, fixed oils

Environmental fate

Degradation studies
Biodegradation by activated sludge, 8.4% of ThOD after 6 hr, 13.5% of ThOD after 12 hr, 21% of ThOD after 24 hr (1).

Mammalian & avian toxicity

Irritancy
Dermal rabbit (24 hr) 500 mg caused severe irritation (2).
Vapour or mist is irritating to the eyes, mucous membranes and upper respiratory tract (species unspecified) (3).

Sensitisation
Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (4).
In vitro Chinese hamster V79 lung cells, induction of forward mutations positive (5).
In vitro primary rat hepatocytes, sister chromatid exchanges positive, induction of micronuclei negative (6).

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N193 nonane

$$CH_3(CH_2)_7CH_3$$

C_9H_{20} **Mol. Wt.** 128.26 **CAS Registry No.** 111-84-2
Synonyms *n*-nonane; nonyl hydride; Shellsol-140
EINECS No. 203-913-4 **RTECS No.** RA 6115000
Uses Solvent. Organic synthesis. Fuel additive.
Occurrence Aroma component of plant oils, cooked meat and fish, and dairy products. In fossil fuels. Residues have been detected in natural and drinking waters and in human milk (1).

Physical properties

M. Pt. -53°C **B. Pt.** 151°C **Flash point** 31°C (closed cup) **Specific gravity** 0.718 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 5.65 **Volatility** v.p. 10 mmHg at 38°C ; v.den. 4.41
Solubility Water: 0.07 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Occupational exposure

FR-VME 200 ppm (1050 mg m^{-3})
JP-OEL 200 ppm (1050 mg m^{-3})

SE-LEVL 150 ppm (800 mg m^{-3}) **SE-STEL** 200 ppm (1100 mg m^{-3})
US-TWA 200 ppm (1050 mg m^{-3})

UN No. 1920 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Ecotoxicity

Bioaccumulation

Estimated log bioconcentration factors of 3.31-3.92 indicate that environmental accumulation may be significant (2).

Environmental fate

Degradation studies

Catabolised by *Pseudomonas oleovorans*. Following oxidation to the fatty acid and further β-oxidation to shorter chain fatty acids, incorporation in polyester takes place (3).

Utilised as sole carbon source by the fungi *Metarhizium anisopliae* and *Normuraea rileyi* (4).

Biodegradation by activated sludge, 0.2% of ThOD after 6 hr, 0.4% of ThOD after 12 hr, 1.1% of ThOD after 24 hr (5).

Abiotic removal

Estimated volatilisation $t_{1/2}$ 3.3 hr in model river water, in model pond water $t_{1/2}$ 78 hr (2,6).

Reaction with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ ~1.5 days (7).

Adsorption and retention

Estimated K_{oc} 13,900-22,250 indicate that adsorption to soil and sediments would be significant (2).

Mammalian & avian toxicity

Acute data

LC_{50} (8 hr) inhalation rat 4500 ppm. Severe cerebral damage was observed. No toxic effects were observed at <2400 ppm (8).

LD_{50} intravenous mouse 220 mg kg^{-1} (9).

Sub-acute and sub-chronic data

Inhalation rat (65 day) no-adverse-effect level 590 ppm for 6 hr day^{-1}, 5 days wk^{-1} (10).

Inhalation rat (7 day), 360, 600 or 1600 ppm for 6 hr day^{-1}. The high dose caused tremor, slight loss of coordination, slight eye irritation and reduced body weight gain. Some fatalities were also reported in the high- and low-dose groups (11).

Metabolism and toxicokinetics

Following rat inhalation exposure to 1000 ppm, 12 hr day^{-1} for 14 days, nonane accumulation in the brain and perirenal fat was determined. The brain/blood ratio was 11.4, and fat/blood ratio was 113 (12).

Metabolised in rats at relatively high rates to hydroxyl derivatives prior to conversion into the corresponding keto form (13).

Irritancy

Inhalation rat, mouse (10 min) threshold for respiratory irritation 3000 ppm (14).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (15).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (16).

The log P_{ow} value exceeds the European Community recommended level of 3.0 (6th and 7th amendments) (17).

Other comments

Physical properties, occurrence and environmental fate reviewed (1).
Physical properties, use, metabolism and toxicology reviewed (18,19).
Adsorption by different grades of microporous carbon was studied (details unspecified).
Autoignition temperature 190°C.

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N194 1-nonanethiol

$$CH_3(CH_2)_7CH_2SH$$

$C_9H_{20}S$ **Mol. Wt.** 160.32 **CAS Registry No.** 1455-21-6

Synonyms nonyl mercaptan

EINECS No. 215-936-7 **RTECS No.** RA 6625000

Occurrence In fossil fuels.

Physical properties

B. Pt. 220°C **Flash point** 78°C **Specific gravity** 0.842

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

Reported to stimulate the germination of rust spores (2).

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N195 1-nonanol

$$CH_3(CH_2)_7CH_2OH$$

$C_9H_{20}O$ **Mol. Wt.** 144.26 **CAS Registry No.** 143-08-8

Synonyms nonan-1-ol; alcohol C-9; *n*-nonyl alcohol; octyl carbinol; pelargonic alcohol

EINECS No. 205-583-7 **RTECS No.** RB 1575000

Uses Organic synthesis. Fragrance and flavour agent. Solvent.

Occurrence Aroma component of fruits, cooked meats, fish and dairy products.

Physical properties

M. Pt. −8 to −6°C **B. Pt.** 215°C **Flash point** 75°C **Specific gravity** 0.8279 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 4.02 **Volatility** v.p. 0.3 mmHg at 20°C ; v.den. 4.98

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow, bleak 5.8-19 mg l^{-1}, flow-through bioassay (1).

Invertebrate toxicity

LC_{50} (96 hr) *Nitocra spinipes* 24 mg l^{-1} (1).

IC_{50} (75 min) mixed bacterial culture 520 mg l^{-1} (1).

IC_{50} (48 hr) *Tetrahymena pyriformis* 24 mg l^{-1} (static bioassay) (2).

Bioaccumulation

Bioconcentration factor 2950 (species unspecified) (2).

Environmental fate

Degradation studies

Biodegradation in activated sludge, 0.9% of ThOD after 12 hr, 9.9% after 24 hr (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 6400 kg^{-1} (4).

LC_{50} (2 hr) inhalation mouse 5500 mg m^{-3} (5).

LD_{50} dermal rabbit 5700 mg kg^{-1} (6).

LD_{50} intraperitoneal mouse 800-1600 mg l^{-1} (4).

Teratogenicity and reproductive effects

Inhalation rat, 150 mg m^{-3} 7 hr day^{-1} on day 1-19 of gestation. No maternal toxicity or foetoxicity or teratogenicity observed (7).

Oral rat, lowest toxic dose, 35,000 mg kg^{-1} day^{-1} on days 1-19 of gestation (foetal mortality) (8).

Metabolism and toxicokinetics

Undergoes oxidation to the carboxylic acid then conjugation with glucuronic acid (species unspecified) (9).

Genotoxicity

In vivo rat bone marrow, chromosomal aberrations and polyploidy positive (10).

Other effects

Other adverse effects (human)

Did not cause skin irritation or sensitisation in 25 volunteers exposed to 2% solution (11).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

The log P_{ow} value exceeds the European Community recommended level of 3.0 (6th and 7th Amendments) (13).

Other comments

Physical properties, toxicity and metabolism reviewed (14).

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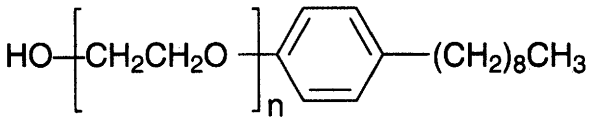
N196 nonoxynol



CAS Registry No. 26027-38-3

Synonyms polyethylene glycol mono(nonylphenyl) ether; polyoxyethylene mono-*p*-nonylphenyl ether; *p*-nonylphenol polyethylene glycol ether; Pannox 18; PEG *p*-nonylphenyl ether; Iconol NP 100; Ipegol Co-630; poly(oxy-1,2-ethanediyl), α-(4-nonylphenyl)-ω-hydroxy-

RTECS No. MD 0905000

Uses Spermicidal agent. Surfactant. Corrosion inhibitor. Used in photographic materials.

Physical properties

M. Pt. 26°C (Ipegol Co-630) **Flash point** 280-290°C (Ipegol Co-630) **Specific gravity** 1.06 (Ipegol Co-630) at 25°C with respect to water at 4°C

Solubility Water: miscible. Organic solvents: corn oil, ethanol, ethylene glycol, ethylene dichloride, xylene

Environmental fate

Degradation studies

>90% removal by *Pseudomonas* KSK-14 at concentrations of 20-1000 mg l^{-1} in wastewater (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 190 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 150-160 mg kg^{-1} (3-5).

Sub-acute and sub-chronic data

Intraperitoneal rat 50 mg kg^{-1} day^{-1} for 5 days caused a significant increase in DNA and collagen content of the liver. Intravaginal administration of the same dose for 15 days caused a significant increase in collagen in the liver and kidney, and DNA was significantly increased in the kidney. Serum glutamic-oxalacetic transaminase activity was increased after a single intraperitoneal dose and after 5 intravaginal doses (4).

Intraperitoneal mouse 0.4 mg $animal^{-1}$ day^{-1} for 24 days caused weight loss, reduced liver weight, and enlarged spleens. The response to sheep red blood cell and leukocyte counts did not differ from controls (6).

Teratogenicity and reproductive effects

In vitro minimum effective spermicidal dose monkey, human, dog, rabbit 0.125, 0.25, 0.25 and 1.0 mg ml^{-1}, respectively (3).

In vitro human sperm 0.25 mg ml^{-1} did not affect morphology of the nuclei, plasmalemma or Y-body. The energy-supplying enzymes and function of the sperm plasmalemma were affected (7).

Oral rat 250 or 500 mg kg^{-1} day^{-1} caused a decrease in maternal weight gain and an increase in the incidence of extra ribs and dilated pelvic cavity in foetuses. No adverse effects were observed in rats given dermal applications of 500 mg kg^{-1} day^{-1} (total exposure not specified) (8).

Metabolism and toxicokinetics

Following vaginal administration of ^{14}C-labelled substance to rats, 13% of the label was absorbed in 6 hr and 38% in 24 hr. The substance was completely metabolised and eliminated, principally in the faeces, secondarily in the urine (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 without metabolic activation negative (8).
Did not induce DNA repair in freshly isolated mouse hepatocytes, did not cause mutations at the HGPRT locus in the T51B rat liver cell lines, germinal cells of mice remain unaffected (10).
Oncogenic transformation (mouse) with fibroblast formation noted at 10 ppm (11).

Other effects

Any other adverse effects
Toxic shock syndrome reported (12).

Other comments

Evidence against an association between the use of spermicidal contraceptive and birth defects (13).
Higher polymers (n >20) are pastes or waxes.

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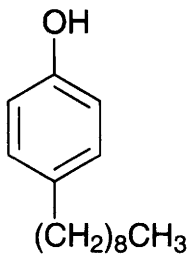
N197 4-nonylphenol



$C_{15}H_{24}O$ **Mol. Wt.** 220.35 **CAS Registry No.** 104-40-5

Synonyms *p*-nonylphenol

EINECS No. 203-199-4 **RTECS No.** SM 5630000

Uses Antifouling agent. Fuel additive.

Physical properties

B. Pt. 288-302°C **Partition coefficient** log P_{ow} 6.35 (1)
Solubility Water: practically insoluble. Organic solvents: soluble in most organic solvents

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 13 mg l^{-1} flow-through bioassay (2).

Exposure of maturing ♂ rainbow trout to 4-nonylphenol (0.5-65 μg l^{-1})caused a clear dose-related increase in vitellogenin production (a process normally dependent on endogenous oestrogens) and a less pronounced dose-related inhibition of testicular growth (3).

Juvenile Atlantic salmon treated with 1-125 mg kg^{-1} body weight suffered an initial increase and then an apparent dose-dependent decrease in progesterone, 6β-, 16α-, and 17α-hydroxylase activities in liver microsomes. 7-Ethoxyresorufin *O*-deethylase and UDP-glucuronosyltransferase activities were also reduced and plasma levels of estradiol-17β fell by 24-43%. Fish treated with the highest dose level showed reductions in ELISA absorbance levels of CYP1A, CYP2K-like, and CYP3A-like proteins, similar to reductions in fish treated with 5 mg estradiol-17β kg^{-1}. The observations are indicative of changes in steroid hydroxylase, cytochrome P450 isoenzyme and conjugated enzyme levels (4).

Juvenile rainbow trout administered a single intravenous injection of [3H]4-nonylphenol had [3H]-labelled residue concentrations 144 hr later in the order bile > faeces > liver > pyloric caeca > kidney > brain, gill, gonad, heart, plasma, skeletal muscle, and skin. Depletion kinetics of [3H]residues from tissues and plasma was biphasic with prolonged β-phase half-lives in muscle and liver of 99 hr. The predominant metabolite in bile was a glucuronide conjugate of 4-nonylphenol (5).

Invertebrate toxicity

Daphnia magna exposed to 25 or 100 μg l^{-1} for 48 hr showed an increase in the accumulation of testosterone supplied in the exposure media. 4-nonylphenol disrupted components of the testosterone metabolic pathway that would lead to a decrease in elimination of testosterone and an increase in androgenic derivatives (6).

Life-cycle test with the midge (*Chironomus tentans*). No-observable-effect concentration 42 μg l^{-1}, lowest-observable-effect concentration 92 μg l^{-1} (7).

LC_{50} (96 hr) bay mussel 3.0 mg l^{-1} (8).

EC_{50} (48 hr) *Daphnia magna* <1 mg l^{-1} (9).

Bioaccumulation

Bioconcentration factor for stickleback 1300 and for mussels 3400 (10).

Bioconcentation factor for salmon 280 (11).

Environmental fate

Degradation studies

When applied to soil in sewage sludge 4-nonylphenol was rapidly degraded (metabolites unspecified) (12).

Degradation in sea water (initial concentration 11 μg l^{-1}) was initially very slow. After 4 wk at 11°C the degradation rate increased rapidly; $t_{1/2}$ ~58 day. The addiction of sediment to the sea water caused an initial higher rate of degradation but degradation, did not increase over a long time period (13).

Under methanogenic conditions using anaerobic digesting sludge at 50 mg of carbon l^{-1}, no biodegradation occurred (14).

Abiotic removal

Adsorption capacity of activated carbon 250 mg g^{-1} carbon (15).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1600 mg kg^{-1} (16).

Other effects

Any other adverse effects

Daphnia magna exposed to 25 or 100 μg l^{-1} for 48 hr showed an increase in the accumulation of testosterone supplied in the exposure media. 4-nonylphenol disrupted components of the testosterone metabolic pathway that would lead to a decrease in elimination of testosterone and an increase in androgenic derivatives (6).

Legislation

The log P_{ow} value exceeds the European Communities recommended level of 3.0 (6th and 7th Amendments) (17).

Other comments

Metabolites of non-ionic surfactants, found in anaerobically treated sewage sludge (10).

Environmental endocrine disruptor (18,19).

Nonylphenol has been identified as an oestrogenic substance released from plastic centrifuge tubes. The authors warn that the oestrogenic properties of alkylphenols, specifically nonylphenols, indicate that the use of plasticware containing these chemicals in experimental and diagnostic tests may lead to spurious results, and these compounds as well as alkylphenol polyethoxylates may also be potentially harmful to exposed humans and the environment at large (20).

The concentrations of nonylphenol found in rivers and estuaries in England and Wales rarely exceed 10 μg l^{-1}, although levels as high as 100 μg l^{-1} have been reached in rivers receiving industrial effluent (21).

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (22).

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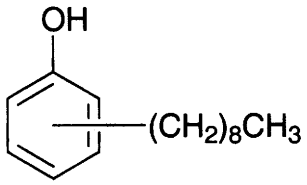
N198 nonylphenol (mixed isomers)



$C_{15}H_{24}O$ **Mol. Wt.** 220.35 **CAS Registry No.** 25154-52-3

Synonyms *n*-nonylphenol; monononylphenol

EINECS No. 246-672-0 **RTECS No.** SM 5600000

Uses Antibody agent. Fungicide. Antioxidant. Polymerisation catalyst. Fuel additive. Waterproofing agent. Organic synthesis.

Physical properties

B. Pt. 293-297°C **Flash point** 149°C **Specific gravity** 0.949 at 20°C with respect to water at 4°C
Volatility v.den. 7.59
Solubility Water: practically insoluble. Organic solvents: benzene, chloroform, ethylene glycol, heptane

Ecotoxicity

Fish toxicity
Predicted LC_{50} (96 hr) fathead minnow, bluegill sunfish, rainbow trout 0.14-0.23 mg l^{-} (QSAR modelling system) (1).
LC_{50} (96 hr) fathead minnow 0.14 mg l^{-1} – flow-through bioassay (2).
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 fish, related to treatment, were still apparent 466 days after cessation of treatment. The ovosomatic index was also significantly affected (3).

Invertebrate toxicity
LC_{50} (6 days) *Anodonta cataracta* 5 mg l^{-1} (4).

Bioaccumulation
Bioconcentration factor for bay mussel 8-12 (5).

Environmental fate

Degradation studies
Partially degraded by bacteria when monitored in groundwater at infiltration depths of up to 7 m (6).
Biodegradation at 1.0 mg l^{-1} 0% after 12 hr in normal and adapted sewage, 0% in normal sewage after 135 hr, 45% in adapted sewage after 135 hr (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1230 mg kg^{-1} (8).
LD_{50} dermal rabbit 2100 mg kg^{-1} (9).

Irritancy
Dermal rabbit (24 hr) 10 mg caused severe irritation, 50 μg instilled into rabbit eye caused severe irritation (exposure unspecified) (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102, TA104 with and without metabolic activation *negative* (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (12).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (13).

Other comments

Degradation product of nonionic detergents (11).
Physical properties, toxicity, environmental impact and health precautions reviewed (14-16).
The concentrations of nonylphenol found in rivers and estuaries in England and Wales rarely exceed 10 $\mu g\ l^{-1}$, although levels as high as 100 $\mu g\ l^{-1}$ have been reached in rivers receiving industrial effluent (17).
Environmental endocrine disruptor (18).
Reported to leach from plastics used in food packaging, such as food grade polyvinyl chloride, and lacquer coatings in food cans (19,20).

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N199 nonyltrichlorosilane

$$CH_3(CH_2)_8SiCl_3$$

$C_9H_{19}Cl_3Si$ **Mol. Wt.** 261.69 **CAS Registry No.** 5283-67-0

Synonyms trichlorononylsilane

EINECS No. 226-113-7 **RTECS No.** VV 4660000

Uses Organic synthesis.

Physical properties

B. Pt. 121-123°C at 5 mmHg **Specific gravity** 1.072 at 25°C

Occupational exposure

UN No. 1799 **HAZCHEM Code** 4XE **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Irritancy

Strong irritant to the skin and mucous membranes (1).

References

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N200 1-nonyne

$$CH_3(CH_2)_6C{\equiv}CH$$

C_9H_{16} **Mol. Wt.** 124.23 **CAS Registry No.** 3452-09-3

Synonyms heptylacetylene

EINECS No. 222-375-1

Physical properties

M. Pt. -50°C **B. Pt.** 150-151°C **Flash point** 33°C **Specific gravity** 0.757 at 20°C

Solubility Organic solvents: diethyl ether, ethanol

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).

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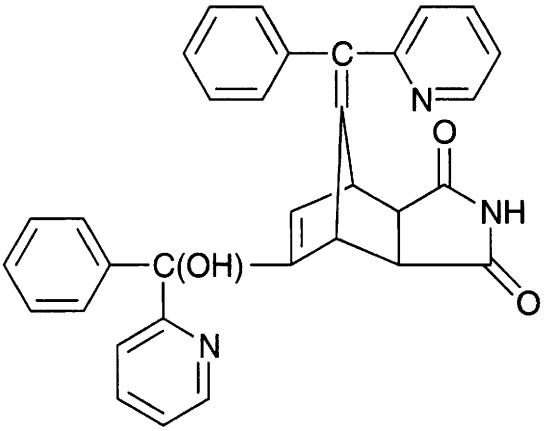
N201 norbormide



$C_{33}H_{25}N_3O_3$ **Mol. Wt.** 511.58 **CAS Registry No.** 991-42-4

Synonyms 5-(α-hydroxy-α-2-pyridylbenzyl)-7-(α-2-pyridylbenzylidene)-5-norbornene-2,3-dicarboximide; 3a,4,7,7a-tetrahydro-5-(hydroxyphenyl-2-pyridinylmethyl)-phenyl-2-pyridinylmethylene)-4,7-methano-1*H*-isoindole-1,3(2*H*)-dione; MCN 1025; Raticate; Shoxin; S-6,999

EINECS No. 213-589-6 **RTECS No.** RB 8750000

Uses Superseded rodenticide.

Physical properties

M. Pt. 190-198°C

Solubility Water: 60 mg l^{-1} at 30°C. Organic solvents: chloroform, diethyl ether, 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)

Mammalian & avian toxicity

Acute data

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

LD_{50} oral rat 3.8-5.3 mg kg^{-1} (2,3).

LD_{50} oral guinea pig 300 mg kg^{-1} (4).

LD_{Lo} intravenous rat 250-650 μg kg^{-1} (3,5).

Other effects

Other adverse effects (human)

Three adult ♂ volunteers received 15 mg kg^{-1} day^{-1} for 3 days without ill-effect (route unspecified) (6).

Humans ingesting up to 300 mg showed a slight transient decrease in body temperature and blood pressure.

Intradermal injection of 0.1 mg $subject^{-1}$ produced no skin reaction or lesions (7).

Any other adverse effects

Single doses of 10-20 mg kg^{-1} to rats, irrespective of route of administration, caused a significant rise in blood glucose levels with a concomitant fall in hepatic glycogen (8).

Intravenous rat, single dose of 250 or 500 μg kg^{-1} caused arrhythmias, although this did not account for the observed myocardial failure (9).
Norbormide is a selective rodenticide against most species of rats in which it produces extreme irreversible peripheral vasoconstriction. It is less toxic to other rodents (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (12).

Other comments

Reviews on human health effects, experimental toxicology, physico-chemical properties listed (13).

References

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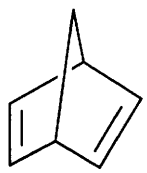
N202 2,5-norbornadiene



C_7H_8 **Mol. Wt.** 92.14 **CAS Registry No.** 121-46-0

Synonyms bicyclo[2.2.1]hepta-2,5-diene; dicycloheptadiene; norbornadiene

EINECS No. 204-472-0 **RTECS No.** RB 6535000

Uses Manufacture of polymers.

Physical properties

M. Pt. −19.1°C **B. Pt.** 89.5°C **Specific gravity** 0.9064 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.201 (1) **Volatility** v.den. 3.2
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol, ligroin, toluene

Occupational exposure

UN No. 2251 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) goldfish 46 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 890, 3900 mg kg^{-1}, respectively (2).
LC_{50} (8 hr) inhalation rat 14,000 ppm (2).
LD_{50} intraperitoneal rat 890 mg kg^{-1} (2).
LD_{50} intravenous mouse 56 mg kg^{-1} (3).

Other effects

Other adverse effects (human)

May be harmful by inhalation, ingestion or skin absorption. Exposure can cause nausea, dizziness and headache and narcotic effects (4).

References

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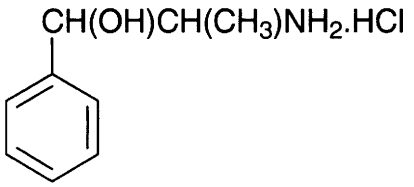
N203 norephedrine hydrochloride



$C_9H_{14}ClNO$ **Mol. Wt.** 187.67 **CAS Registry No.** 154-41-6

Synonyms phenylpropanolamine hydrochloride; α-(1-aminoethyl)benzenemethanol hydrochloride; (±)-2-amino-1-phenyl-1-propanol hydrochloride; α-hydroxy-β-aminopropylbenzene hydrochloride; *d,l*-norephedrine hydrochloride; Nobese; Propardrine

EINECS No. 205-826-7 **RTECS No.** DN 4200000

Uses Vasoconstrictor used in cough medicines, nasal decongestants and over-the-counter diet aids.

Physical properties

M. Pt. 190-194°C

Solubility Water: freely soluble. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 150, 1490 mg kg^{-1}, respectively (1,2).
LD_{50} intraperitoneal rat, mouse 160, 428 mg kg^{-1}, respectively (3,4).
LD_{50} subcutaneous rabbit, mouse 225, 600 mg kg^{-1}, respectively (3,5).
LD_{50} intravenous rabbit 50 mg kg^{-1} (3).

Metabolism and toxicokinetics

In humans, readily and completely absorbed from the gastro-intestinal tract with peak plasma concentrations 1-2 hr after dosage. Excreted largely unchanged in urine (6).

Other effects

Other adverse effects (human)

A 20-yr-old woman who took the recommended dosage of Dexatrin (containing 50 mg norephedrine hydrochloride and 10 mg caffeine) suffered a right frontal intracerebral haemorrhage (7).
Cases of hypertension following ingestion of cough and cold preparations containing norephedrine hydrochloride have been reported. Episodes occurred after as little as 10 min and lasted for 1-2 hr (8,9).
A 35-yr-old patient treated with 50 mg day^{-1} gradually developed paranoid schizophrenia, disordered thinking, and delusions of grandiosity and persecution. It is not clear whether this was caused by norephedrine hydrochloride (10).
Chronic abuse by a 29-yr-old female resulted in psychotic behaviour and grand mal seizures. The patient responded to treatment but when challenged with an oral dose of 50 mg, seizure activity recurred (11).
A 25-yr-old male suffered acute renal failure with tubular necrosis following an overdose but a causal relationship was not established (12).

Any other adverse effects

♂ Wistar rats administered 0, 1, 2, 4, 8, 16, 32 mg kg^{-1} intraperitoneally showed dose-related blood pressure and hyperactivity at >4 mg kg^{-1}. Myocardial necrosis was observed in animals killed 24 hr after receiving >8 mg kg^{-1} (13).

Other comments

The increased incidence of mental adverse effects in Europe compared with the US, where hypertension is more common, may be because the isomer *d*-norpseudoephedrine is sometimes used in Europe whereas the *d,l*-norephedrine racemic mixture is always used in North America. Adverse effects in Australia may involve the isomer *l*-norephedrine, but this has not been confirmed (14).

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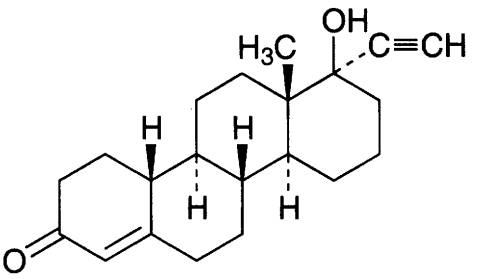
N204 norethisterone



$C_{20}H_{26}O_2$ **Mol. Wt.** 298.43 **CAS Registry No.** 68-22-4

Synonyms (17α)-17-hydroxy-19-norpregn-4-en-20-yn-3-one; enhydroxynorprogesterone; ethynylnortestosterone; 17α-ethynyl-19-nortestosterone; norethindrone; 19-norethisterone; 19-nor-17α-ethynyl-17β-hydroxy-4-androsten-3-one; 19-nor-17α-ethynyltestosterone; Anovlar 21; Norinyl; Orthonovum; Prinolutin

EINECS No. 200-681-6 **RTECS No.** RC 8975000

Uses ♀ oral contraceptive. In treatment of conditions such as amenorrhoea, dysfunctional uterine bleeding, endometriosis, dysmenorrhoea and premenstrual tension. To delay or prevent menstruation.

Physical properties

M. Pt. 203-204°C

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

Mammalian & avian toxicity

Acute data

LD_{50} *oral* mouse 12,000 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).

Oral rat, mouse, 2-5 × human contraceptive dose, 5-150 × human contraceptive dose or 200-400 × human contraceptive dose (amounts unspecified) in diet for life. Norethisterone, or its acetate were administered alone or in combination with oestrogens. An increased incidence of benign liver-cell tumours occurred in groups of ♂ mice treated with norethisterone and its acetate (33/120 and 35/120, compared with 18/20 and 19/20 in the 2 groups of controls, respectively). Incidences of pituitary tumours were increased in ♀ mice fed norethisterone alone (23/120 in treated mice given norethisterone acetate; ethinylrestradiol (50:1) (from 2/120 to 25/120 in ♂, and from 6/120 to 32/120 in ♀) and in ♂ and ♀ mice given norethisterone: mestranol (20:1) (from 2/120 to 15/120 in ♂, and from 6/120-31/120 in ♀). No increase in the incidence of pituitary tumours was observed in mice administered norethisterone as the acetate alone. Rats administered norethisterone or it acetate alone or norethisterone: mestranol (20:1) at the same dosages. Incidences of benign liver-cell tumours were increased in ♂ (28/120 in treated compared with 5/120 controls) in rats treated with norethisterone alone and with mestranol. The same treatments induced benign and malignant mammary tumours in ♂ rats (5/120 and 14/120, respectively, compared with none in controls). Administration of norethisterone: mestranol resulted in increased incidence of malignant mammary tumours in ♀ rats (26/120 compared with 6/120 in controls. Feeding of norethisterone as the acetate: ethinylestradiol (50:1) induced an increase in the incidence of benign mammary tumours in ♂ rats (34/120 compared with 2/120 in controls) (3).

Subcutaneous implantation ♀ mouse, pellets containing 40% norethisterone and 60% cholesterol, with estimated adsorption of 3.6-15.9 μg day^{-1} (mean 7.7 μg day^{-1}) induced granulosa-cell tumours of the ovary in 13/25 animals: only 2 could be seen macroscopically (4).

Teratogenicity and reproductive effects

Oral or injection mouse (route unspecified) 0.5 or 1.0 mg kg^{-1} day^{-1} on days 8-16 of gestation induced anomalies in 3-57% foetuses. These included retarded development, hydrocephalus, clubfoot and minor skeletal anomalies (5).

Subcutaneous rat, 1-10 mg $animal^{-1}$ day^{-1} on days 15-20 of gestation induced pseudohermaphrodism and an altered sex ratio (6).

Intramuscular rhesus monkey 25 mg $animal^{-1}$ day^{-1} 5 days wk^{-1}, starting from day 27-35 of gestation and continuing until delivery, terminated 8/10 pregnancies. ♀ Foetuses showed virilisation of the external genitalia and hypoplastic ovaries; ♂ foetuses showed cryptorchidism (7).

Metabolism and toxicokinetics

Metabolites identified in humans include: 5β,17α-19-norpregn-20-yne-3β,17-diol and 5β,17α-19-norpregn-20-yne-3α,17-dione (8).

Readily absorbed following oral administration of 1 mg to human subjects. Serum elimination $t_{1/2}$ 7.6 hr and mean bioavailability 53.6 ng ml^{-1} hr^{-1}. There were large inter-subject variations in these parameters (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (10).
Escherichia coli WP2 *uvr*A with and without metabolic activation negative (10).
In vitro Chinese hamster lung cells, chromosomal aberrations positive (10).
In vitro human lymphocytes chromosomal aberrations negative (11,12).
In vitro primary rat hepatocytes, unscheduled DNA synthesis positive (13).
In vivo ♀ mouse, dominant lethal assay positive (acetate) (14).
In vivo mouse bone marrow micronucleus assay negative (10).

Other effects

Other adverse effects (human)

There were 6 cases of jaundice among 107 patients with breast cancer treated with norethisterone as the acetate. The jaundice was reversible and of an obstructive type (15).

Ectopic pregnancies have been reported in women using low-dose progestogen and contraceptives (300 μg norethisterone) (16).

Abnormalities seen in the offspring of women who had received norethisterone during pregnancy (either alone or in combination with ethinyloestradiol) included hypospadias, masculinisation of ♀ infants, meningomyelocele or hydrocephalus, and neonatal choreoathetosis (16).

Other comments

Trace amounts have been detected in natural waters (17).

A survey of sewage effluents, natural and drinking waters in south east of England established that levels were <20 ng l^{-1}, a value considered unlikely to present a significant risk to human health (17).

Oral thyroidectomised or parathyroidestomised rat 500 μg kg^{-1} wk^{-1} (norethisterone acetate) reduced urinary ^{45}Ca excretion and conserved bone (18).

Physical properties, use, occurrence, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (19).

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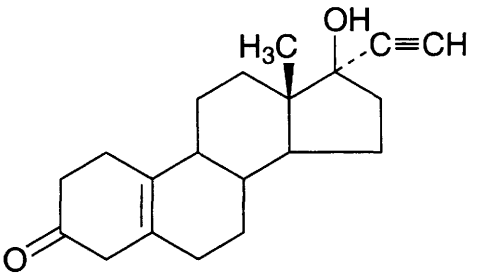
N205 norethynodrel



$C_{20}H_{26}O_2$ **Mol. Wt.** 298.43 **CAS Registry No.** 68-23-5

Synonyms 17α-ethynyl-17-hydroxy-5(10)-estren-3-one; (17α)-17-hydroxy-19-norpregn-5(10)-en-20-yn-3-one; 17-hydroxy-19-nor-17α-pregn-5(10)-en-20-yn-3-one; Conorid; Enidrel; Previson; Norolen

EINECS No. 200-682-1 **RTECS No.** RC 8980000

Uses Oral ♀ contraceptive. In treatment of dysfunctional uterine bleeding and endometriosis.

Physical properties

M. Pt. 169-170°C

Solubility Organic solvents: acetone, chloroform, diethyl ether, ethanol, hexane, methanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (1).

Oral rat and mouse (80 wk) 1.25 mg kg^{-1} day^{-1} alone or in combination with 0.05 mg kg^{-1} day^{-1} mestranol for 50-80 wk. In mice benign hepatocellular tumours were observed in 0/50 and 2/50 administered norethynodrel alone and in combination, respectively. 1/50 controls developed a similar tumour (2).

Oral mouse, 2-5 × human contraceptive dose, 50-150 × human contraceptive dose or 200-400 × human contraceptive dose (amounts unspecified) in diet for 80 wk. Both nonethynodrel alone and in combination with mestranol induced an increased incidence of pituitary tumours in ♂ and ♀ mice 30/120-47/120 in treated groups compared with 2/120 and 8/120 in controls. Eight malignant mammary tumours were found in treated animals of which 5/120 occurred in high-dose ♀ mice, compared with 4/240 controls. In rats administration of norethynodrel alone increased the incidence of benign liver-cell tumours in ♂ from 4/120 to 86/360, mostly at the

medium- and high-dose levels. Malignant hepatomas occurred in 29/360 ♂ rats, mostly in the medium- and high-dose groups, compared with 0/120 in control. ♀ Rats had lower incidences of benign liver-cell tumours and no malignant liver cell tumours. Norethynodrel alone induced pituitary tumours in 43% ♂ rats compared with none in ♀ and 6% of controls, and 15% in ♂ and 20% in ♀ given the combined treatment. Both benign and malignant mammary tumours were seen in ♂ rats given norethynodrel with or without mestranol (15-19% compared with 0 in controls). In ♀ rats the incidence of malignant tumours was increased only in the combined treatment group (20% compared with 7% in controls) (3).
Subcutaneous ♀ mouse, 0.1 mg Enovid (98.5% norethynodrel, 1.5% mestranol) animal^{-1} 2 × wk^{-1} for 21 months induced mammary tumours in 30/100 treated mice compared with 14/100 in controls (4).
Subcutaneous implantation ♀ mouse, pellets containing 40% norethynodrel and 60% cholesetrol, with estimated absorption of 5.5 μg day^{-1} induced granulosa-cell tumours of the ovary in 2/24 animals (5).

Teratogenicity and reproductive effects
Oral mouse, 10 mg kg^{-1} day^{-1} on day 8-15 of gestation caused significant embryolethality (98.9%), but not when administered on days 14-17 of gestation (6).
Oral mouse, 0.2-2.4 mg kg^{-1} norethynodrel or its 3-hydroxy metabolite, either singly or on three consecutive days between day 6-16 of gestation induced congenital abnormalities in the offspring (restricted development, hydrocephalus, clubfoot and minor skeletal anomalies) (7).
Subcutaneous rat, 0.5 or 1.0 mg kg^{-1} day^{-1} on days 2,3 and 4 of gestation terminated a significant number of pregnancies (8).

Metabolism and toxicokinetics
Major metabolites in rats, mice, guinea pigs and rabbits are the 3α- and 3β-alcohols, and norethisterone. In most species polyhydroxylated metabolites occur, which have not been characterised (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (10).
In vitro human lymphocytes, induction of polyploidy negative (11,12).
In vitro primary rat hepatocytes, unscheduled DNA synthesis negative (13).
In vivo rat bone marrow, chromosomal aberrations negative (14).

Other comments

Used as an oral contraceptive, mostly in combination with an oestrogen such as mestranol (9).
Physical properties, use, analysis, carcinogenicity, mammalian toxicity, metabolism and mutagenicity reviewed (9).

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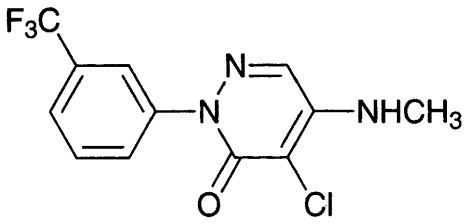
N206 norflurazon



$C_{12}H_9ClF_3N_3O$ **Mol. Wt.** 303.67 **CAS Registry No.** 27314-13-2

Synonyms 4-chloro-5-(methylamino)-2-[3-(trifluoromethyl)phenyl]-3(2*H*)-pyridazinone; 4-chloro-5-(methylamino)-2(α,α,α-trifluoro-*m*-tolyl)-3(2*H*)-pyridazinone; Evital; Solicam; Telok; Zorial; Predict

EINECS No. 248-397-1 **RTECS No.** UR 6150000

Uses Selective pre-emergent herbicide used to control germinating annual grasses and broadleaf weeds in fruits, vegetables, nuts, cotton, peanuts, soybeans, and various non-agricultural and industrial areas.

Physical properties

M. Pt. 174-180°C **Partition coefficient** log P_{ow} 2.45 at pH 6.5, 25°C (1) **Volatility** v.p. 2.9×10^{-8} mmHg at 20°C **Solubility** Water: 33.7 mg l^{-1} at 25°C. Organic solvents: acetone, ethanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} catfish, goldfish >200 mg l^{-1} (exposure unspecified) (1).

Invertebrate toxicity

Practically non-toxic to bees, LD_{50} >0.24 mg bee^{-1} (1,2).

Environmental fate

Degradation studies

Degraded slowly in aerobic soil $t_{1/2}$ 130 days (2).

Degraded in an aerobic aquatic study to desmethyl norflurazon $t_{1/2}$6-8 months (2).

Persistent with $t_{1/2}$ 8 months under anaerobic conditions (2).

Desmethyl norflurazon is persistent under aerobic and anaerobic conditions (2).

Abiotic removal

Rapidly degraded by sunlight. Soil $t_{1/2}$ 21-28 days, for photodegradation and volatilisation (1).

Completely removed from water (as determined by removal of injury to plants) at a ratio of 10 parts activated charcoal to 1 part norflurazon. Ratios of 100-300 were required for complete removal in a sand matrix (3).

Stable to hydrolysis (2).

Adsorption and retention

Soil K_{oc} ~5.7 (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 8000-9400 mg kg^{-1} (1,5).

LD_{50} oral bobwhite quail, mallard duck >1250 mg kg^{-1} (1).

LD_{50} dermal rabbit >20 g kg^{-1} (1).

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

Sub-acute and sub-chronic data
Oral dog (90 day) no-adverse-effect level 12.5 mg kg^{-1} day^{-1} (1).

Carcinogenicity and chronic effects
Oral rat (2 yr) no-adverse-effect level 19 mg kg^{-1} body weight day^{-1} (1).

Teratogenicity and reproductive effects
Reported to have no teratogenic or adverse reproductive effects (1).

Metabolism and toxicokinetics
In rats, norflurazon metabolism is principally via two pathways, reaction with glutathione or *N*-demethylation followed by conversion into a sulfoxide (this was the major metabolite). Following dosages of 2 and 110 mg kg^{-1}, 19-28% was excreted in the urine and 65-80% in the faeces within 4 days (6).

Irritancy
Practically non-irritating to rabbit eyes and skin (2).

Genotoxicity

Nonflurazon is not considered to be mutagenic (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (8).
WHO Toxicity Class Table 5 (9).
EPA Toxicity Class IV (4).
ADI 0.02 mg kg^{-1} body weight (4).

Other comments

Absorbed by the roots of plants. Reduces carotenoid biosynthesis which causes chlorophyll depletion and hence inhibition of photosynthesis (1).
Metabolic pathways reviewed (10).

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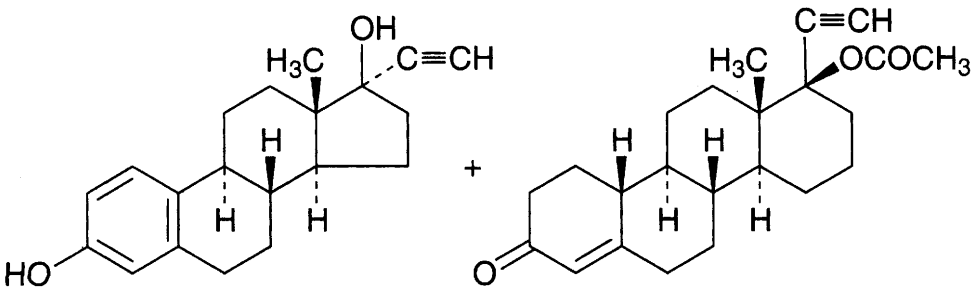
N207 Norlestrin



CAS Registry No. 8015-12-1

Synonyms (17α)-17-(acetyloxy)-19-norpregn-4-en-20-yn-3-one, mixture with (17α)-19-norpregn-1,3,5(10)-trien-20-yne-3,17-diol; norethisterone acetate mixture with ethinylestradiol; Anovlar; Controvlor; estostep; etalontin; gynovlar; Lo-estrin; orlest; primidos; Sinovula; Zorane

RTECS No. RC 8990000

Uses Female oral contraceptive.

Physical properties

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

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (overall evaluation for combined oral contraceptives) (1).

Gavage ♀ rat, 0.075 mg ethinylestradiol plus 6 mg norethisterone acetate animal^{-1} day^{-1} for 1 yr initiated hepatocarcinogenesis by increasing the oestrogen-oestrogen receptor complex in the nucleus, directly acting on DNA (2).

Oral rat 0.25 mg norethisterone:ethynyloestradiol, 50:1 day^{-1} for 10 days resulted in an increased incidence of mammary tumours induced by a single oral dose of 8 mg 7,12-dimethylbenz[*a*]anthracene from 17/38 to 18/22 rats. Pretreatment with 1 mg norlestrin day^{-1} for 10 days had no significant effect on the incidence of tumours produced by 7,12-dimethylbenz[*a*]anthracene (3).

Teratogenicity and reproductive effects

Oral monkey and baboon, at concentrations ranging from 1-1000 fold the human equivalent dose on days 20-50 of gestation. Embryolethality was increased in both species relative to controls in the 100-1000-fold human equivalent dose group, and maternal lethality occurred in high-dose monkeys (4).

Metabolism and toxicokinetics

Following oral administration to lactating women, ~10% was transferred from maternal sera to milk (5).

Genotoxicity

In vivo mouse bone marrow, chromosomal aberrations positive, induction of micronuclei negative (6).

Other effects

Other adverse effects (human)

Norlestrin had a minimal effect on clotting factors, carbohydrate metabolism and the concentration of plasma lipids when administered to normally menstruating women (7).

Other comments

Physical properties, use, analysis, mutagenicity, mammalian toxicity, metabolism and mutagenicity of norethisterone and ethynyloestradiol, individually and combination, reviewed (1,8).

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N208 norspermidine

$$(NH_2CH_2CH_2CH_2)_2NH$$

$C_6H_{17}N_3$ **Mol. Wt.** 131.22 **CAS Registry No.** 56-18-8

Synonyms 3,3-iminobis(propylamine), *N*-(3-aminopropyl)-1,3-propanediamine; 3,3-diaminodipropylamine; di(3-aminopropyl)amine; aminobis(propylamine); iminobispropylamine; iminobis-3-isopropylamine; Caldine

EINECS No. 200-261-2 **RTECS No.** JL 9450000

Uses Polymer manufacture. Vulcanising agent. Wood preservative.

Physical properties

M. Pt. −14°C **B. Pt.** 151°C at 50 mmHg **Flash point** 118°C **Specific gravity** 0.938 at 20°C with respect to water at 4°C **Volatility** v.den. 4.52

Occupational exposure

UN No. 2269 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Supply classification very toxic
Risk phrases Harmful if swallowed – Toxic in contact with skin – Very toxic by inhalation – Causes severe burns – May cause sensitisation by skin contact (R22, R24, R26, R35, R43)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S28, S36/37/39, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, guinea pig, mouse 210-435 mg kg^{-1} (1).
LD_{Lo} dermal rat 110 mg kg^{-1} (2).

Irritancy

Dermal rat 470 mg (open) caused moderate irritation and 47 mg instilled into rabbit eye caused severe irritation (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (4).

Other effects

Any other adverse effects

Norspermidine inhibits B cell growth and differentiation by interfering with the polyamine metabolic pathway (5).

Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (6).

In vivo antitumour activity against L1210 leukaemia, 3LL carcinoma and EL4 lymphoma in mice. In combination with α-difluoromethylornithine, norspermidine accumulation in tumour cells increased by ≥50% compared with cells from animals receiving norspermidine only (7,8).

Norspermidine levels in cockroach ovary increased during maturation but declined in sperm cells in ♂ crickets during spermatogenesis (9).

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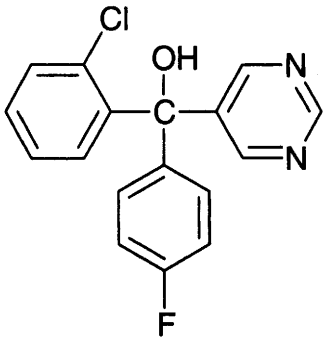
N209 nuarimol



$C_{17}H_{12}ClFN_2O$ **Mol. Wt.** 314.75 **CAS Registry No.** 63284-71-9

Synonyms (±)-2-chloro-4'-fluoro-α-(pyrimidin-5-yl)benzhydryl alcohol; (±)-α-(2-chlorophenyl)-α-(4-fluorophenyl)-5-pyrimidinemethanol; dipropylenetriamine; Cidorel; Gandural; Gauntlet; Murox; Trimidal; Tridal; Triminol

EINECS No. 264-071-1 **RTECS No.** UU 9279700

Uses Fungicide.

Physical properties

M. Pt. 126-127°C **Partition coefficient** log P_{ow} 3.176 at pH 7.0 (1) **Volatility** v.p. 1.5×10^{-8} mmHg
Solubility Water: 26 mg l^{-1} at 25°C and pH 7. Organic solvents: acetone, methanol, *n*-hexane, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 12 mg l^{-1} (1).
In 7-day trials no adverse effect to bluegill sunfish at 1.1 mg l^{-1} (flow-through bioassay) (2).

Invertebrate toxicity
LC_{50} contact bee >1 g l^{-1} (2).

Environmental fate

Degradation studies
Undergoes microbial degradation (1).

Abiotic removal
Undergoes photodegradation (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail 200 mg kg^{-1} (1).
LD_{50} oral rat, mouse 1250, 3000 mg kg^{-1}, respectively (1).
LD_{50} oral dog 500 mg kg^{-1} (1).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1,2).

Carcinogenicity and chronic effects
Oral rat and mouse, no-adverse-effect level 50 mg kg^{-1} diet in 2-year feeding trials (1).

Metabolism and toxicokinetics
Rapidly eliminated following oral administration to rats (1).

Irritancy
Slight eye irritant in rabbits (1).
Dermal rabbit, rat irritant at 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).
The log P_{ow} value exceeds the European Community recommended value of 3.0 (6th and 7th amendments) (5).
WHO Toxicity Class III (6).
EPA Toxicity Class III (2).

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N210 nystatin

$C_{47}H_{75}NO_{17}$ **Mol. Wt.** 926.11 **CAS Registry No.** 1400-61-9

Synonyms Biofanal; Candex; Chinyfungin; Diastatin; Fungicidin; Mycostatin; Nysfungin; Nystan; Stanycin

EINECS No. 215-749-0 **RTECS No.** RF 5950000

Uses Antibiotic used principally for fungal skin infections. Feed additive; as a growth promoter.
Occurrence Produced from *Streptomyces noursei*

Physical properties

M. Pt. 160°C (decomp.)
Solubility Water: 4 mg l^{-1} at 28°C. Organic solvents: acetone, chloroform, ethanol, dimethylformamide, ethyl acetate, ethylene glycol, methanol

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 8000, 10,000 mg kg^{-1}, respectively (1,2).
LD_{50} subcutaneous mouse 120 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse, rat 4.4, 24 mg kg^{-1}, respectively (4,5).
LD_{50} intravenous mouse 3 mg kg^{-1} (6).

Teratogenicity and reproductive effects

Oral rat, lowest toxic dose, single dose of 100 mg kg^{-1} on day-9 of gestation (teratogenic effects) (7).

Metabolism and toxicokinetics

Absorption from gastro-intestinal tract, skin and mucous membranes is negligible (8).

Genotoxicity

In vivo mouse bone marrow cells, chromosomal aberrations positive (9).

Other effects

Other adverse effects (human)

Nausea, vomiting and diarrhoea have occasionally been reported following oral administration. Rarely, irritation may occur after topical use (10).

Other comments

Nystatin contains mainly tetraenes, the principal component being nystatin A_1 (10).

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